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Hybrid Manufacturing System to Produce 3D Structures for Osteochondral Tissue Regeneration

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Abstract : One utmost challenge in Tissue Engineering is the production of 3D constructs capable of mimicking the functional hierarchy of native tissues. This is well stated for osteochondral tissue due to the complex mechanical functional unit based on the junction of articular cartilage and bone. Thus, the aim of the present study was to develop a new additive manufacturing system coupling micro-extrusion with hydrogels printing. An integrated system was developed with 2 main features: (i) the printing of up to three distinct hydrogels; (ii) in coordination with the printing of a thermoplastic structural support. The hydrogel printing module was projected with a 'revolver-like' system, where the hydrogel selection was made by a rotating mechanism. The hydrogel deposition was then controlled by pressured air input. The use of specific components approved for medical use was incorporated in the material dispensing system (Nordson EDF Optimum® fluid dispensing system). The thermoplastic extrusion modulus enabled the control of required extrusion temperature through electric resistances in the polymer reservoir and the extrusion system. After testing and upgrades, a hydrogel modulus with 3 syringes (3cm3 capacity each), with a pressure range of 0-2.5bar, a rotational speed of 0-5rpm, and working with needles from 200-800µm was obtained. This modulus was successfully coupled to the extrusion system that presented a temperature up to 300˚C, a pressure range of 0-12bar, and working with nozzles from 200-500µm. The applied motor could provide a velocity range 0-2000mm/min. Although, there are distinct printing requirements for hydrogels and polymers, the novel system could develop hybrid scaffolds, combining the 2 moduli. The morphological analysis showed high reliability (n=5) between the theoretical and obtained filament and pore size (350µm and 300µm vs. 342±4µm and 302±3µm, $p>0.05$, respectively) of the polymer; and multi-material 3D constructs were successfully obtained. Human tissues present very distinct and complex structures regarding their mechanical properties, organization, composition and dimensions. For osteochondral regenerative medicine, a multiphasic scaffold is required as subchondral bone and overlying cartilage must regenerate at the same time. Thus, a scaffold with 3 layers (bone, intermediate and cartilage parts) can be a promising approach. The developed system may give a suitable solution to construct those hybrid scaffolds with enhanced properties. The present novel system is a step-forward regarding osteochondral tissue engineering due to its ability to generate layered mechanically stable implants through the double-printing of hydrogels with thermoplastics.

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