Surface Adsorption of rhBMP-2 to Hydroxyapatite Reinforced PEEK Scaffolds

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Statement of Purpose: Polyetheretherketone (PEEK) interbody spinal fusion cages are augmented with autograft, or recombinant human bone morphogenetic protein-2 (rhBMP-2) absorbed in a collagen sponge, in order to promote fusion [1]. PEEK cages with BMP-2 have excellent fusion rates [1], but leakage of BMP-2 from the sponge has been reported to cause inflammation, hematoma, and bony cysts [2]. Therefore, a clinical need exists for improved control in the delivery of BMP-2. BMP-2 is known to exhibit an affinity for hydroxyapatite (HA) and can thus be adsorbed onto HA surfaces [3]. In fact, the bioactivity of HA *in vivo* is due to the adsorption of endogenous growth factors [4]. HA-reinforced PEEK scaffolds and implants were recently prepared such that HA crystals were exposed on the scaffold strut surfaces (Fig. 1) [5-7]. Therefore, the objective of this study was to investigate the surface adsorption of BMP-2 to PEEK and HA-reinforced PEEK scaffolds.

Methods: HA-reinforced PEEK scaffolds were prepared by previously established methods [5-7]. Scaffolds 4 mm in diameter and height were prepared with 75% porosity and either 0 or 40 vol% HA whisker reinforcements (n = 21/group). Scaffolds were sterilized in ethanol, rinsed and wetted with PBS under centrifugation. Scaffolds were loaded with 10 µL of 100 µg/mL rhBMP-2 (Peprotech) solution and then incubated in 100 µL sterile PBS at 37°C for 24 h to allow protein binding to scaffolds. Scaffolds were removed, placed in 1 mL PBS (pH 7.52) containing 0.1% bovine serum albumin to ensure protein stability, and incubated at 37°C. BMP-2 release was measured after 1, 2, 3, 5, 7, 10, and 14 days by removing and replacing the solution. Solution samples containing eluted protein were frozen at -80°C. After collecting all samples, the BMP-2 concentration in each sample was measured via ELISA (Peprotech).

Results: HA-reinforced PEEK scaffolds were able to adsorb and deliver a five-fold greater dose of BMP-2 compared to otherwise identical PEEK scaffolds (Fig. 1). HA-PEEK scaffolds were able to be loaded with nearly 100% of a clinically-relevant dose of BMP-2, which was subsequently was released from HA-PEEK scaffolds over 5-7 days *in vitro* (Fig. 1). In contrast, PEEK scaffolds were only able to be loaded with ~20% of the BMP-2 dose which was also released over 5-7 days *in vitro* (Fig. 1). The ability to load and deliver a significantly greater dose of BMP-2 in HA-PEEK compared to PEEK scaffolds suggested specific binding interactions to HA. Thus, loading and delivery of a clinically-relevant dose of BMP-2 was facilitated by surface adsorption to HA crystals and the high scaffold surface area. In contrast, the BMP-2 that was able to be loaded in PEEK scaffolds was mostly likely only trapped within fluid-filled pore spaces and/or non-specifically adsorbed to PEEK surfaces.

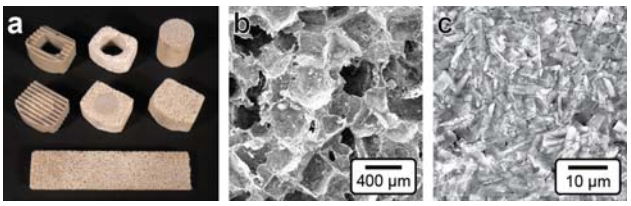

Figure 1. (a) HA-reinforced PEEK scaffold and implants prepared with 75% porosity and 40 vol% HA whisker reinforcement [8]. SEM micrographs show (b) interconnected pores and (c) HA whiskers exposed on scaffold strut surfaces.

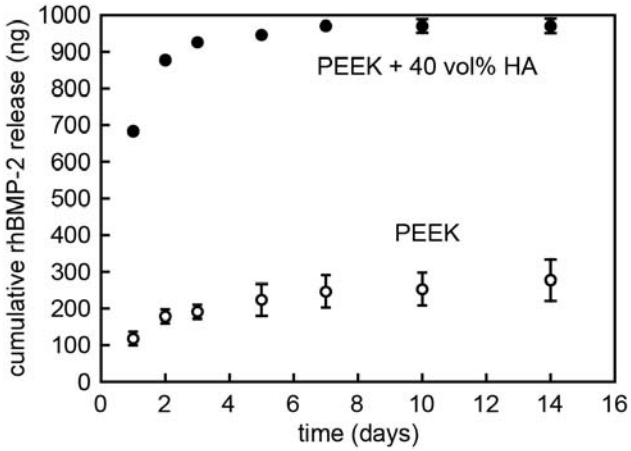

Figure 2. Cumulative release of rhBMP-2 from PEEK scaffolds containing 0 and 40 vol% HA after loading scaffolds with a solution containing a 1000 ng dose. Error bars show one standard deviation.

Conclusions: HA reinforced PEEK scaffolds were able to load and deliver a clinically-relevant dose of rhBMP-2 through surface adsorption to HA crystals exposed on high surface area scaffolds. Moreover, HA-PEEK scaffolds were able to adsorb and deliver a five-fold greater dose of BMP-2 compared to otherwise identical PEEK scaffolds. Therefore, the results of this study suggest that HA reinforced PEEK scaffolds may be able to serve as a delivery vehicle for BMP-2.

References:

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