Osseointegration Effect of BMP-2 on Dental Implants: A 3-6 Week *In Vivo* Study

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Statement of Purpose: Recombinant human bone morphogenic protein type 2 (rhBMP-2) plays a critical role in the development of bone as a potent recruiter and inducer of osteoblast activity. Previous studies have demonstrated titanium is an unsuitable material for proper surface adsorption of BMP-2 due to its surface characteristics, while calcium phosphate possesses none of the same restrictions. We hypothesized that coated plasma-spray treated calcium phosphate (PSCaP) implants adsorbed with rhBMP-2, containing healing chambers, would result in increased novel bone formation and osseointegration with the implant surface.

Methods: Prior to implantation, Ti implants were plasma spayed with CaP (PSCaP implants) as such a technique is thought to grant a more hydrophilic environment that is more conducive and favorable for BMP-2 uptake. Titanium (textured) and PSCaP implants are then submerged in rhBMP-2, 4.67 mg/mL, Medtronics, Minneapolis, MN) for 5 seconds prior to surgical placement. Both the experimental and uncoated control groups were implanted within five sheep iliac bones for 3 and 6 weeks each. Following animal sacrifice, the implants were nondecalcified, processed, reduced to thin slides, stained (Stevenel's Blue and Van Giesons Picro Fuschin stain), and analyzed via histomorphometric examinations upon image capture (Aperio, Vista, CA). The bone-implant contact (BIC) and the bone area fraction occupancy (BAFO) were quantified. Statistical analysis used a 95% level of significance after ranking the raw statistical data and generated a general linear model with BIC and BAFO as the dependent variables and implant surface, BMP presence, and time in vivo as independent variables.

Results: Purely qualitative examinations depicted the novel bone formation and osseointegration to all implant surfaces after 3 weeks in vivo [Figure 1]. Quantitative histomorphometric analysis showed significantly higher BIC in PSCaP implants coated with rhBMP-2 at 3 weeks when considering the implant surface type, time *in vivo*, and effects of rhBMP-2 as independent individual or group variables [Figure 2]. At 6 weeks, an overall increase in BIC and BAFO was observed in relation to the 3 week time point. However, no significant effects of all the other independent variables excepting time *in vivo* and implant surface type were detected at this time point.

Conclusions: Earlier studies have demonstrated the superiority of calcium phosphate as a material component

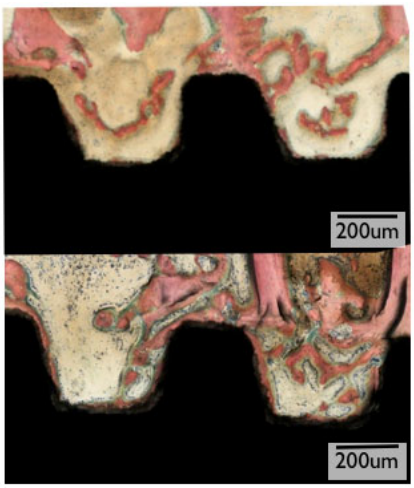

Figure 1: Histologic section of PSCaP implant surfaces at 3 weeks displaying bone (red) and cells (blue) without (top) and with rhBMP-2 (right).

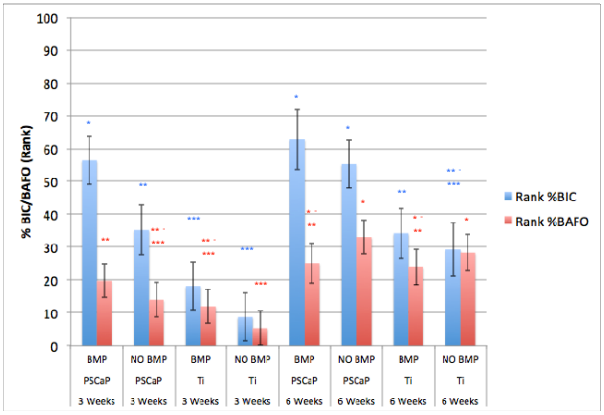

Figure 2: Statistical summary for all outcomes and combination of time in vivo, implant surface, and the presence of BMP (mean ± standard error of the mean).

in dental and bone implants when compared to titanium. Thus, the significant difference in osseointegration between the two surface types is not an unexpected result. As an implant surface, plasma-spray treated calcium phosphate exhibited a higher degree of bone-implant contact over that of titanium with more than a 50% increase in the presence of rhBMP-2 at 3 weeks relative to its uncoated counterpart. Our results suggest that the PSCaP implant surface is more amenable to adsorption of bone morphogenic protein for early healing release. For future studies, earlier time points must be considered in order to further investigate the effect of rhBMP-2 on osseointegration in terms of measurable parameters and kinetics.