Effects of teriparatide (human parathyroid hormone 1-34) on the bone formation in the unidirectional porous beta-tricalcium phosphate

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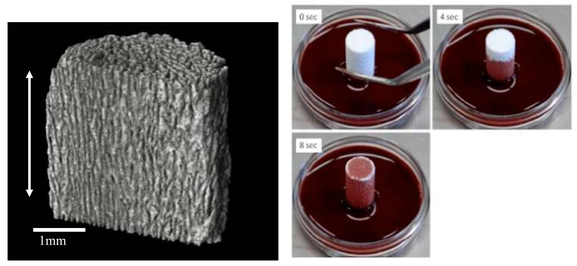
Introduction

Unidirectional porous beta-tricalcium phosphate (UDPTCP) is a novel artificial bone (Affinos®, Kuraray, Co. Inc., Tokyo, Japan), having a unidirectional porous structure (pore size: 25-400 μm) with a porosity of 57%. UDPTCP is characterized by an appropriate balance between bone formation and material resorption[1]. β-TCP is commonly used in orthopaedic surgery and teriparatide is often used in combination with it because of the osteogenic potential. However, its effect on UDPTCP is unknown.



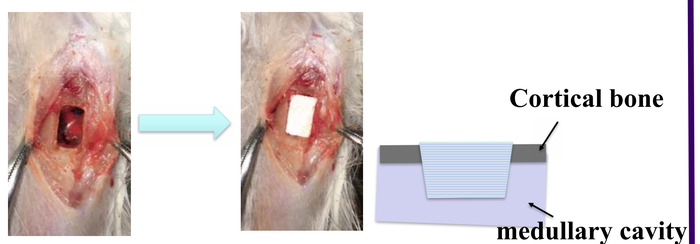
Objective

This study aimed to evaluate the effect of intermittent teriparatide treatment on changes in bone formation using UDPTCP in a rabbit bone defect model.

Methods

All protocols involving animals were approved by the institutional review board for animal testing. Twelve Japanese white rabbits were used in this study. General anesthesia was induced by injecting a mixture of ketamine (50 mg/kg body weight) and xylazine (14 mg/kg body weight) intramuscularly.

A 5×8-mm rectangular area of periosteum was resected, followed by preparation of a cortical bone defect in a 4.5×7-mm rectangular shape using a high-speed bur. UDPTCP was embedded in the defect in the direction of the pores, parallel to the axis of the tibia[2].

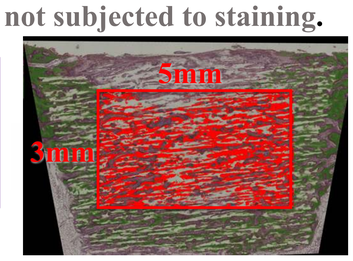


Rabbits in the teriparatide group (n=6) were subcutaneously injected with 30 μg/kg of chemically synthesized teriparatide three times per week.
Rabbits in the control group (n=6) were injected with a hormone stock solution according to the same schedule. Tissue samples were harvested at 6 weeks after implantation.

Observation of newly formed bone

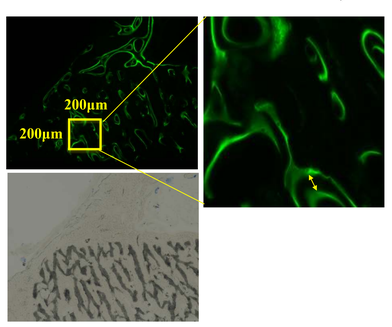
Histological Analysis: Villanueva-Goldner (VG) stain on sagittal sections. In addition, an axial section was cut 3 mm from the proximal end of the UDPTCP that was not subjected to staining.

- A region of interest (ROI) with a height of 3 mm and a width of 5 mm was set in the center of the artificial bone.
- The area ratio of the newly formed bone was calculated by dividing the area of the extracted portion by the area of the ROI.



