

Layer-by-Layer Systems for Craniomaxillofacial Bone Repair

By

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Technical Summary

The treatment of craniomaxillofacial bone defects with drug-eluting synthetic implants is a promising treatment currently being investigated. It is becoming increasingly recognized that release rate of growth factor proteins signaling bone regeneration and vascularization is a key optimization parameter since these proteins are rapidly cleared from the body and can have safety ramifications when released too rapidly. A clear delivery challenge exists to produce a synthetic bone implant which can deliver growth factors in safe doses with appropriate delivery time frames locally to the bone defect site. A technology that can potentially meet this challenge is layer-by-layer (LBL) self-assembly, which can be used to coat defect-relevant implants with nanoscale thickness films that elute growth factors with tunable release kinetics and dose.

In this work, we first developed LBL film architectures deliver osteogenic growth factor, bone morphogenetic protein-2 (BMP-2), over four different time scales ranging from 2 days to 30 days by changing the method of diffusional barrier incorporation. We next implanted formulations with rapid or slow release of a minimal dose of BMP-2 in a rat calvarial defect model to determine the influence of BMP-2 release kinetics on bone growth. We then investigated the effects of combination growth factor therapies incorporating angiogenic growth factors vascular endothelial growth factor (VEGF) or platelet-derived growth factor (PDGF) to determine if dual-protein delivery could enhance bone regeneration. Finally, we translated BMP-2-eluting films to customized 3D-printed scaffolds and implanted these formulations into a rabbit mandibular defect model to investigate the effects of differential BMP-2 release kinetics in a larger animal model with a load-bearing bone defect.

As a result of this research, we developed LBL diffusional barrier tools that can be used to engineer targeted release kinetics of growth factor proteins. These tools could be applied to various growth factors or other biologic therapeutics in order to address delivery challenges in other disease and injury applications. We also leveraged the power and flexibility of LBL technology to enable investigation into optimal delivery parameters for single or dual growth factor delivery in two different craniomaxillofacial bone defects. These findings inform optimization and formulation of future clinical products incorporating growth factors for bone regeneration.

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