Implant Coating Technology with New Bioadhesive Materials

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Introduction: Clinical success of implants in orthopaedic surgery is critically related to the interaction between the implant surface and the surrounding tissue. Biodegradable materials that bonds to hard tissues such as bones and teeth are needed for medical and dental applications in both tissue engineering and regenerative medicine. Unfortunately, such materials are not currently available in clinical practice. We showed the development of a novel hard-tissue bioadhesive using biodegradable phosphopullulan (PP) before. And in this study, we coated implants with PP, and evaluated the new bone formation on the implant surface.

The purpose of this study was to construct a novel phosphopullulan bioadhesives coating incorporated with hydroxyapatite (HA) on the implant, and evaluating its biomechanical effects, an elemental analysis, and a histological examination. In an experimental study, a new method for coating implant material was tested for stability of the bone-metal interface.

Methods: We used that the arcam-surfaced titanium alloy (Ti-6Al-4V) implants. The implant form was cylindrical (5 mm in diameter, 15 mm long). We made 2% concentration PP solution and 2% PP+HA solution. And we coated the implants with PP or PP+HA, spraying while making them rotating in a concentric fashion by the coating machine. We sprayed 1ml at intervals of 3mm, 5 times.

In vivo experiment

Adult New Zealand White Rabbits weighing 3.0-3.5 kg were used and kept in cages with free access to food pellets and water. During the experimental period, the animals were kept under the same conditions of food and temperature. General anesthesia was induced by mask inhalation of Isoflurane with oxygen at an Isoflurane concentration of 3.5-4% for induction and 2.5-3% for maintenance after intramuscular injection of 2ml of Ketamine hydrochloride. Before the surgery, a single dose of antibiotic, Gentamicin 4mg/kg, was administered intramuscularly. After a standard skin disinfection technique, a local injection of 1.5 ml Lidocaine without vasoconstrictor was then performed. A straight 2-3cm skin incision was made at the medial side of the knee, and the medial condyle of the femur was exposed through a directed approach. We drilled the rabbit’s femoral condyles from the medial to the lateral with 5.2mm diameter drill. The implants were then inserted into the bone holes. The rabbits were implanted with three different foils (control, PP, PP + HA) each randomly with respect to type to eliminate any positional influence and individual difference on the results. This process was carried out in both the right and left femur. The rabbits were free to move and were fully weight-bearing after surgery. These rabbits were divided into 2 groups, with observation periods of 2, 4 weeks. 2 or 4 weeks after of the surgery, the rabbits were sacrificed by injecting air to heart, and bilateral distal half of the femora containing the implants were retrieved.

Mechanical examination
About 1 week after 10% formalin fixation, removal torque testing (mechanical push-out measurement) was performed to evaluate the interfacial shear strength between the implant and the bone of each group. We obtained maximum mechanical push-out strength, while the implants moved 3mm.

Elemental analysis
Two samples were selected from each groups after the mechanical examination, the elementary analysis was performed quantitative elemental analysis of the surface of these implants. We selected 9 elements, C, N, O, Al, P, Cl, Ca, Ti, V, and mapped the elements on the implant surface matching.

Histological examination
On an equality with elementary analysis, two samples were selected from each groups, and the histological and histomorphometric analysis was made 4 weeks after the implantation. This test was performed separately from mechanical examination. Each sample was cut into sagittal plane in the rabbits, such as parallel to the femoral diaphysis and perpendicular to the long axis of the implant. The samples were mounted on glass slides, and stained with hematoxylin and eosin. We measured the amount of bone inside the threaded area and the percentage of direct bone contact length on the implant surface to the entire implant surface length.

**Results:** In the mechanical examination, the removal torque values for the PP+HA group was 860 N (478-1400 N); corresponding values for the control group and PP group were 687 N (217-1175 N) and 737 N (394-1132 N) at 2 weeks after surgery. There was no significant difference in each group. 4 weeks after surgery, the removal torque values for the PP+HA group was 1235 N (968-1898 N); corresponding values for the control group and PP group were 944 N (546-1272 N) and 1152 N (775-1629 N). The removal torque values of the PP group and PP+HA group were 22% and 31% significantly greater than those of control group (P = .03, P = .002) (Figure.1).

In the quantitative elemental analysis after the mechanical examination, the PP+HA and PP coated implant groups showed a higher amounts of P elements and Ca elements than the uncoated implant group.

In the histological examination, there was evidence of bone neoformation on the surface of the implants (Figure.2). The percentage of periprosthetic bone in the groove gap of the implant was 35% in the control, 56% in the PP coating, and 75% in the PP+HA coating. The bone implant contact length percentage of the implant whole circumference was 40% in the control, 44% in the PP coating, and 53% in the PP+HA coating.

**Discussion:** In the mechanical examination, there was no significant difference in the 3 groups in 2 weeks. But, in 4 weeks, the interfacial shear strength of the PP coating and PP+HA coating implants was greater than that of uncoated implants. The PP group and PP+HA group had a positive effect on bone remodeling compared to the control group, 4 weeks after implantation.

In the quantitative elemental analysis, P and Ca elements were higher in the PP and PP+HA coating implants. We observed that the PP+HA group had increased bone volume per tissue, bone implant contact and new bone formation on the implant surface. But it was possible that the P and Ca elements of the implant surface may show variations about new bone formation, such as a strong cellular proliferation and differentiation resulting in bone neoformation or fibrous connective tissue with a high degree of organization. C element was higher after the mechanical examination than before surgery in all groups. We considered that this showed organic matter such as osteoblast, granulation tissue or signs of necrosis.
In the histological examination, there was greater new bone formation on the surface of the implants in the PP and PP+HA groups. According to these results, we speculate that the higher bone implant contact and bone area fraction occupancy observed at the PP and PP+HA implants in vivo were likely related to the amount of P and Ca observed in the quantitative elemental analysis. And with mechanical testing results, the PP coating and PP+HA coating implants had beneficial effects on interfacial shear strength and peri-implant new bone formation in rabbit femurs during the early stages of bone healings. The phosphopullulan bioadhesives may be useful as a new coating material for titanium alloy implants. There is more abundant documentation in favor of PP coated implants.

**Significance:** The PP coating had a beneficial effect on interfacial shear strength and peri-implant new bone formation in rabbit femurs during the early stages of bone healings.

![Mechanical push-out measurement chart](chart.png)