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Development and in vivo implantation of LEGO-like 3D printed bone scaffolds

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Abstract

The leading cause of failure for current bone replacements, is lack of vascularization. Ideal synthetic bone scaffolds provide structural rigidity, allow cellular migration, vascularization, have a modular design to fit defect geometry. Advancements in 3D printing technology offers materials such as Beta tricalcium phosphate (βTCP) ceramics and Gelatin methacrylate (GelMA). GelMA is a biocompatible, mechanically tunable, photocrosslinkable, and 3D printable material with the potential to seed both stem cells and growth factors into the medium. The present studies in-vitro development and preliminary in vivo implantation of a novel, modular, LEGO-like synthetic scaffold comprised of rigid βTCP scaffold and embedded GelMA matrix, and compares cellularization, vascularization and tissue invasion of two different GelMA designs within the construct.

TCP scaffolds were designed as modular, open, interlockable pieces with hollow core and wall openings analogous to LEGO blocks. βTCP scaffolds were SLA 3D printed (Lithoz) while GelMA microgels were printed using an Ember 3D printer. Microgels contained VEGF, PDGF-BB, and BMP-2 and were placed in the hollow core structures.

Hydrogel-impregnated' samples consisted of LEGO-like constructs filled with GelMA hydrogel containing growth-factors and photopolymerized. The second group, termed 'Microgels' consisted of growth-factor laden GelMA microgel using 3D printing to, fabricate microgels before placement in the construct

In vitro cellular migration and penetration into Hydrogel-impregnated and microgel constructs was examined by seeding constructs with 1:1 HUVECs and hMSCs and examined via confocal microscopy. In vivo cellularity, tissue invasion and vascularization were immunohistologically examined via subcutaneous implantation in rats.

Microgel incorporation increased hydrogel macro porosity and diffusion of nutrients to the core of the construct. In both the in vitro and the in vivo studies, microgels constructs showed increased cell spreading and invasion farther into the core than hydrogel-

impregnated samples. Both in vitro and in vivo, microgel samples showed increased cellularity over bulk hydrogel.

3D printed LEGO-like constructs demonstrated promising signs of cellularization and vascularization both in vitro and in vivo. These constructs, which are modular, synthetic, and do not require living tissue culture, may eventually provide an answer to critical-size bone defects.