Silk-fibroin based scaffold 3D bioprinting deposition: mathematical modeling and experimental characterization

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INTRODUCTION:Robotic dispensing-based 3D bioprinting strategies are widely used to print cell-laden hydrogel constructs. This enables the fabrication of neo-engineered constructs able to maintain cells alive and to regenerate tissues. Nowadays, efforts in this field are mainly driven by experiments and trial-and-error approaches. In order to predict the deposited filament width through extrusion-based 3D bioprinting, a mathematical model[1] was applied considering different printing parameters such as pressure and printing speed. The printing parameters were chosen to print silk fibroin(SF)-gelatin(G) based scaffolds laden with human-derived mesenchymal stromal cells (hMSCs).
METHODS:The rheological characterization of cell-friendly SF-G bioink used in our previous study[2] was used to define the viscosity and the power law index. A mathematical model of deposition was formulated including the following parameters: printing pressure (0-3 bar), speed (0.5-3 mm/s) and cylindrical stainless-steel needle features (diameters: 0.2, 0.41 and 0.5 mm and lengths: 6.35, 12.7 and 25.4 mm). Then, an experimental characterization was carried out to validate the model monitoring filament width as the output. Shear stress values were also estimated to ensure cell viability during the process. Printing parameters were chosen to print 3D cell-embedded construct with open and interconnected pores to guarantee nutrients permeability. Cell viability and cartilage genes expression were investigated at different time points (days 14 and 28).
RESULTS:The mathematical model was successfully validated by experimental data: the smallest discrepancy (1.5%) was found with needle diameter of 0.2 mm and length of 6.35 mm, whereas, the largest discrepancy (65.8%) with needle diameter of 0.5 mm and length of 25.4 mm. The model helped to define the best printing parameters to achieve a filament width of 200 µm using a pressure of 1.2 bar and a printing speed of 1.5 mm/s. The selected printing parameters and SF-G bioink ensured open pores formation and good cell viability until day 28. Moreover, we confirmed an increase expression of typical chondrogenic markers (SOX9, COLL2), at day 28 by both gene expression and immunofluorescence analyses.
DISCUSSION & CONCLUSIONS:This study evidenced that the proposed model can be used to predict the features of the silk-based hydrogels permitting to save time and resources by avoiding trial-and-error approaches. Moreover, we confirmed that SF-G bioink enhanced cartilaginous matrix formation.
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