Successful posterolateral fusion using a collagen-mineral composite material in rabbits

Introduction:
Clinical studies comparing different materials and their in vivo responses are lacking. Preclinical data, however, based on a standard and well reported model can provide a basis for comparison and understanding. Posterolateral fusion in the adult rabbit [1] is one such model that provides insight into the in vivo performance.

The use of osteoinductive molecules (e.g. bone morphogenetic proteins) or tissue (autologous bone graft, or demineralized bone matrix) can often improve the performance of osteoconductive ceramic scaffolds. The addition of a collagen matrix to ceramic materials represents a simple strategy to couple the osteoinductive response of the two phases (mineral and organic) as well as the porosity and interconnectivity within the materials to support and encourage cell proliferation and differentiation. This study evaluated the performance of a calcium phosphate-collagen composite bone graft material (FormaGraft, NuVasive, Inc. San Diego, CA) in the New Zealand white rabbit posterolateral spinal fusion model [1]. The effect of adding cellular components from either bone marrow aspirate or iliac crest autograft was investigated and compared to autograft alone.

Materials and Methods:
A single-level posterolateral lumbar fusion was performed at L5-L6 in 69 adult New Zealand white rabbits, as developed by Dr. Boden and co-workers, [1] following ethical approval. A sample size of n=6 was used at 6 weeks considering only radiographic and histological endpoints while this was increased to n=12 at 12 weeks where mechanical testing was also performed. Three test groups were examined; FormaGraft alone, FormaGraft plus BMA, and FormaGraft plus autograft and BMA were compared to autograft (1.5 cc/side) (positive control) and empty decorticated (negative control). In the FormaGraft and FormaGraft plus bone marrow aspirate (BMA) groups, the two 10x20mm strips were laid on top of each other; for the FormaGraft plus autograft group one 10x20mm strip was used with 0.75cc of autograft laid on top. A total of 3cc of bone marrow was aspirated from the proximal tibia through a puncture in the anteromedial cortex. The FormaGraft strips were soaked with BMA in a 1:1 mix, based on volume, and allowed to soak for 5 minutes prior to implantation between the decorticated transverse processes.

Fusion rigidity was manually assessed. AP Faxitron radiographs and axial computed tomography slices taken for all animals. DICOM data was imported and analyzed with MIMICS software (Version 12, Materialise, Belgium). Three-dimensional models were created to visualize the fusion masses between the transverse processes as well as individual slices and sagittal planes. Tensile mechanical testing (12 weeks only) was performed using an MTS Bionix testing machine. Sagittal and coronal plane histology was evaluated in a blinded fashion using H&E, Tetrachrome, and Pentachrome stains. Assessment included overall bony response on and between the transverse processes. New bone formation within the porous domains of the mineral was examined. Mechanical data was analyzed using ANOVA followed by Games Howell post hoc test when appropriate (SPSS 15, SPSS Inc., Chicago IL).

Results:
No significant inflammatory reaction to the implanted material was noted at harvest. Manual assessment of the fused level revealed stable constructs bilaterally in nearly all animals with 2 sides out of 24 (8.3%) in each of the FormaGraft plus BMA group and FormaGraft plus autograft and BMA group found to be unstable at 12 weeks upon manual assessment. Autograft at 12 weeks was found to be unstable in 2 out of 12 sites (16.7%). Radiographic evidence of new bone formation at the margins of the material was present at 6 weeks and 12 weeks in all animals with FormaGraft as well as autograft alone with no differences between groups observed. Softening of the edges of the FormaGraft was observed from 0 to 6 weeks and progressed with time at 12 weeks. Radiographic fusion rate of the autograft control was 50% (3/6 sites) at 6 weeks and increased to 83% (10/12 sites) at 12 weeks. The empty decorticated controls did not fuse.

Discussion:
No statistically demonstrable benefits or adverse effects of the addition of BMA were found in the current study based on macroscopic, radiology or mechanical data. This may reflect, in part, the good to excellent results of the collagen HA/TCP composite material alone in a well healing bony bed. However, qualitative differences present at the histological level were detected with the addition of BMA with respect to new bone formation, although these differences did not manifest themselves in the macroscopic, radiographic or mechanical endpoints. This highlights the sensitivity of different endpoints where differences need to be large for radiographs to demonstrate effects or sample size increased to large numbers to detect smaller differences between treatment groups. FormaGraft is a safe and efficacious device when used alone, or preferentially with BMA or autograft, in the New Zealand white rabbit, which may be a good indication of safety and efficacy in the human clinical environment.

References: