Title: Patterning decellularised human bone and vascular allograft bioinks via 3D bioprinting for skeletal tissue engineering

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Abstract

Autologous grafts or metal implants are commonly used for repairing critical bone defects, but typically fail to offer a long-term clinical solution. Autologous bone implants are limited by the size and availability of explanted bone portions, while allogeneic or synthetic bone grafts lack osteoinductive properties. Metal implants, although supportive, do not guarantee physiological repair and require periodic revisions increasing healthcare costs. Therefore, there is an urgent need for a functional biomimetic alternative for skeletal repair. Thus, we investigated the potential use of hydrogels derived from decellularized human tissues for skeletal regeneration. The decellularized materials have been found to retain native proteins and growth factors essential for cellular differentiation and tissue homeostasis. The use of human bone extracellular matrix (hbECM) in the realization of skeletal constructs offers the possibility of recreating an osteogenic microenvironment appropriate for human bone marrow skeletal stem cells (HBMSCs) survival and differentiation but lacks the mechanical stability necessary for bioprinting processes. The addition of nanoclay (Laponite®) and sodium polyacrylate showed an improving of physicochemical properties of hbECM hydrogels, enhancing the rheology properties for the printing and improving both scaffolds vascularization and mineralization. Using an innovative microfluidic 3D bioprinting strategy, we will develop 3D constructs able to stimulate osteogenesis and angiogenesis with the use of HBMSCs printed in a hbECMs-based bioink, and human umbilical vein endothelial cells (HUVECs) deposited in an extracellular matrix of decellularized human chorion placenta (hpcECM)-based bioink, offering a new approach for personalized skeletal tissue repair.