

Evaluation of Healing of Ovine Bilateral Femoral Defect with Calcium Phosphate Cements

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INTRODUCTION: Currently-marketed calcium phosphate cement (CPC) devices leave room for significant improvements that could be made to their handling, resorption kinetics, and support for bony healing. The objective of this study was to investigate osseointegration and local histopathology response of two proprietary CPC formulations (CoLOSSIS™, which contains collagen, and MacroSET™, which contains collagen and polymer microspheres) mixed with saline or mixed with Bone Marrow Aspirate (BMA), compared to Stryker HydroSet™ and a negative control (Sham) in an ovine bilateral femoral critically-sized defect model. Based on their compositions, the two proprietary CPC formulations were hypothesized to improve *in vivo* remodeling via generation of an overall lower-density implant compared to more dense CPCs.

METHODS: The materials evaluated in this study included two calcium phosphate cement (CPC) formulations – CoLOSSIS™ and MacroSET™ – for comparison to a market leading device, Stryker HydroSet™, as well as a negative control (sham). To evaluate the performance of the devices and compare the groups, an ovine model was utilized with critically sized defects. Following defect creation, the CPC devices (n≥5 per group) were prepared and implanted, after which timepoints were collected throughout the study up to 1-year. Images and radiography were taken throughout the study, as well as histological staining to evaluate remodeling. Histological slides, as well as histomorphometry and pathology results produced were evaluated for cellular responses by the Study Pathologist for a number of parameters regarding the safety and efficacy of the Test Articles, Control Article, and Negative Control-Sham at each time point. This animal experiment was approved by an institutional review board conforming to the laws and regulations of the United States.

RESULTS: No substantial differences in performance were found among the groups at the short-term time points of 4, 8, and 12 weeks. At the 1-year time point, histomorphometry data indicate a significant difference in bone area when comparing the HydroSet™ control to both MacroSET™ groups and the CoLOSSIS™ group hydrated with BMA (Image 1). Radiographic imaging indicates that the HydroSet™ material remains a dense structure at 1-year, while the CoLOSSIS™ and MacroSET™ groups show densities closer to the surrounding bone (Image 2).

DISCUSSION: The data demonstrates superior long-term integration and bone formation with the CoLOSSIS™ and MacroSET™ materials due to the presence of collagen and microspheres, as well as the ability to mix the materials with autogenous BMA. Based on the overall trends observed in the study, it is anticipated that both the saline and BMA MacroSET™ groups as well as the CoLOSSIS™ BMA group would continue to integrate and remodel at a more rapid rate than the HydroSet™ material. These test groups each demonstrated a greater potential for bone ingrowth and remodeling compared to the HydroSet™ implant and empty defects.

SIGNIFICANCE/CLINICAL RELEVANCE: The design intent of the formulations tested within this pre-clinical model was to create materials that will remodel faster than current marketed products; this potential has been demonstrated in this study. Further data is needed to assess the clinical relevance with regards to patient recovery, but the results indicate a lower-density implant with long-term improved remodeling capabilities.

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IMAGES AND TABLES:

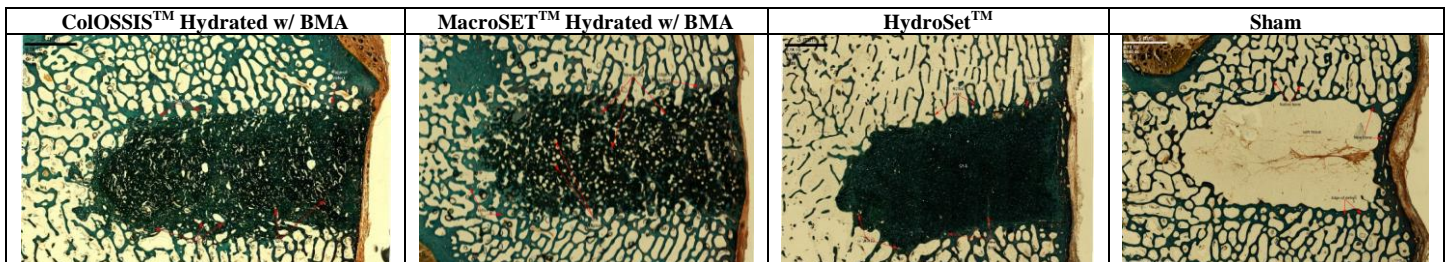
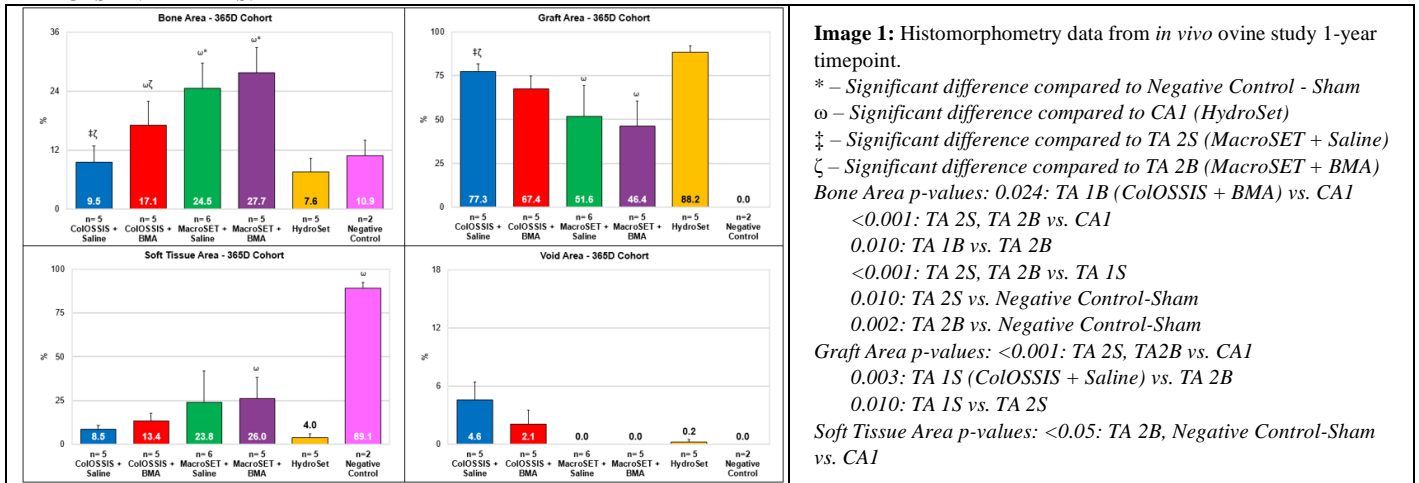


Image 2: Goldner Trichrome stain of 1-year *in vivo* test sites, at 4x magnification. Within the staining, light green coloring indicates new bone formation, black signifies implanted test article, and yellow/orange/tan shows porosity for vascular supply and/or fatty marrow.