Biomimetic Calcium Phosphate Coatings as rhBMP-2 Delivery Systems in Posterolateral Lumbar Fusion
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INTRODUCTION:
The osteoinductive characteristics of BMP-2 are well-characterized and are capable of inducing bone formation ectopically. Currently, BMP-2 is delivered by soaking a collagen sponge in an aqueous solution of the protein immediately prior to implantation. During the soaking process, BMP-2 is physically adsorbed to the collagen. Physical adsorption of BMP results in poor binding, which leads to rapid diffusion away from the carrier upon implantation. Rapid diffusion yields an initial burst of BMP-2 at the fusion site, which tapers off significantly within the first 12 hours of implantation.

Recently, a method by which the BMPs can be delivered in a sustained, localized fashion was developed. The method involves the incorporation of BMPs within the physical structure of a calcium phosphate (CaP) coating, which can be biomimetically deposited on implant surfaces. Since the BMPs are incorporated within the coating, in vivo delivery will be more localized and sustained, as compared to the physical adsorption technique.

The goals of this study were to (1) determine the efficacy of biomimetic CaP films as BMP delivery systems in spine fusion and (2) compare BMP delivery via hybrid CaP+rhBMP-2 coatings to the current best practice of physical adsorption.

METHODS:
This study consisted of four treatment groups, as described in Table 1. Calcium phosphate (CaP) films were biomimetically deposited on 2.5cc collagen strips (Healos, Depuy Spine). The strips were immersed in a supersaturated calcium phosphate solution (SCPS) for 72 hours, with daily solution refreshments. Hybrid rhBMP-2+CaP coatings were deposited by immersing the collagen strips in an SCPS, which also contained a 1.2mg/mL aqueous solution of rhBMP-2. Physical adsorption of BMP-2 was accomplished by wetting the CaP-coated sponges with an aqueous solution immediately prior to implantation.

Eighteen (18) New Zealand White Rabbits underwent a non-instrumented spinal fusion procedure using a posterolateral approach to the lumbar spine in accordance with IACUC standards. Transverse processes of L5 and L6 were decorticated to yield a bleeding bone surface. Graft material was placed on the decorticated transverse processes. Rabbits were followed radiographically for 6 weeks. At 6 weeks, the animals were sacrificed and the lumbar spines were harvested. Degree of fusion was assessed using manual palpation, radiographs and CT scans.

RESULTS:
Deposition of CaP coatings on the Healos material resulted in distinct enhancements of nanoscale surface topography, as shown in Figure 1. Animals tolerated the procedure well with only one loss to anesthesia complications and no losses to infection. Serial fluoroscopic follow-up of the rabbits revealed vigorous bone formation as early as 2 weeks, in treatment groups using rhBMP-2. Radiographic fusion was obtained at 4 weeks in Group 3 (incorporated BMP-2) animals and at 5 weeks in Group 2 (adsorbed BMP-2) and Group 4 (incorporated and adsorbed BMP-2). At all time points (weeks 2-6), animals in Group 3 received the highest score of radiographic fusion.

Computed tomography and subsequent 3D reconstruction of harvested spines yielded differences in the fusion masses between all treatment groups, as shown in Figure 2. The intended fusion site in Group 1 animals was characterized by thickening of the transverse processes. Fusion masses in Group 2 often extended beyond one level, with some evidence of resorption of the mass. Group 3 fusion masses were confined to a single level, with one animal showing evidence of mass resorption and extension beyond one level. Group 4 fusion masses often extended beyond a single level, and showed some evidence of resorption.

DISCUSSION:
This study examined the efficacy of biomimetic CaP films to act as rhBMP-2 delivery systems in posterolateral fusion of the lumbar spine. Preliminary biochemical assays suggest that the amount of rhBMP-2 incorporated into the CaP coatings is 10-20% of the amount that is physically adsorbed to collagen and/or CaP. Despite the disparity in the amount of rhBMP-2, fluoroscopic, CT and manual palpation analyses indicate comparable levels of fusion amongst Groups 2, 3 and 4. This result is in line with a previous report that combining a collagen sponge with BMP-2-loaded bone chips, or TCP granules enhances fusion, which allowed the dosage to be halved.1

Isolated resorption of the fusion mass was observed in all animals in Group 2 and 3 animals in Group 4. This resorption is likely mediated by a previously described, dose-dependent response of osteoclast activity to rhBMP-2.2

Future studies will be undertaken to examine the threshold dosage of BMP-2, which can be incorporated into the CaP films while still inducing fusion.

REFERENCES:

ACKNOWLEDGEMENTS:
The authors thank Depuy Spine for providing the Healos material used in this study. We also acknowledge financial support from the William Beaumont Hospital Research Institute.