COMPARATIVE EVALUATION OF THE OSTEOINDUCTIVE POTENTIAL OF COMMERCIALLY AVAILABLE DEMINERALIZED BONE MATRICES IN AN ATHYMIC RAT POSTEROLATERAL SPINAL FUSION MODEL

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INTRODUCTION
The use of demineralized bone matrix (DBM) materials for bone grafting procedures in orthopaedic surgery represents an alternative or supplement to the use of harvested autologous bone. Demineralized bone matrices are prepared by treating allograft bone in an acid solution to remove the majority of mineral content. Harsh demineralization processes can alter the naturally occurring growth factors within DBM, resulting in lower overall concentrations of active growth factors compared to those found in native bone. Thus, it is important that the demineralization process be as controlled as possible to reduce damage to the proteins and retain the overall osteoinductivity of the resulting DBM. Because of differences in processing methods and carriers, previous studies have demonstrated that commercially available DBM products have varying osteoinductive capacities.

Recently, there has been significant interest in the use of recombinant human bone morphogenic proteins (rhBMPs). Because rhBMPs are isolated proteins, the dosage required to fuse a single spine level in humans is in extreme excess and disproportion to the BMP concentrations found in native bone. In contrast, DBM grafts that have been demineralized to an optimal residual mineral level offer all BMPs at their low native levels. This is important because each individual BMP in the TGF-β family of growth factors plays a role in the multi-step sequence of bone formation. Though each DBM will differ based on its processing methods, work is currently being done to characterize the levels of BMPs present in DBM.

The athymic rat spinal fusion model has been developed to evaluate bone grafts in an immunocompromised animal, and in this case minimize the potential of an inflammatory response to xenogenic tissue grafts. Several authors have used this model to study the efficacy of human DBM products. In this study, the efficacy of six different commercially available DBM materials were evaluated for their potential to induce spinal fusion in an athymic rat posterolateral model.

MATERIALS AND METHODS
All animal procedures and surgeries were performed under an approved IACUC protocol at outside laboratory, Toxikon (Bedford, MA). Sixty 8-9 week old athymic male Sprague Dawley rats underwent a single-level non-instrumented PLF. Twelve animals were implanted with Grafton® putty (Osteotech), 12 with Regenaform® RT (Regeneration Technologies, Inc), 12 with Optium® putty (LifeNet), 6 with DBX® putty (Musculoskeletal Transplant Foundation), 6 with Allomatrix® (Isotis OrthoBiologics), and 6 with Allomatrix® Injectable Putty (Wright Medical). Six animals served as controls and underwent decortication only. Each animal was implanted bilaterally with the same test material.

The surgical levels were identified by referencing from the sacrum with manual palpation. A dorsal midline incision was made in the lumbar region of the skin, and the transverse processes of L4 and L5 were identified and exposed through two paramedian fascial incisions. The transverse processes of L4 and L5 were decorticated bilaterally with a high-speed burr and 0.2cc of graft material was implanted on each side (0.4 cc total). Following implantation, the sites were closed in 2 layers, fascia with 3-0 Vicryl and skin with skin staples. At 8 weeks post-surgery, all animals were sacrificed.

Manual palpation of the spine segments was performed by three independent graders who were blinded to treatment group. The explanted spine segments were fixed in 10% neutral-buffered formalin and contact radiographs were taken. Explanted spine segments were evaluated for radiographic evidence of fusion by two independent observers who were blinded to the treatment group. A 4-point scoring system was used (0: no bone formation; 1: bone formation but not fused; 2: unilaterally fused; 3: bilaterally fused). If different between observers, the lowest of two scores was used. The scoring results were assessed with a nonparametric Kruskal-Wallis test. In addition, volumetric small animal computed tomography (μCT) and histology analysis were performed. These analyses are ongoing and results are to follow.

RESULTS
All animals survived the procedures well and completed the 8-week postoperative period. There were no fusions present in the empty group that underwent decortication alone. Figure 1 illustrates average radiographic fusion scores by group:

Figure 1: Radiographic Fusion Scores

By radiographic analysis (Figure 2), Optium demonstrated the highest total fusion rate (91.6% or 11/12) as well as the highest bilateral fusion rate (7/12) among all groups. This difference was significant with respect to Regenaform, Allomatrix, and the empty control groups (p<0.05). Grafton and DBX were the only other materials that had bilateral evidence of fusion (2/6 and 1/6 respectively). DBX and Accell DBM 100 had equal total fusion rates (5/6), and demonstrated a higher bone induction potential than Regenaform RT (4/12) and Allomatrix (0/6).

Figure 2: Representative 8-week Radiographs

DISCUSSION
Due to varying demineralization processes and carriers used, commercially available DBM products differ in osteoinductive capability. The results of this study indicate the importance of choosing a DBM that has been process controlled to retain all of the natural BMPs that carry bone inducing potential.

REFERENCES

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