INTRODUCTION:
Composites of purified collagen and calcium phosphate salts have been widely used to produce osteoconductive scaffolds for fracture healing and spinal fusion. The effects of different calcium phosphate additives in a collagen scaffold was previously investigated in a rat model of ectopic bone formation induced by a mixture of bovine bone derived growth factors. It was found that osteoinductivity was significantly enhanced by moderately acidic dibasic calcium phosphate salts but inhibited by hydroxyapatite and β-tricalcium phosphate [1]. In this study, the efficacy of a novel bone graft substitute - CopiOs® Sponge Bone Void Filler (composite of collagen and dibasic calcium phosphate) - was studied in a rabbit radial critical size segmental defect model to compare with autograft and the predicate device Healos® II Bone Graft Substitute (BGS).

METHODS:
CopiOs® Sponge (Fig 1) is a highly porous, osteoconductive composite scaffold of Type I bovine collagen and dibasic calcium phosphate (Zimmer, Inc., Warsaw, IN). Healos II BGS is comprised of Type I bovine collagen and hydroxyapatite mineral (DePuy Spine, Raynham, MA). Eighty male rabbits were randomly assigned to each of 4 groups defined by the implant material to be received: CopiOs Sponge soaked with autologous bone marrow aspirate (BMA), Healos II BGS soaked with autologous BMA, autogenous bone implant (ABI), or empty defect. A 1.5 cm mid-diaphyseal defect was created in the right radius of each animal and the excised segment was homogenized for autogenous bone implant according to group assignment. CopiOs Sponge and Healos II BGS were cut to fit the prepared defect and combined with BMA harvested from femur at the time of surgery. Radiographs were taken at the time of surgery and 7, 11 and 23 weeks to assess healing. Animals were euthanized at 12 or 4 weeks and both the right and left radius were harvested for gross osteotomy site scoring, histology and mechanical testing. All studies were approved by the Institutional Animal Care and Use Committee at MPI Research, Inc. (Mattawan, Michigan).

RESULTS
Radiographic evaluation at 11 weeks post-implantation revealed that the CopiOs Sponge filled defects had completely healed and remodeled, as evidenced by a dense cortical wall (exterior intensification) and enhanced translucency within the marrow cavity that appeared equivalent to autograft (Fig. 2). In contrast, the radiographs of the defects filled with Healos II BGS appeared evenly diffuse, with no evidence of cortical rim formation at 11 weeks. All groups, except empty defects, were completely healed at 23 weeks by radiographic assessments.

Gross morphological examination was used to score post-explantation osteotomy sites using the following 3 point system: 3 = Complete defect healing; 2 = Defect bridging with moderate instability; 1 = Slight bridging, weak stability; and 0 = Complete nonunion. Twelve week measurements revealed no significant difference between the CopiOs Sponge and either the ABI or Healos II BGS groups. CopiOs Sponge and ABI both had equal median scores of 3, while Healos II BGS had a median score of 2; all of the empty defects were scored 0. The mean morphological scores were: ABI 2.8 ± 0.63; CopiOs Sponge 2.4 ± 0.17; Healos II BGS 2.0 ± 1.1. At 24 weeks all of the implant defects had healed compared to empty defects, which had not. The histomorphometry evaluation confirmed the above qualitative data and showed at 12 weeks that ABI and CopiOs Sponge had the greatest amount of new bone formed/area, 51.5±11.5% and 51±15.8%, respectively. Empty defects contained the least amount of new bone formed (26±14.6%), while the Healos II BGS group was 37.8±17.7%. The amount of bone remained unchanged at the 24 week time point in all groups.

DISCUSSION:
This study was conducted to evaluate the efficacy of CopiOs Sponge Bone Void Filler as a treatment for bone defects in rabbits compared to the gold standard, ABI, and the predicate device, Healos II BGS. CopiOs Sponge performed equivalent to ABI in promoting bone healing in this model. In addition, the evidence of healing at 12 weeks demonstrated CopiOs Sponge was significantly better than Healos II BGS at this early time point, and indicates CopiOs Sponge accelerates the healing process compared to the predicate device.

The safety and efficacy of dibasic calcium phosphate in promoting bone formation is well documented in various animal models [2, 3]. The unique chemical nature of dibasic calcium phosphate in CopiOs Sponge Bone Void Filler helps to create a moderately acidic microenvironment with abundant soluble mineral ions [1]. The microenvironment produced by CopiOs Sponge preserves the solubility and bioavailability of osteoinductive growth factors and may prove beneficial for bone healing.

REFERENCES:

Healos is a registered trademark of DePuy Spine, Inc. CopiOs is a registered trademark of Zimmer Spine, Inc.