Large Segmental Bone Defects Treated with 3D Printed Scaffolds and Autologous Stem Cells Demonstrate Increased Stiffness Following Hardware Removal

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Introduction

- Large critical size segmental long bone defects do not reliably heal despite numerous surgical treatment options.
- Biometric scaffolds, produced from micro-CT images of trabecular bone, result in 500% increased bone regeneration compared to scaffolds with simple geometric pores.
- Biometric scaffolds coated in beta-tricalcium phosphate, and seeded with autologous adipose derived stem cells, can bridge a 4.2cm mid-diaphyseal femoral defect in a sheep within 3 months.
- Strain gauges incorporated into the scaffolds can measure loads passing through the scaffold during healing.
- The purpose of the current study was to compare the mechanical properties of bone regenerated using biometric stem cell seeded senescent scaffolds when the supporting metal hardware in non-dynamized, dynamized, or following complete removal of the hardware.

Methods

- Polybutylene terephthalate (PBT) scaffolds 4.2 cm in length were 3D printed with an internal structure based on micro-CT images of sheep femoral heads.
- Three, 1000 Ω strain gauges were waterproofed and attached to each scaffold. Scaffolds were compressed to 294 N at 294 N/S to generate linear stress-strain calibration curves.
- Scaffolds were coated in beta tricalcium phosphate, sterilized in ethylene oxide, and seeded with autologous adipose derived stem cells obtained from the tail fat pad of sheep two weeks prior to surgical placement.
- Scaffolds were surgically placed into a 4.2 cm mid-diaphyseal femoral defect in three sheep. Scaffolds were stabilized using an intramedullary nail with a locking screw placed proximal and distal to the defect.
- Following surgery sheep were walked on a treadmill for 15 minutes up to three times per week. Radiographs of the femur were taken monthly.
- Scaffolds were dynamized by removal of the proximal locking screw at six months, and the intramedullary nail was removed nine months following scaffold placement.
- Following sacrifice, the femora were explanted for mechanical testing, micro-CT imaging and histological analysis of regenerated bone.

Results

- All sheep demonstrated bridging bone across the anterior, medial and lateral sides of the defect by three months.
- Monthly radiographs demonstrated evidence of remodeling in the regenerated bone three months after dynamization, with continued remodeling three months after hardware removal (Figure 1).
- Scaffolds did not demonstrate a significant change in loading prior to and immediately following dynamization, but demonstrated decreased peak loads 3 months following dynamization, just prior to hardware removal (Figure 2).
- Sheep femora demonstrated significantly increased axial stiffness compared to control and non-dynamized femora (Figure 3).
- CT imaging and histology (Figure 4) demonstrate extensive bone formation.

Discussion

- Sensate biometric PBT scaffolds coated in tricalcium phosphate particles and seeded with autologous adipose derived stem cells are able to regenerate a large 4.2 cm mid-diaphyseal femoral.
- Six months following scaffold placement the regenerated bone is supporting a significant proportion of limb loading.
- Dynamization of the construct facilitates additional bone formation and remodeling around the scaffold.
- Regenerated bone is supporting limb loading by 9 months, allowing safe removal of all hardware.
- Regenerated bone demonstrates an increased stiffness in axial loading following removal of all supporting hardware.

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