

## Release Profile Characterization of a Biphasic Implant Porous Metal Enhanced Coating

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**Statement of Purpose:** A novel titanium alloy porous material manufactured via a Direct Metal Laser Sintering (DMLS) process has been developed [1]. Because of this manufacturing process versatility, an optimized configuration ideal for biologic fixation can be fabricated [Figure 1]. To further facilitate bone apposition and the immediate surrounding host bone, an enhanced coating incorporating the bisphosphonate alendronate is applied to the porous metal. The porous metal titanium surface is partially hydroxyapatite (HA) coated, such that the outermost portion of the porous surface is coated with a thin layer of HA and the interior portion is bare (non-HA coated) metal. Bisphosphonates attach readily to HA because of their high binding affinity for calcium phosphate. Thus, after application of an aqueous solution containing alendronate to the partially HA-coated porous implant, the alendronate that contacts the outer HA-coated part of the porous titanium bonds to the HA covalently. The balance of the alendronate coats the inner bare metal struts of the porous titanium as a soluble coating. This enhanced coating-implant combination offers a new and improved platform suited to increase the rate and volume at which bone forms around the porous metal on the implant. The purpose of this study was to quantify the amount of alendronate released from the porous metal using various implant model geometries (porous rods and acetabular shells).

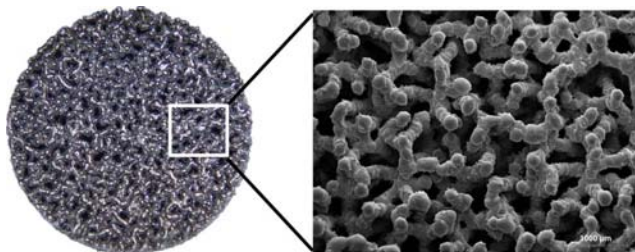


Figure 1. Ti6Al-4V porous disc (left). Scanning electron micrograph (SEM) image of the DMLS porous metal configuration (right).

**Methods:** Alendronate-HA coated (experimental) and alendronate (control) Titanium 6Al-4V alloy 9 mm (diameter) x 25 mm (length) porous rods and acetabular shells were manufactured by Pipeline Biotechnology (Parsippany, NJ). The thickness of the porous region for both implant models was 1.5 mm. The porosity of this layer was approximately 65% with pores measuring an average of 410 microns and struts approximately 185 microns in diameter. Experimental samples processing consisted of the partial HA coating [Figure 2] followed by the application of known amounts of an alendronate solution evenly throughout the implant porous region. Control samples were processed identically and left as bare metal without the HA coating. To quantify the amount of alendronate released from the samples, *in vitro* release studies were performed by placing individual

samples in phosphate buffer saline (PBS). During the release study, samples were incubated at 37 °C with agitation using a controlled environment incubator-shaker at 80 rpm. At pre-determined time points (1 hr intervals) aliquots were withdrawn to determine the amount of alendronate release from the samples. The concentration of alendronate in solution was determined by UV-Vis spectrophotometry via complex formation of alendronate with o-phthalaldehyde (OPA) [2].

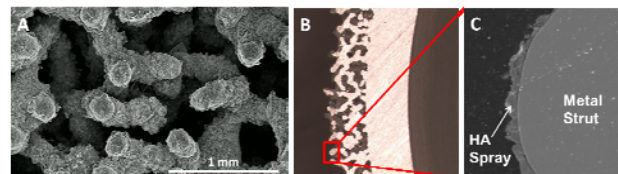


Figure 2. (A) SEM image of HA coated porous metal configuration. (B) Cross-section photomicrograph of a partially HA coated acetabular shell. (C) SEM image showing thin HA layer covering the outer most portion of the metal strut highlighted in image B.

**Results:** *In vitro* studies demonstrate that the amount of alendronate released from the surface of porous metal rods and acetabular shells upon implantation was approximately 40% of the total alendronate amount. The range for the alendronate release profile for the sample of porous rods and acetabular shells was 33.1% - 41.0% with a mean and standard deviation of  $38.7\% \pm 2.7\%$  and 36.0% - 48.1% with a mean and standard deviation of  $41.1\% \pm 4.1\%$ , respectively. Alendronate release from control samples was  $97.9\% \pm 1.6\%$  for porous rods and  $97.3\% \pm 1.2\%$  for porous acetabular shells. These results corroborate no alendronate is lost during the alendronate application and that the remaining alendronate is covalently bonded to the stable HA.

**Conclusions:** *In vitro* studies of alendronate release from both porous metal rods and acetabular shells demonstrate that the parameters employed during the HA coating and alendronate application of the implants results in an alendronate release of approximately 40%. It is reasonable to assume that this controlled amount of alendronate would be released to the peri-implant space due to hydration and diffusion of the alendronate from the innermost, non-HA coated porous structure. This should provide an increase in bone volume immediately surrounding the implant. In addition, it is expected that the remaining alendronate (~ 60%) covalently bonded to the stable HA coating will promote apposition of bone to the porous metal struts which in turn should strengthen the bone-to-implant interface.

**References:** [1] Cohen RC. ISTA Meeting 2013; Abstract # 2233. [2] Tzanavaras P. Anal. Chim. Acta. 2005; 547(1):98-103.