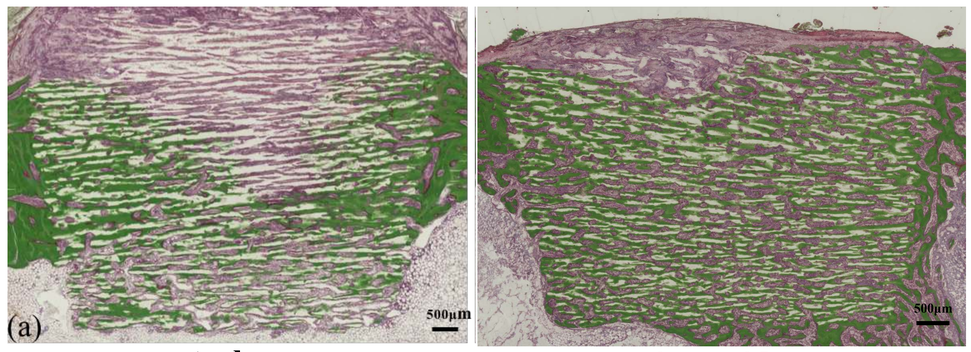
A double-fluorochrome labeling: Calcein was subcutaneously injected into each rabbit twice, at a dose of 8 mg/kg body weight, nine and two days before sacrifice.

- Within the ROI, five randomly selected regions measuring 200 μm on one side and extending to the most elongated part of the double fluorescent label were identified.
- The average of 6 specimens was calculated and compared between the two groups.

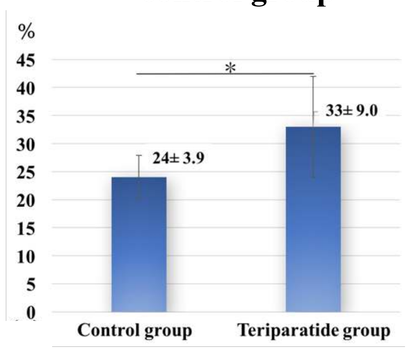


All data were presented as mean ± standard deviation. Statistical analysis was performed using Student's t-test. P<0.05 was considered to indicate a statistically significant difference.

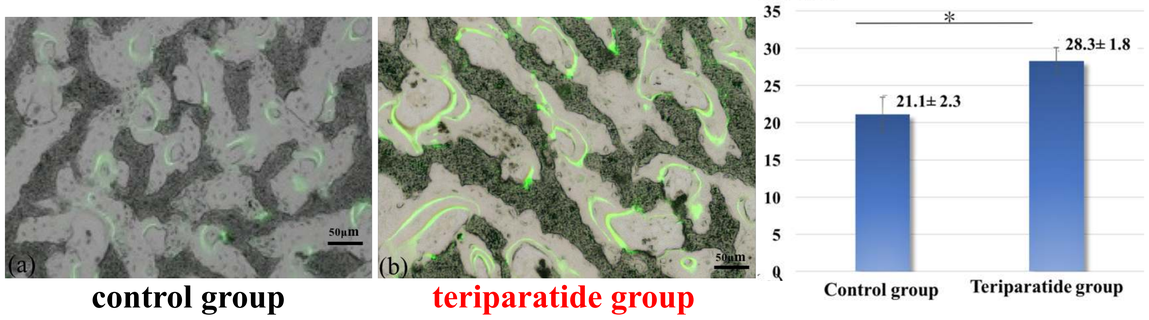
Results



control group — teriparatide group



The percentage of new bone area in the ROI was significantly larger in the teriparatide group (33 ± 9.0%) than in the control group (24 ± 3.9%).



control group — teriparatide group

The calcification rate was significantly faster in the teriparatide group (28.3 ± 1.8 μm/week) than in the control group (21.1 ± 2.3 μm/ week).

Discussion

- Tissue invasion into artificial bone is an important factor in bone replacement. Several studies have reported that new active bone formation occurs with osteoblastic lining cells in direct contact with β-TCP[3]. This experimental result suggested that the unique pore structure contributes to remodeling in the material.
- Intermittent administration of teriparatide resulted in osteoblastic proliferation and differentiation, thereby leading to an increase in bone mass. Our histological findings revealed that intermittent administration of teriparatide enhances new bone formation within UDPTCP.

Conclusion

UDPTCP used alone sufficiently causes new bone formation, but as combined use of teriparatide further enhances new bone formation, promotion of bone fusion can be expected, leading to better clinical outcomes when applied to surgical procedures in real-world settings.

References:
[1] Makihara T, et al., 2016, Key Eng Mater, 177-182;
[2] Iwasashi M, et al., 2008, Key Eng Mater, 396-398;
[3] Chazono M, et al., 2004, J Biomed Mater Res; 70:542–9

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