INTRODUCTION: For decades, bone auto- and allografts have been regarded among the most effective techniques to enhance orthopedic repairs. These techniques are not without complications such as second site morbidity and potential disease transmission. To limit the possible occurrence of these complications, natural and synthetic bioceramic bone substitutes, with a composition similar to that of natural bone (apatite), have been investigated. Despite encouraging results, these products too have their shortcomings, such as limited osteoconductivity and/or resorbability. To address such limitations, the purpose of this study was to compare the biological behavior of a new synthetic apatite calcium phosphate bone void filler (α-BSM® - ETEX Corp. [BSM]) to that of a porous medical grade calcium carbonate/calcium phosphate bioceramic (ProOsteon-500R® - Interpore-Cross, Intl. [PO]). Bone ingrowth and implant resorption were compared over 24 weeks, using a rabbit tibial metaphyseal defect model. Our hypotheses were that BSM would promote bone ingrowth without evidence of foreign body reaction, that BSM would support bone ingrowth earlier than PO and that BSM would be resorbed faster and more completely than PO.

METHODS: All procedures were approved by the Institutional Animal Care and Use Committee. Bilateral 5x12mm cortical defects were surgically created in the medial aspect of the proximal tibia metaphysis of 30 mature, male, New Zealand White rabbits. Each defect was randomly implanted with PO or BSM, or was left empty (E) to serve as a control. Mean implant weights were 0.16g (PO) and 0.38g (BSM). Nine rabbits were killed at 6, 12 and 24 weeks (n=6/treatment) and 3 fresh cadavers were used to evaluate PO and BSM defect filling at time 0 (n=3/treatment). Radiographic and histologic evaluations were conducted at 0, 6, 12 and 24 weeks. High-resolution contact radiographs were obtained (Faxitron HP) to qualitatively evaluate implant resorption and defect mineralization at each time period. Qualitative histology and quantitative histomorphometry (Bioquant™ T CW-98 image analysis) were performed on 3 undecalciﬁed, longitudinal sections per specimen. Sections were divided into cortical and marrow regions coinciding with the original defect. Regional bone ingrowth and overall implant resorption at each time period and over time were compared using one-way ANOVA followed by Tukey’s post-hoc test when significant differences (p<0.05) were found.

RESULTS: There was neither morbidity nor mortality during this study. Radiography: Empty: Despite a subtle increase in radiographic density, empty defects did not heal by 24 weeks. PO: While granule de ﬁnition decreased after 12 weeks, there was no obvious reduction in PO over time. By 24 weeks, blurring of the defect margins and a slight increase in radiographic density suggested moderate bone ingrowth. BSM: At time 0, BSM showed homogeneous radiographic density throughout the defects. Resorption of implant material created fissures by 6 weeks, resulting in large radiolucent areas by 12 weeks. By 24 weeks, “islands” of residual BSM with indiscernible margins were visible in the defects. These ﬁndings suggest continuous BSM resorption, with progressive bone ingrowth over time (Fig. 1).

Histology: At 24 weeks, immature trabecular bone was present in the cortical space of the empty de ﬁcits; the narrow space remained ﬁlled with hematopoietic and adipose tissues. While regional cancellous bone ingrowth occurred on the surface of both BSM and PO materials between 6 and 24 weeks, osteoblastic activity was more substantial in the BSM group, producing more mature bone over time. There was minimal evidence of PO resorption before 12 weeks, and by 24 weeks, residual PO persisted in both cortical and marrow spaces. Although numerous multinucleated giant cells were seen on the PO implant surface, the absence of Howship’s lacunae and resorption pits suggested that PO degradation occurred via hydrolysis or dissolution. In contrast, marked BSM resorption occurred by 6 weeks as the result of osteoclastic activity, and continued throughout the study. BSM fragmentation was associated with the presence of relatively few foreign body giant cells. By 24 weeks, most BSM specimens showed mature bone in the cortical region of the defect, and almost complete implant resorption. The inﬂammatory response was greater around PO than BSM and was associated with a larger number of mononuclear and foreign body giant cells.

DISCUSSION: This study demonstrates that BSM is capable of supporting earlier cortical bone ingrowth compared to PO in a critical size metaphyseal defect model. Indeed, BSM implants resulted in the production of an equal or greater amount of bone in both cortical and marrow defect regions at each time point when compared with either empty controls or PO-ﬁlled defects. The rapid bone ingrowth seen with BSM was associated with early, and near complete, implant resorption by 24 weeks, and may result from the fact that BSM resorption occurred via cell-mediated events involved in normal bone remodeling. In contrast, approximately 25% of the PO remained at the defect site at the end of the study. This slower rate of resorption, possibly via simple dissolution, may explain the scant bone ingrowth at 12 weeks. These ﬁndings suggest that BSM may act as a more effective osteoconductive scaffold than PO for bone void ﬁlling.

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Fig. 1 - High-resolution contact radiographs of representative empty (left), PO (center) and BSM (right) specimens at time 0 and 24 weeks.

Fig. 2 - Bone ingrowth (A) and implant resorption (B) over time. Signiﬁcantly more bone (#) formed with BSM than PO at 12 weeks. Significant resorption occurred before 12 weeks with BSM ($) and after 12 weeks with PO (¥).