VISIONS FOR THE FIELD BY A BIOFABRICATION OF 3D HARD-SOFT AND COMPOSITE CONSTRUCTS FOR BONE REGENERATION

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Biofabrication encompasses the use of additive manufacturing techniques for fabricating complex constructs from a wide range of biomaterials, cells and bioactive substances as well as their maturation for the formation of tissue. The fabricated constructs should provide mechanical stability, porosity, and accurate positioning of cells. The aim of this work was the creation of hybrid constructs consisting of a combination of a thermoplastic hard polymer with and without addition of bioactive glass particles and a soft hydrogel matrix with immobilised cells. The hard phase should enhance the limited mechanical performance of the soft hydrogel phase. Moreover the addition of bioactive glass will enhance the local bioactivity of the scaffolds, of relevance for bone tissue engineering [1]. The hydrogel composition, based on alginate, was tailored to enable the proliferation, migration and differentiation of cells. The mechanical properties and the degradation kinetic of the constructs were investigated. Alginate-dialdehyde (ADA) gelatine (GEL) hydrogel (= ADA-GEL) containing murine bone marrow derived stroma cells (ST2) and polycaprolactone (PCL), polyethylene glycol (PEG) blends were used. Processing was done by additive manufacturing using a dispense plotter equipped with multiple cartridges. Process parameters like plotting speed, pressure and temperature were optimized for the two material systems. Porosity, degradation behaviour and mechanical stability of the PCL-PEG frame structure scaffolds were tested as well as the response of ST2 cells. The presence of bioactive glass leading to enhance local formation of hydroxyapatite was investigated. The cell behaviour and cell development were characterized by assessing the morphology and by measuring the viability of the immobilized cells in the ADA-GEL over an incubation period of 28 days. Both materials could be processed in a defined manner with optimized process parameters. The PEG phase could be dissolved and porous (bioactive) struts forming a framework structure were created. The viability of immobilized ST2 cells after hydrogel plotting was proven as well as their attachment, migration and proliferation by SEM and fluorescence microscopy images. Thus, two promising material systems for creating hybrid constructs were successfully evaluated. The two phase plotting approach enables the fabrication of hydrogel constructs with improved mechanical properties and bioactivity, which exhibit high potential for applications in bone regeneration.

[1] A. J. Leite, et al., Bioplotting of a bioactive alginate dialdehyde-gelatin composite hydrogel containing bioactive glass nanoparticles, *Biofabrication*, 8, pp. 035005 (2016)