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3D printing technologies and bio-ink materials for medical applications

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Additive manufacturing, also known as 3D printing, is one of the fastest developing technologies nowadays. It allows for the fabrication in one process parts with complex geometries from different materials what was not possible to achieve with standard methods. Advances in 3D printing technologies together with novel ink materials may overcome current limits in the development of advanced medical devices, 3D tissue models, drugs, or treatment methods. They allow for simultaneous deposition of biological components and biomaterials, mostly in a layer-by-layer fashion, to form 3D well-organized heterogeneous bio-structures that can mirror physiologically and morphologically relevant complex biological architectures. Moreover, these emerging fabrication technologies provide tools for the development of a patient-specific medical devices delivery drugs exclusively targeting diseased tissues with controlled doses of bio-actives compounds.

Our additive manufacturing approach is based on a microfluidic system coupled to a co-axial needle extruder for high-resolution computer-controlled 3D deposition of hydrogel fibers laden with different cells. By formulating tailored hydrogel based bio-inks and precisely controlling the 3D spatial organization of the bio-fibers, this novel 3D bioprinting method has been tested for the fabrication of advanced engineered bio-constructs for the regeneration of musculoskeletal tissues. Depending on application, the biomimetic hydrogels were composed of modified biopolymers like gelatin, alginate, hyaluronic acid, or PEG-fibrinogen. The gels were laden with different types of cells including mesenchymal stem cells, muscle precursor cells or chondrocytes. The obtained with high resolution (~ 100 um), a fiber-based 3D printed living constructs mimic organized tissues like cartilage, tendon and muscle. Additional post-processing including biochemical and mechanical stimulation influenced cells proliferation, alignment, and differentiation and enhanced extracellular matrix deposition in 3D biofabricated constructs. Moreover, these constructs have shown an extraordinary capacity in regenerating musculoskeletal tissues in *in vivo* experiments.

In summary, the 3D printing together with novel bio-ink materials play a significant role in developing new-generation medical devices and 3D tissue models with new properties not possible to reach with traditional fabrication techniques.