Society of Engineering Science 51st Annual Technical Meeting

1–3 October 2014

Purdue University, West Lafayette, Indiana, USA

3D Bioprinting of functionalized graphene nanoplatelet-doped hydrogel for neural regeneration

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ABSTRACT

Each year more than 20 million Americans are affected by peripheral nervous system damage, leaving them in pain and with restricted mobility. Various cell therapies and implants have been investigated, yet a comprehensive treatment to that grants full functional recovery has still not been elucidated. Traditional neural guidance constructs lack the ability to incorporate biomimetic nanofeatures, well-controlled 3D geometry, and appropriate electrical conductivity in the same scaffold, limiting their effectiveness. To address these problems, this study aims to leverage stereolithography based 3D bioprinting and graphene nanoplatelets (GNPs) to create a biomimetic, conductive nanocomposite scaffold for successful neural tissue regeneration. For this purpose, a series of highly aligned 3D computer models were created via CAD software, and printed using our lab's novel stereolithography based bioprinter. In brief, a hydrogel solution is created by mixing biocompatible Poly(ethelene) glycol, Poly(ethelene) glycol di-acrylate, and a photoinitiator appropriate for the wavelength and energy of the laser used. This solution is then added layer by layer into a vat and subsequently cured via UV laser radiation into a 3D hydrogel scaffold. Similar hydrogel constructs with added graphene nanoplatelets with COOH or NH_2 functional groups were successfully fabricated as well. The scaffolds were compared with the pure hydrogel construct through scanning electron microscopy (SEM) imaging, PC-12 cell proliferation and differentiation studies in vitro. The SEM images highlight the homogenous incorporation of the GNPs throughout the scaffold, yet still present on the surface, allowing for direct interaction between GNPs and cells. The conductivity of the GNP scaffolds was shown to be significantly better than the control scaffolds without GNPs, which make the scaffold promising for neural regeneration. Cell proliferation and confocal microscopy shows that the graphene doped scaffolds are biocompatible and allow PC-12 cells to grow and align along the channels.