**Novel Concept of Bioactive Pedicle Screw: Biocompatibility and Bone-bonding Ability Improved by Chemical and Heat Treatments**

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**Disclosures:**

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**Introduction:** The use of spinal instrumentation with a pedicle screw (PS) system has become increasingly common in spinal surgery during the last two decades, and is usually in place in the spine over long periods or semi-permanently. Titanium (Ti) and Ti-6Al-4V alloys have been widely used as an endosseous implant in orthopedic fields, including a PS system, because of their good mechanical properties and biocompatibility with bone tissue. However, Ti and its alloy have no potential for direct chemical bonding with the bone; there remains a significant clinical problem including the loosening and back-out of PSs[1]. Several strategies have been proposed to augment PS-to-bone fixation; modifications in screw design[2] and screw surfaces[3]. During the last decade, a novel technology to produce bioactive Ti by chemical and heat treatments, which induce the spontaneous formation of a layer of hydroxyapatite (HA) on the surface of Ti materials in vitro and vivo, has been reported[4-6]. A porous bioactive Ti implant[7] has recently been utilized for spinal interbody fusion in a prospective clinical trial[8]. In an effort to add a high level of biological function to spinal instrumentation, we applied this bioactivation technology to a PS system. The purpose of this study was to examine the effect of bioactivation of Ti-6Al-4V PSs on (1) the ability of hydroxypatite (HA) to form in vitro, and (2) bone-bonding ability in vivo.

**Methods:** Preparation of bioactive PSs: Pedicle screws (2.5 mm in diameter, 14 mm in length) were prepared from Ti-6V-4Al alloys (Century Medical, Inc., Tokyo, Japan). For bioactivation[6], the screws were first soaked in 5 M aqueous NaOH solution at 95°C for 24 hours (alkali treatment). The screws were subsequently soaked in 100 mM CaCl2 solution at 40°C for 24 hours, heated to 600°C in an electrical furnace for 1 hour, and then placed in ultrapure water at 80°C for 24 hours. Evaluation of hydroxyapatite formation: The hydroxyapatite (HA)-forming ability of bioactive PSs was examined by incubation in simulated body fluid (SBF) with ion concentrations nearly equal to those of human blood plasma at 36.5°C. After soaking in SBF for 3 days, the screws were removed and HA formation on the surface of screws was evaluated by field emission scanning electron microscopy (FE-SEM) and energy dispersive X-ray analysis (EDX). HA-forming ability was also evaluated on bioactive PSs that had been removed after insertion into the pedicle of cryopreserved canine lumbar spines. Animal study: Three 11-month-old female beagle dogs were used in this study. Under general anesthesia, PSs were placed from L1 to L6 using fluoroscopy. The bioactive PSs were inserted into one pedicle or the other of each lumbar level at random. The controls PSs (without bioactivation) were similarly inserted into the contralateral side of the pedicle. The dogs were euthanized three months after surgery, and the lumbar spines were removed followed by micro computed-tomography (µCT) analysis. One level of vertebra was removed, and processed for histological analysis. The other levels of lumbar spines were separated and stored at -30°C until biomechanical analyses.

Biomechanical study: A torsional screw extraction analysis (control PS: n=8, bioactive PS: n=9) was performed to evaluate the mechanical strength of the bone-implant interface. Samples were secured in plaster and connected to a testing machine. The screws were extracted at a uniform rate (1.0 rpm) for four minutes (4 revolutions). Angular displacement and torque were recorded at 100 Hz for the duration of each test. Peak and averaged torque (mN-mm) were determined. For evaluation of pull-out strength (control PS: n=5, bioactive PS: n=6), the specimens were secured in polymethyl methacrylate (PMMA) and connected to the testing system. The direction of pull-motion was parallel to the long-axis of the screw. Maximum resistance against the pull-out force was calculated on the basis of the tensile curve recorded. Histological analysis: The PSs with surrounding bone were then immersed in formalin solution, and then embedded in methyl methacrylate. The samples were cut in the long axis of the screws. The specimens were stained using the Villanueva-Goldner method. The length of contact area between bone tissue and screw surface was assessed using image analysis software.

**Results:** A total of 34 PSs were inserted into the pedicles of canine lumbar spines. Two screws failed to insert during surgery. CT-image analysis revealed that 94.1% (32/34) of PSs were adequately placed into the pedicle. Hydroxypatite-forming ability: The surface analysis of bioactive PSs by FE-SEM showed that substantial HA deposits covered the entire surface. A similar observation was also found on the surface of bioactive PSs after removal from cryopreserved lumbar spines. EDX analysis showed that the HA deposits contained a small amount of Mg, Na and C, in addition to Ca and P, which were taken from Mg2+, CO32-, and Na+ ions in SBF, and thus should be bone-like HA.
Biomechanical study: The maximum extraction torque was 1.4 times higher in bioactive PSs compared to those of untreated PSs. The averaged extraction torque was significantly higher in bioactive PSs compared to that of the control PSs ([mN.m] 65.0±17.2, 45.9±18.3, respectively, p<0.05). There were no significant differences on pull-out strength between control and bioactive PSs. Histological analysis: In the control (untreated) group, a fibrous tissue layer was interstitially spread between the bone tissue and screw surface, while bone tissue, including bone matrix and bone marrow, was closely attached to the surface of bioactive PSs (Figure). The ratio of contact area between bone tissue and screw surface was 1.5 times higher in bioactive PSs compared to that of control PSs.

**Discussion:** We have, for the first time, shown that the novel concept of bioactive PSs prepared by chemical and heat treatments has the potential to form a layer of HA on the surface of screws in vitro and to increase the biocompatibility and bonding ability with bone in vivo. Bioactive PSs may prevent screw-loosening and improve clinical outcomes of spinal instrumentation surgery. The effect and safety of bioactivation on PSs should be examined in a long-term future study.

**Significance:** We have, for the first time, shown that the novel concept of a bioactive pedicle screw prepared by chemical and heat treatments has the potential to form a layer of HA on the surface of screws in vitro and to increase the biocompatibility and bonding ability with bone in vivo. Bioactive PSs may prevent screw-loosening and improve clinical outcomes of spinal instrumentation surgery.

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