**Introduction:** One of the most difficult challenges for orthopaedic surgeons is the management of bone loss resulting in a segmental bone defect. Segmental bone defects are ubiquitously difficult to treat, require multi-phase surgery and have frequent complications. Current treatment options include autografts, allografts and distraction osteogenesis, all of which have significant complications and none have satisfactory success rates. A promising new strategy involves combining tissue engineering techniques with the delivery of biologically active proteins to facilitate bone regeneration.

The ideal bioengineered scaffold should possess the following 4 characteristics:

1. The surface chemistry of the carrier should allow for cell attachment, differentiation and deposition of extra cellular matrix.
2. The degradable carrier should provide sufficient initial mechanical strength to sustain the load and maintain the gap before bone bridging or union occurs. In other words, to allow immediate weight bearing.
3. The carrier design should be easily allow for incorporation of biologically active factors and be effective in factor release after implantation.
4. The degradation byproducts from the degradable carrier should cause minimal adverse effects to the surrounding tissue.

The purpose of this study is twofold. First, to investigate whether a cylindrical, biodegradable load-bearing scaffold, stabilized with an intramedullary (IM) nail, will facilitate early weight bearing in a critical sized canine defect model. The second objective is to investigate if rhBMP-2, transported by the biodegradable carrier, will enhance bone formation and healing across a critical sized canine defect.

**Materials and Methods:** 10 mature, female mixed-mongrel dogs underwent the creation of a critically sized, tibial diaphyseal defect of 3 cm in length. A cylindrical, biodegradable scaffold of (poly)propylene fumarate was inserted into the defect. The tibia was then stabilized with a locked intramedullary nail. The nail was passed in an antegrade fashion, first through the proximal tibia, next through the central lumen of the scaffold and finally through the distal tibia. Half of the scaffolds were impregnated with 300 μg rhBMP-2 (n=5) and half remained as controls (n=5). The animals were allowed immediate weight bearing post-operatively.

X-rays were obtained immediately post-operatively and at weeks 1, 2, 3, 6, 12, 18, and 24. X-rays were assessed for loss of height, integrity of the scaffold, and presence of bridging callus formation at all time points.

All animals were sacrificed at 24 weeks. Two specimens from each group were sent for micro-CT and histological evaluation. Three specimens from each group were subjected to biomechanical testing. Bones were tested to failure by four-point bending tests to measure flexural strength of the treated bones in comparison to contra-lateral controls. Destructive testing was performed using a custom made four-point bending fixture, using an 858 MiniBionix Materials Testing System.

**Results:** The animals that received scaffolds treated with rhBMP-2 showed abundant callus formation on X-ray. Statistically significant differences in callus formation, defect height and hardware failure were seen between the 2 groups. Callus formation in the BMP group was seen at 3 weeks. Complete bridging callus (bridging on 4 cortices) was observed by 6 weeks. These BMP specimens maintained height of the defect, overall length of the tibia and showed no hardware failure.

The animals that received scaffolds without rhBMP-2 (controls) demonstrated minimal callus formation at all time points. By 3 weeks significant loss of defect height was observed. By 6 weeks failure of hardware (breakage of interlocking screws and/or screw loosening) was evident.

Histological evaluation confirmed bridging callus in the BMP specimens and absence of bridging in the controls. Micro-CT showed similar results. Remnants of the scaffold remained present in both control and BMP specimens.

A statistically significant difference in bending strength was seen in the BMP animals compared to controls.

**Discussion:** This study shows that biodegradable scaffolds, treated with rhBMP-2, when implanted in a critical sized defect, facilitate bridging callus formation and healing across the defect. This data indicates that biodegradable scaffolding made of (poly)propylene fumarate is a suitable carrier for rhBMP-2. The scaffolds studied in this investigation have demonstrated the ability to:

1. Maintain the biologically active protein (rh-BMP-2) within the defect
2. Allow the release/interaction of the protein with the surrounding tissues to facilitate bone growth
3. Provide sufficient initial structural support for weight bearing
4. Cause no detrimental effect on the surrounding tissues during scaffold degradation.

Further investigation into the use of these scaffolds as carriers for other biologically active proteins, cells and antibiotics is warranted.


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