A Regenerative Bone Adhesive Improves Fixation and Promotes Bone Healing as an Augmentation to Metal Hardware in an Ovine Distal Femur Intra-Articular Fracture Model

Sourabh Boruah, Brittany McDonough, Jeremiah Easley, Benjamin C Gadomski, Uzma Mhate, Molly Shutt, Brian J. Hess, Hans Peter Van Lancker, Michael John Weaver

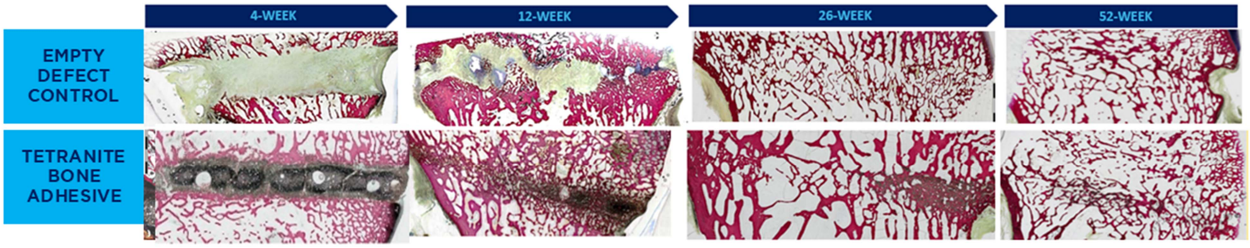
INTRODUCTION: Each year, an estimated 6.3 million fractures are reported in the US. Intra-articular fractures are especially challenging to treat and often caused due to a high energy trauma resulting in comminution. These fractures substantially increase the risk of long-term joint instability and cartilage damage, contributing to early progression of post-traumatic arthritis. The current standard of care for these fractures involves surgical fixation using metal hardware such as locking compression plates (LCP) and screws. Depending on the comorbidities (underlying bone conditions), fracture complexity and fixation alignment, this approach often leads to revision surgeries. The failure rate of these fixations due to non-union has been reported to be as high as 20%, while the rate of early fixation failure has been documented at 13.6%. This study uses a novel bone adhesive formulated with a chemical composition of Tetracalcium Phosphate and Phosphoserine (TTCP-PS) to reinforce the metal hardware and provide rigid bone-to-bone adhesion to mitigate these risks. TTCP-PS also includes trace amounts of Calcium Carbonate for optimal porosity when acting as a scaffold for new bone formation and Barium Sulfate for radiopacity to visualize intra-operative placement and post-operative healing. This adhesive is self-setting in a wet or dry field, has sufficient load-bearing strength within minutes, and is osteoconductive to promote healing. TTCP-PS offers a solution to improve surgical technique and post-operative outcomes for complex intra-articular fractures.

METHODS: In this study, a total of forty-five (45) sheep were treated to evaluate the safety and efficacy of TTCP-PS as an adjunct to hardware fixation in an unstable intra-articular fracture model in the distal femur. A 1-cm base wedge osteotomy was performed in the distal femur to represent an unstable metaphyseal fracture. The bone was stabilized using a stainless-steel locking compression plate (LCP) fixed on the lateral aspect of the femur using stainless-steel locking screws. TTCP-PS was implanted to fill the osteotomy in animals assigned to the Treatment Group. The osteotomy performed in the Control Group was treated with the same stainless-steel LCP and screws, but the osteotomy gap was left empty. At respective timepoints, the assigned animals were humanely euthanized and submitted to necropsy for gross evaluation. In vivo procedures included lameness assessment to determine post-operative return to function. Ex vivo procedures of the affected limb included dissection and radiographic imaging, micro-CT imaging, biomechanical testing, and histopathology.

RESULTS: Successful surgery in all animals resulted in all animals scoring a lameness of 1 (out of 4) or lower by 4-weeks, with both test groups exhibiting similar trends in lameness score severity and timing throughout the study. No abnormal results were reported during gross necropsy and examination, and no significant differences were found between control and treatment groups for synovial fluid assessment or histopathology. All study animals, regardless of experimental group, displayed robust tissue healing and new bone formation with progression to complete healing of the femoral osteotomy site over time from the 4- to 52-week timepoint. Tier 1 Organ histopathology showed that there were no treatment/test-compound related adverse effects. At 4-weeks post-treatment, cartilage health was better in the treatment group, while at all other timepoints they were equivalent. Across all timepoints, histomorphometry showed that the Control group had significantly increased percent void area in the wedge as compared to the Treatment group ($p = 0.004$). From 4 to 52 weeks, the percent TTCP-PS area decreased from 40 to 10%, while the percent bone area increased from 10 to 30%, indicating sustained remodeling of TTCP-PS to bone over one year. The percentage bone area was not statistically significantly different between the two groups. Biomechanical testing showed that while the measured parameters did not vary significantly with treatment group in the ex-vivo specimens, cadaver sheep femurs tested within 2 ± 1 hours of treatment showed that bone strain was significantly greater in the treatment group (63 μstrain) in comparison to the control group (34 μstrain; $p \leq 0.047$), indicating a favorable load distribution between plate and bone in the treatment group with diminished strain on the plates and screws.

DISCUSSION AND CONCLUSION:

The study showed that utilizing TTCP-PS as an augment to plates and screws in a fracture could improve post-operative stability of the fixation, especially in the early time points, by maintaining native bone strains and preventing fibrous tissue ingrowth, as shown by significantly reduced void area in the defect by 30% to 40% and improved bone strain by an average 99% in this model. Intra-articular applications showed that TTCP-PS could be safely used adjacent to the joint, improving cartilage health outcomes and stabilizing bone fragments in comminuted fractures, including those involving articular joint surfaces.


4-WEEK
12-WEEK
26-WEEK
52-WEEK
EMPTY DEFECT CONTROL
TETRANITE BONE ADHESIVE