Implant Coatings based on Enzymes improve Osteogenic Responses in vivo

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Introduction: Modulation of implant surfaces to optimize biological responses is a major topic in biomaterials and implantology. For bone implants, the state-of-art comprises either topographical modulation (gritblasting followed by acid etching; GAE) or chemical alterations (calcium phosphate coatings; CaP). However, both of these approaches result in rather 'passive' surfaces, whereas an 'active' surface might be preferable to enhance bone-to-implant contact (BIC) and bone volume (BV). Inspired by the physiological mineralization process, the current study focused on the application of enzyme-based coatings utilizing alkaline phosphatase as an active surface component. These ALP-coatings had previously demonstrated to induce surface mineralization upon immersion in culture medium[1] and enhance osteoblast-like cell behavior in an established cell culture model.[2] the current study aimed to evaluate the bone response to ALP-coatings and ALP/CaP composite coatings using a rat model. GAE implants and CaP-coatings served as controls.

Methods: Bovine intestine ALP (1 mg/ml; Sigma) and freshly-prepared CaP-nanoparticles (0.36 mg/ml) were used as coating solutions. Electrostatic spray deposition (ESD) was used to fabricate ALP-, ALP/CaP-, and CaP-coatings on cylindrical GAE titanium implants (Ø: 2.5 mm, length: 6 mm) with a gap of 1 mm. Implants were inserted in the femurs of rats for 1 and 4 weeks. Evaluation consisted of histological and histomorphometrical analyses of osteogenic responses (BIC and BV) to the implants at various areas of the implant (Figure 1).

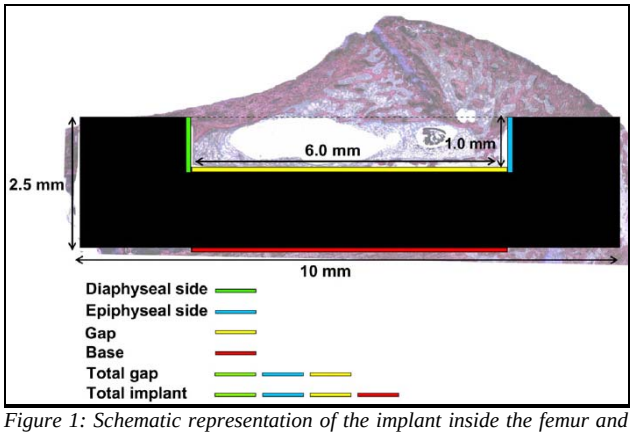

Figure 1: Schematic representation of the implant inside the femur and the evaluation areas for analyses of the osteogenic responses.

Results: During the experiment, all animals remained in good health and no signs of infection or adverse tissue response were observed at implant retrieval.
After 1 week of implantation, variable amounts of callus tissue formation were observed in the gap area of all implants, predominantly at the drill margins of the pre-existent bone tissue. Generally, little or no bone tissue was present at the implant surface of the gap, regardless of experimental group. However, soft tissue formation was seen mostly for the GAE implants.
After 4 weeks of implantation, the callus tissue inside the gap was replaced by fatty bone marrow. Furthermore, apparent BIC was observed for all experimental implants, which was extending from the epi- and diaphyseal sides of the gap. For GAE implants, higher magnifications showed interposed fibrous tissue at the bone/implant interface.

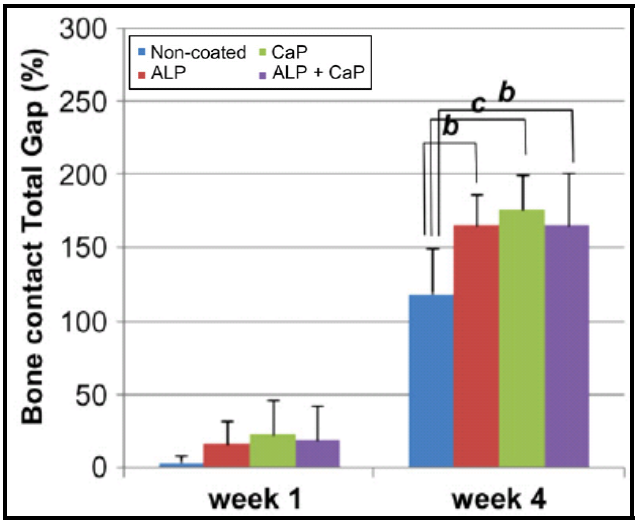

Figure 2: Histomorphometrical analysis of BIC for total gap. (b, p<0.01; c, p<0.001)

Histomorphometrical analysis demonstrated a significant decrease of bone volume in the gap from 1 to 4 weeks of implantation for all experimental groups individually ($p<0.01$). In contrast, BIC showed significant implant-related differences at 4 weeks after implantation (Figure 2). Furthermore, conduction of bone tissue along the implant surface preferentially originated from the diaphyseal side ($p<0.001$).

Conclusions: Electrosprayed ALP-, ALP/CaP-, and CaP-coatings showed improved osteogenic responses compared to non-coated, GAE control implant, more specifically regarding bone-to-implant contact. Furthermore, positional determinants for osteoconduction were observed, showing preference for diaphyseal implant sides.

References:

(1) De Jonge LT. Adv Funct Mater. 2009;19:755-762
(2) De Jonge LT. Acta Biomater. 2009;5:2773-2782