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Bone Tissue Engineering: Scalability and Optimization of Densified Collagen-Fibril Bone Graft Substitute Materials

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ABSTRACT

Over 240 million people missing teeth worldwide experience lingering problems such as difficulty speaking and eating, undesirable aesthetics, and resorption of bone supporting neighboring teeth. The gold standard of treatment utilizes grafts to attach a function-restoring implant to supporting bone. Current graft materials suffer from problems including autologous donor site morbidity, long resorption time, incomplete integration with the maxillae or mandible, and structural weakness. Patient-specific, cellularized bone grafts may be a solution to these issues by accelerating and improving the quality of regenerated bone. Recently, encapsulation of mesenchymal stem cells within self-assembling type I collagen oligomer matrices has been shown to support rapid mineralization of small-scale bone constructs (cylinders with diameter and height of 6mm and 1mm, respectively) *in vitro*. However, this method's volume and geometric constraints for nutrient transport and cell viability are still unknown. In this study, the effects of construct size and medium formulation on mineralization were investigated using conventional static culture methods. To create constructs, human adipose stem cells (hASCs) were embedded in oligomer matrices, allowed to polymerize, and compressed to final cell and fibril densities of 3×10^7 cells/mL and 50 mg/mL, respectively. Varying construct sizes (maximum diameter and thickness of 11 mm and 0.81 mm) were cultured for 1 week in growth medium or osteogenic medium with varying calcium concentrations. Alizarin red staining was used to detect calcium deposits indicative of cell-induced mineralization. Preliminary data suggests that culture in osteogenic medium supplemented with both 8 mM and 16 mM calcium may induce rapid, uniform mineralization across all sizes tested, and 16 mM calcium supplementation induces greater mineralization. However, additional validation by direct measurement of cell viability and osteogenic differentiation will be needed to better compare bone regeneration as a function of scale.

KEYWORDS

Engineered Bone Construct, Bone Regeneration, Adipose Stem Cells, Type I Oligomer Collagen, Mineralization