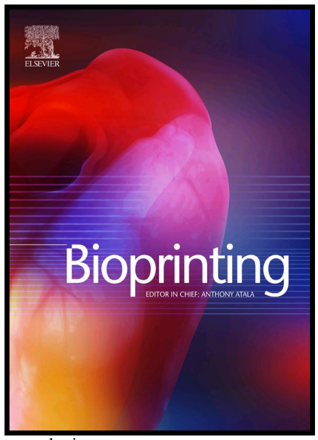

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CELLULAR BIOINK SURFACE TENSION: a TUNABLE BIOPHYSICAL PARAMETER for FASTER BIOPRINTED-TISSUE MATURATION

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ABSTRACT

Bioprinting provides an exceptional platform for tissue engineers to deposit cells onto substrates with precision, and to construct three-dimensional (3D) biological structures such as tissues and organs. In extrusion bioprinting of cells, cellular bioink particles in the form of multicellular systems are printed on supportive materials such as agarose. Post-printing and before implantation, the 3D biological structure undergoes a complex maturation process governed by both biological and physical mechanisms. Controlling the maturation time to expedite the regeneration of human tissues remains challenging. Herein, we provide evidence that the fusion of cellular bioink (a critical step in tissue maturation) can be accelerated by higher apparent tissue surface tension (ATST) of the cellular bioink particles. Two different preparation methods, namely the egg holder aggregate maker and cylindrical aggregate fabrication, were used to fabricate cellular bioink of Chinese hamster ovary (CHO) and human skin fibroblast (HSF) cells. Each method produced distinct ATSTs from aggregates of the same cell type. The characteristic fusion times for CHO aggregates with 14.71 dyne/cm and 22.8 dyne/cm were found 181.95 hours and 93.15 hours respectively. The same trend was observed for HSF as aggregates with a higher surface tension fused faster. Therefore, controlling tissue fusion can be achieved through adjusting the ATST of bioprinted spheroids via our fabrication method. This is an essential initial step towards engineering tissues of defined anatomical and histological structures.

Keywords: bioprinting, apparent tissue surface tension, cellular bioink, maturation time

1. Introduction

Tissue engineering is the process of constructing tissues and organs *ex vivo* to be applied in regenerative medicine [1,2]. The delicacy, precision, and reproducibility achieved by printers have made possible advances in electronics [3-6], renewable energy [7,8], and tissue engineering [9,10]. Bioprinting is a versatile tool to deliver cells and biomaterials with high speed, accuracy, and reproducibility. It has been used extensively to advance tissue engineering and build three-dimensional (3D) biological constructs [11,12]. Cells have been successfully printed with a high degree of viability when using the inkjet (piezoelectric and thermal) [13-15], laser-assisted [16], and extruder methods [17,18]. Although most types of printers can deliver cells and cell-laden biomaterials, extrusion printers have emerged as one of the most useful systems for the engineering of 3D biological constructs on the scale of tissues [19].

Tubular structures play critical roles in the body, as they constitute the majority of organs. Specific structures such as nerve and blood vessel conduits have been successfully printed using extrusion printers [17,18]. In the latter example, the printer facilitates the delivery of the cellular bioink particles made with cellular types composing the wall of blood vessels (collection of endothelial cells, smooth muscle cells, and fibroblasts at a specific ratio) into an initial configuration compatible with the tubular geometry [17].