

## BIOPRINTING CARTILAGE GRAFTS

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Bioprinting is an emerging technology for the fabrication of patient-specific, anatomically-complex tissues and organs. A novel bioink was developed based on two unmodified regulatory-compliant polysaccharides, gellan and alginate, which undergoes cell friendly gelation in the presence of cations. Rheological properties of the bioink revealed optimal shear thinning and shear recovery properties for high fidelity bioprinting. Tensile testing of bioprinted dumbbell-shaped specimens revealed a strong, ductile material. To make the bioink tissue-specific and bioactive, extracellular matrix particles can be added, or the polymers can be sulfated for growth factor binding affinity. As proof of concept, clinical product BioCartilage® (cartilage extracellular matrix particles) and bovine chondrocytes were added to the bioink. 3D auricular, nasal, meniscal and vertebral disc grafts were printed based on computer tomography (CT) data or generic 3D models. The bioink containing BioCartilage supported proliferation of chondrocytes and, in the presence of transforming growth factor beta-3 (TGF- $\beta$ 3), supported strong deposition of cartilage matrix proteins. A clinically-compliant bioprinting method is presented which yields patient-specific cartilage grafts with good mechanical and biological properties. The versatile method can be used with any type of tissue particles to create tissue-specific and bioactive scaffolds.

## 3D CELL AND TISSUE CULTURING UNDER PERFUSION

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The in vitro culture of primary cells typically involves monolayer expansion on tissue culture plastic (e.g., on Petri dishes) and serial replating of the cells onto new dishes upon confluence. This technique fails to recapitulate a physiological environment and is associated with a loss of characteristics and functionality of the expanded cell progeny. Cell culture in a 3D setting (e.g., within the pores of 3D scaffolds), which in turn requires the use of perfusion-based bioreactor systems to maintain suitable mass transfer rates, has the potential to recapitulate features of a