Histological Evaluation of a Calcium Phosphate / DBM Composite Cement in a Sheep Anterior Lumbar Interbody Fusion Model

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Statement of Purpose:

Autograft substitute materials are playing an increasing role in spinal fusion procedures, eliminating complications associated with graft harvesting, and in some indications, are showing improved performance over autograft. Bone morphogenic proteins (BMPs) demonstrate equivalent performance in specific indications but are expensive and are not indicated for all fusion methods. Pure synthetics, such as calcium phosphates (CaP), exhibit superior osteoconductivity but do not have the osteoinductivity necessary for spinal fusions (Boyan BD. Bone Graft Substitutes. 2003; 231-259). Demineralized bone matrix products (DBMs) have been used extensively as autograft extenders, and have demonstrated osteoinductive potential, but concerns over the reliability of these products, such as donor to donor variability, and poor handling properties have limited their use (Poynton AR. Bone Graft Substitutes. 2003; 13-29). Combining CaP with DBM may yield graft substitutes efficacious for spinal fusion.

The purpose of this study is to demonstrate histologically, the ability of CaP / DBM cement to achieve complete arthrodesis between vertebral bodies in a sheep interbody fusion model.

Methods:

The CaP / DBM material was prepared by mixing a high strength CaP cement (ETEX Corporation, Cambridge, MA) with DBM prepared from sheep cadaver bone. The CaP was prepared by high energy milling of an amorphous calcium phosphate with a dicalcium phosphate dihydrate (Tofighi A. US Patent App. 0120351 A1/2003). The DBM was prepared by grinding and sieving cortical bone from sheep long bones and sieving them to 53-125 microns. The bone powder was then exposed to multiple washes of 0.5 normal HCl to remove the mineral component, followed by multiple washes of deionized water and a dilute sodium phosphate buffer. The DBM was then lyophilized and stored in a desiccator until use. The CaP and DBM powders were mixed in a 70:30 (CaP:DBM) ratio and then the combination of CaP and DBM was mixed with saline to achieve a moldable, self-setting cement.

Three skeletally mature female sheep underwent a two-level, instrumented, lumbar interbody fusion procedure at levels L/4/L5 and L5/L6. A single cylindrical, fenestrated titanium interbody device (INTERFIX^{TM}, MSD) was used to maintain disc height and contain the graft material. One set of pedicle screws and rod was used for fixation. The interbody devices were packed with either the CaP / DBM composite (n=3) or the DBM alone (n=3). All sheep were sacrificed after 6 months. Undecalcified histological slides were prepared and evaluated for: 1) the efficacy of the graft to induce *de novo* bone within the titanium cage device, 2) the efficacy of the titanium cage device filled with graft to induce histological fusion, and 3) the cytological response to the graft within the titanium device. These results were compared to a previous study (Sandhu HS. Spine. 2002; 27(6): 567-575) performed in an identical model by the same surgeons and evaluator, in which the device was filled with either a rhBMP-2–collagen (n=6) or with an autogenous iliac crest bone graft (n= 6).

Results/Discussion:

The composite material, as well as the DBM alone, was able to generate *de novo* bone within the cages. All levels treated with the titanium cage and composite material, as well as the DBM alone, achieved histological fusion (continuous superior to inferior bony bridging) (Fig.1). Very slight to no inflammation was observed in both the composite material and the DBM alone. In the previous study autograph exhibited a histological fusion rate of only 37%, while rhBMP-2 exhibited a histological fusion rate of 100%.

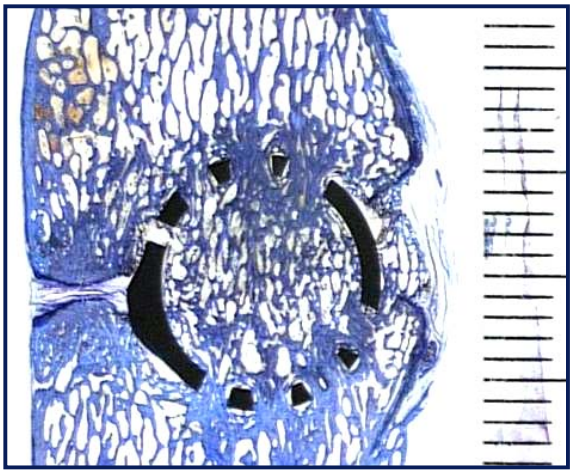

Figure 1: Representative histological sections of fusion area from animals receiving CaP/DBM cement

Conclusions:

In a sheep lumbar interbody fusion model, CaP / DBM achieved fusion rates of 100%, better than those reported for autograft and comparable to those reported for rhBMP-2. In conclusion, this composite material, which possesses handling properties which are superior to DBM alone, shows promise as an autograft substitute in interbody fusion indications.