INTRODUCTION: Calcium sulfate pellets have been used successfully as a synthetic bone graft for treatment of contained bone defects at sites without substantial compressive loads [1]. There are many bone defects, notably subcondral and vertebral, where calcium sulfate with increased compressive strength would be beneficial. A new, modified calcium sulfate with a different crystalline structure and a compressive strength similar to many calcium phosphate materials but with a more rapid resorption profile has been developed. We hypothesized that new bone formation in defects treated with pellets made of the modified calcium sulfate would be substantially equivalent to treatment using the conventional pellets. A canine bilateral defect model was employed at 6, 13 and 26 weeks to compare the amount and compressive strength of newly formed bone in defects treated with the two pellets types.

MATERIALS AND METHODS: Under an IACUC-approved protocol, 13 skeletally mature, male hound-type dogs weighing 26–33 kg. had a cylindrical, critical, axial medullary defect (13mm diameter X 50mm) created bilaterally in the proximal humerus. In each dog, one humeral defect was treated with 50 (4.8mm X 3.3mm circular) pellets of the test material (modified alpha hemihydrate calcium sulfate, MIIG-X3tm, Wright Medical Technology). The contralateral humerus received 50 similar pellets of the control material (conventional medical grade calcium sulfate, Osteoset®, Wright Medical). The animals were observed postoperatively for 6 weeks (N=3), 13 weeks (N=5) or 26 weeks (N=5). Radiographs were obtained immediately postoperative and at 2, 6, 13 and 26 weeks and graded for changes in pellet density and new bone in the defects.

The specimen humeri were cut using a positioning jig to produce comparable transverse slices of the right and left bone pairs. Proximal, middle and distal undecalcified, plastic-embedded sections were analyzed for the area fraction of new bone and residual material in the defects by computer analysis of backscattered electron SEM images. Following this analysis, the sections were further ground and stained with basic fuchsin and toluidine blue for characterization by light microscopy of the nature of new bone and residual implant material in the defects.

Biomechanical tests were conducted using an 8mm dia. X 16mm test cylinder cored in the long axis of the defect between the mid and distal sections [2]. Unconfined, uniaxial compression tests were performed at a compressive strain rate of 0.5 mm/min. Data for the axial deformation and the applied load was acquired at 10 Hz. The compressive strength and 1% secant modulus were calculated from the stress-strain curve.

Mechanical tests were also conducted on 8 modified formulation and 8 conventional calcium sulfate pellets to characterize their initial compressive strengths.

The histomorphometric and biomechanical data from the 13 and 26-week groups were analyzed using the Friedman and Mann-Whitney tests. A p < 0.05 was considered significant.

RESULTS: The ultimate compressive strengths of the unimplanted pellets were 87.79 ±7.15 MPa for the MIIG-X3 modified formulation pellets and 34.94 ±2.04 MPa for the Osteoset conventional calcium sulfate pellets (p<0.001).

In the in vivo study, there were no intraoperative or postoperative complications. All of the dogs returned to weight bearing within 2 days of the surgical procedure and completed the study period without any clinical incident related to the treatments.

The clinical radiographs revealed substantial resorption of both types of pellets beginning at 2 weeks and generally continuing by 6 weeks. Circular densities associated with sites of pellet resorption remained more prominent in defects treated with the MIIG-X3 pellets compared to the Osteoset pellets even after 13 or 26 weeks. With both types of pellets, the defects resumed a density comparable to the surrounding bone in the 13 and 26-week radiographs.

The mean area fraction of new bone in the defects was similar in the MIIG-X3-treated defects compared to the Osteoset-treated defects at 6, 13 and 26 weeks (Figure). At 6 weeks, the mean area fraction was 15.0% ±3.0% for the MIIG-X3-treated defects and 13.3% ±2.2% for the Osteoset-treated defects. At 13 weeks, the mean area fraction of bone was significantly greater in the MIIG-X3-treated defects (10.0% ±3.1%) compared to the Osteoset-treated defects (7.7% ±2.3%) (p=0.025). After 26 weeks, the difference in the area fraction of new bone, comparing the MIIG-X3-treated defects (11.1% ±1.9%) and the Osteoset-treated defects (10.1% ±1.8%), was not statistically significant (p=.180).

The area fraction of residual material was overall very low for both types of pellets and decreased with time (p<0.047) with the MIIG-X3 pellets resorbing more slowly. At 6 weeks, the area fraction of residual material was 4.3 % ±1.8% in MIIG-X3-treated defects and 3.3% ±0.3% in defects treated with Osteoset pellets. At both 13 and 26 weeks, the amount of residual material was significantly greater in the MIIG-X3-treated defects (2.1% ±1.5% at 13 weeks and 0.4% ±0.3% at 26 weeks) compared to Osteoset-treated defects (0.4% ±0.3% at 13 weeks and 0.2% ±0.1% at 26 weeks) (p=0.025).

The stained histological sections showed a similar pattern of new bone formation and pellet resorption for the two treatments; but at each time point, there was more residual material in the MIIG-X3-treated defects than in the Osteoset-treated defects. In all of the animals, the pellets resorbed leaving small sites of residual material incorporated into new bone. Both the MIIG-X3 and Osteoset-treated defects were restored with bone trabeculae, marrow, and only focal areas of fibrous tissue.

The mean compressive strength of the 26-week cored samples was not statistically different comparing the MIIG-X3-treated (0.62 ±0.44 MPa) and Osteoset-treated (0.61 ±0.21 MPa) defects (p=.100). The stress-strain curves for the cored samples showed a typical pattern of brittle fracture of trabecular bone under compression in 4 of 5 dogs at 26-weeks. The stress-strain curves did not consistently demonstrate a definable yield point for several of the cores of Osteoset-treated defects at 13 weeks. The mean compressive strength for MIIG-X3-treated defects at 13 weeks was 0.57 ±0.27 MPa.

The modulus of the cored cylinders was not significantly different between the MIIG-X3-treated and Osteoset-treated defects at either 13 or 26 weeks (p>.180). For both treatments, the bone samples became stiffer with time, but the differences were not significant (p>0.655).

<table>
<thead>
<tr>
<th>Time (wks)</th>
<th>MIIG-X3-treated (MPa)</th>
<th>Osteoset-treated (MPa)</th>
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<tbody>
<tr>
<td>13</td>
<td>9.6 ±9.1</td>
<td>7.2 ±10.5</td>
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<tr>
<td>26</td>
<td>24.9 ±31.7</td>
<td>33.1 ±27.1</td>
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DISCUSSION: The altered crystalline structure and increased initial compressive strength of the modified calcium sulfate pellets allows their use in a broader range of defects. In spite of these modifications, there was no difference in the area fraction or compressive strength of new bone formation after 26 weeks in comparison with conventional calcium sulfate pellets. Although restoration of the defects with bone and marrow was similar and the majority of the calcium sulfate had been resorbed with both pellet types, the modified calcium sulfate pellets showed slightly slower resorption, reflecting the relatively higher density of these pellets. The findings of this study indicate that the modified calcium sulfate pellets were as effective as conventional calcium sulfate pellets in restoration of model bone defects.


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