

+Novel Antibiotic Eluting Polymer Sleeve Outcome in an Infected Ovine Fracture Model

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Statement of Purpose: The development of deep wound and bone infections secondary to traumatic bone injury is a well-documented clinical problem. In fact, many centers prophylactically treat open fractures with local antibiotic therapy¹ to avoid such complications. The primary objective of this study was to evaluate the efficacy of an antibiotic eluting plate sleeve² to control bacterial colonization and improve clinical outcomes in an infected sheep fracture model. A secondary objective of this work was to develop an optimized model for conducting these studies. Towards these goals, the efficacy of the eluting sleeve was evaluated by escalating the dose of a *S. Aureus* bacterial inoculum.

Methods: A unilateral mid-diaphyseal tibial osteotomy was created in 19 Dorset-cross ewes, with fixation using a stainless steel locking compression plate (LCP). Ten animals received plates without sleeves (control cohort) and nine animals received the gentamicin loaded polymer sleeve over the plate (treatment cohort). After closure, the site was inoculated with *Staphylococcus aureus* (ATCC 25923) at a dose of either 10⁴, 10⁶, 10⁸, or 10¹⁰ CFU. The sheep were regularly scored by three independent clinicians for clinical signs of pain and infection (pain score). Sheep were euthanized one month post-op. The plate was removed and the adjacent and underlying tissues were scored. Scores pertaining to the level of healing observed in the osseous and soft tissues were recorded as well as the extent of abscess formation. The plates were aseptically collected then individually sonicated to liberate any adherent bacteria. The resulting sonicate was serially diluted and plated. Colonies were then counted to determine the amount of bacteria recovered from each plate. A paired two-tailed t-Test was performed on scored data.

Results: Two sheep sustained fixation failure within 1 week post-op and were excluded from the study. At explant, all polymer sleeves had completely degraded without leaving any noticeable debris.

Clinical & Explant Scores

At necropsy, the animals treated with the antibiotic eluting sleeve demonstrated a dramatic reduction in gross evidence of infection, as well as improved healing of the osteotomy ($p < 0.00003$) and the overlying soft tissues. The pain scores in the treatment cohort also demonstrated significantly better outcomes ($p < 0.004$) in comparison to their control cohorts.

Microbiology

The pooled results of bacteria recovered from the plates, independent of inoculum level, shows 1/9 plates were colonized in the sleeve group and 6/10 plates were colonized without sleeve (Figure 1). The 10¹⁰ inoculum group (highest inoculum) resulted in the most consistent infection among the controls (Figure 2).

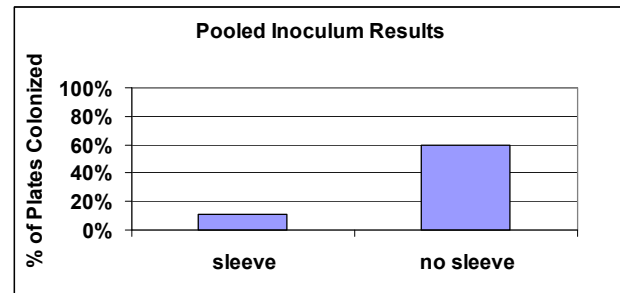


Figure 1: Pooled inoculum results showing the percentage of plates colonized with and without sleeves. (Fischer exact test p-value = 0.038)

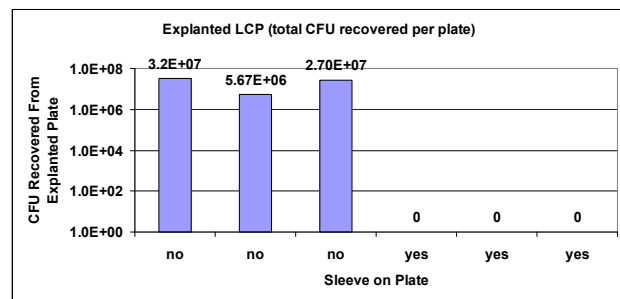


Figure 2: Bacterial recovery from the explanted plates shows no bacteria when a plate sleeve is used and consistent colonization on the control plates.

Conclusions: These data show that the gentamicin loaded polymer plate sleeve significantly reduced bacterial colonization of the plate in this large animal infection model. The sleeve also improved the quality of the fracture repair at 1 month, as well as the composite pain scores. These results further showed that the colonization of the plate was inconsistent in the control groups at the lower inoculum levels. At the highest inoculum level, consistent colonization (100%) of the plate was achieved in the control animals without any signs of sepsis, suggesting that the 10¹⁰ CFU dose may be the optimal dose range for this model. Taken together, these data indicate that an antibiotic eluting plate sleeve may be a clinically safe and effective means for reducing infection rates associated with the open reduction and internal fixation of bone fractures.

References:

1. Zalavras, et al. Clin Orthop and Rel Res, 427 (86-93), 2004
2. Armbruster, et.al. Elution of gentamicin and triclosan from bioabsorbable polymer films. 2007 Society for Biomaterials Annual Meeting Transactions.