EVALUATION OF RHBMP-2 WITH VARIOUS CERAMIC/COLLAGEN SPONGE CARRIERS IN POSTEROLATERAL SPINE FUSION IN THE RABBIT AND NON-HUMAN PRIMATE

INTRODUCTION: Autogenous iliac crest bone graft remains the current gold standard graft material for spine fusion. However, fusion success rates are less than 100%, supply of autograft is minimal, and the morbidity of graft harvest is significant with up to 20% of patients having complications. Recombinant bone morphogenetic protein –2 (rhBMP-2) when delivered in a resorbable collagen sponge was successful in rabbit and canine models of spine fusion. Unfortunately, the plain collagen sponge was too compressible for large animals in a posterolateral spine fusion model. We subsequently demonstrated good bone induction using biphasic ceramic phosphate (BCP) granules [60% hydroxyapatite (HA)/40% tricalcium phosphate (TCP)] as the carrier matrix for rhBMP-2 in rhesus monkeys. A limitation of 60:40 BCP was its slow resorption time due to the high HA content, making radiographic detection of new bone formation very difficult. Therefore, the purpose of this study was to test two new faster resorbing compression resistant matrices for spine fusion in the rabbit and non-human primate.

METHODS: Adult NZW rabbits (n=14) underwent posterolateral spine arthrodesis at L5-L6. A Wiltse paraspinal muscle-splitting approach was used and the transverse processes were decorticated with an electric bur. Bone graft implants consisted of 5:95 BCP (5% HA/95% TCP) impregnated type I collagen sponges (15X35X3mm-2 per side) loaded with 0.86 mg rhBMP-2.

Adult rhesus monkeys (n=6) underwent posterolateral arthrodesis at L4-L5 with ceramic/collagen sponge carrier loaded with 9 mg rhBMP-2 per side. Two monkeys received 15:85 BCP (15% HA/85% TCP) with 2 pieces sponge/side; two received 5:95 BCP (5% HA/95% TCP) with 2 pieces/side and two received 5:95 BCP with 4 pieces/side.

The rabbits were euthanized after 5 weeks and the monkeys after 24 weeks; the spines were evaluated by manual palpation, radiographs, tensile mechanical testing (rabbits only), and non-decalcified histology.

RESULTS: rhBMP-2 delivered in the 5:95 BCP/collagen sponge achieved spine fusion in 100% of rabbits and had improved handling properties compared to the BCP granules. The granules handled similar to wet sand whereas the BCP/collagen sponge was a single unit easily lifted and deposited into the surgical site.

Biomechanical testing results (strength and stiffness relative to the adjacent unfused control spinal level) with 5:95 BCP/collagen carrier were comparable to those obtained with the 60:40 BCP granules and superior to those of autogenous bone graft (p < .05). rhBMP-2 delivered in the 15:85 or the 5:95 BCP/collagen sponge carrier (2 pieces/side) induced spine fusion in non-human primates with normal bone histology. The monkeys with the 9 mg BMP-2 distributed over 4 sponges per side, instead of two sponges, had half the effective rhBMP-2 concentration per sponge and yielded inferior results with much less bone formation.

DISCUSSION: The translation of successful preclinical studies with BMPs to clinical trials has been slower than desired. Two important variables include growth factor dose and the delivery matrix or carrier for the protein. In fact, the delivery matrix can be as important as the choice of osteoinductive growth factor for bone induction. While the BCP granules were a biologically suitable carrier and successfully induced bone and spine fusions, the inability to radiographically detect new bone formation was a relative drawback. In contrast, the new compression resistant BCP/collagen sponge matrices were biologically compatible with rhBMP-2 bone formation and had improved handling and radiographic resorption properties that permit easy radiographic visualization. These data suggest that clinical trials with this carrier matrix are warranted.