INTRODUCTION:
A variety of synthetic ceramic bone void fillers are available with the most common based on calcium sulfate or calcium phosphate. Many of the calcium phosphate materials do not resorb or incorporate into the host skeleton quickly enough to be clinically satisfying. Conversely, many of the calcium sulfate based products resorb too quickly to be adequately replaced by new host bone. The objective of this research was to evaluate a novel injectable bone substitute (Cerament™) that contains: 40 wt % hydroxyapatite (HA) granules, and 59.6 wt % calcium sulfate hemihydrate plus 0.4 wt % calcium sulfate dihydrate cements that are mixed with a solution of iohexal (USP 30) to create an injectable material with radiocontrast properties. The hypotheses were that Cerament-filled defects would heal more quickly and completely than empty defects, producing more new bone formation.

METHODS:
Under an institutional animal care and use committee approved protocol, twelve six-month-old female New Zealand white rabbits had bilateral distal femoral cancellous defects created and they were either left empty or filled with Cerament randomly assigned to the right or left leg. A drill-hole (8.0 mm deep, 5.0 mm dia) was placed in each lateral femoral condyle from a lateral approach. The cement was delivered through a syringe, filling the defect in a retrograde fashion. Bone wax was used to seal the defects. Rabbits were sacrificed after three (n=6) and twelve weeks (n=6) with calcein injections given three days prior to sacrifice. The six rabbits in the twelve week group had in vivo µCT scans (voxel resolution of 28 µm) of each femur at three, seven, and twelve weeks to observe volumetric defect occupancy with mineralized material.

Histological analyses were performed on decalcified samples using hematoxylin and eosin (H and E) staining to quantify the bone tissue in the defect. Cellular material was also observed to qualitatively determine the tissue response using a 0 to 3 grading scale (0=no activity, 3=extensive cellular activity with new bone extending to the defect center). Undecalcified samples were observed under fluorescence microscopy to demonstrate new bone formation activity. All measures were analyzed with two-way ANOVA (time, group) followed by post-hoc t-tests.

RESULTS:
The µCT scanning (Figure 1) showed minimal filling of the Empty defects over twelve weeks with only periosteal bridging/healing. The Cerament filled defects remained filled and demonstrated consolidation over time.

DISCUSSION:
The empty defect results in this model were as expected, showing only periosteal bridging of the drill-hole opening. The interior of the cylinders showed marrow-like appearance, but no bone formation. The presence of an osteoconductive scaffold within the Cerament filled defects greatly improved the ingrowth of new bone in this cancellous defect model. Unlike with pure HA cements, there was significantly greater new bone formation with Cerament compared to Empty defects. The dissolution of the calcium sulfate phase of Cerament is relatively rapid, but the remaining osteoconductive HA becomes surrounded by infiltrating precursor cells and new bone.

ACKNOWLEDGMENT:
This work was supported by BoneSupport AB, Lund, Sweden.

REFERENCES:
1) Bajammal et al., JBJS-A, 2008;90:1186-1196.