A COMPLEX OF HIGHLY PURIFIED BETA-TRICALCIUM PHOSPHATE (BETA-TCP) AND HYALURONATE AS BONE SUBSTITUTE FOR BONE DEFECTS

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Introduction
Autografts remain the gold standard for bony defects. Recently, we have developed highly purified beta-TCP, and reported that a block of this material was able to be a bone substitute for autogenous graft. The objective of this study is to investigate the efficacy of a complex of highly purified beta-TCP granules and hyaluronate as bone filler.

Materials and Methods
Bilateral cylindrical bone defects (4 x 12 mm) were created in the distal femoral metaphysis of 36 adult New Zealand White rabbits. These were divided into three groups. Twenty-four animals received a complex of 0.1g of beta-TCP granules with 50-500 pm and 0.1ml of 3.5% hyaluronate (group 1) and a block of beta-TCP (dia. 4mm x 10mm) (group 2) bilaterally. Twelve animals received sham operations bilaterally as controls (group 3). Nine rabbits each were sacrificed at 2, 4, 6 and 8 weeks postoperatively. For histological examination, femoral specimens were cut in half in the sagittal plane to obtain decalcified and non-decalcified sections. Decalcified sections were stained with hematoxylin and eosin (H&E) and tartrate-resistant acid phosphatase (TRAP). On the other hand, non-decalcified section was used to analyze resorption rate of beta-TCP and mineral apposition rate using color-based thresholding by the image analyzer (Adobe Photoshop 5.0®). A Mann-Whitney U test was used to compare group 1 with group 2 at 95% confidence level.

Results
Histological findings revealed new bone ingrowth into beta-TCP scaffolds both granules and block at 2 weeks. Osteoblasts were present with the woven bone (Fig. 1). Most of TRAP-positive multinucleated giant cells were contact with beta-TCP (Fig. 2). The thickness of trabecula of newly formed bone increased and became similar to adjacent cancellous bone at 8 weeks postoperatively. However, histologic analysis of the specimens in the control group showed only minimal bone formation around the bony defects at 8 weeks. Thus, a complex of beta-TCP and hyaluronate possessed significant osteoconductive effects. There was no significant difference between the complex and the block in new bone formation (Fig. 3). On the contrary, resorption of the complex of beta-TCP and hyaluronate was significantly faster than that of the block (Fig. 4), however, mineral apposition rate between the complex and the block was almost equal at all time-periods.

Discussion
The results from this study suggest that not only a block of beta-TCP but also a complex of highly purified beta-TCP and hyaluronate support bone growth into a defect in metaphyseal bone of rabbit. Biological process of resorption of bioceramics is known as two kinds of biore sorption: solution-mediated disintegration and cell-mediated disintegration. Histological examination at 2 weeks post implantation reveals that cell-based resorption of beta-TCP and osteoblastic apposition of new bone directly on the surface of beta-TCP has occurred both granules and block, suggesting that a coupling-like phenomenon could be occurred in the beta-TCP filling bone defect. Thus, beta-TCP can be considered as a resorbable material through cell-mediated disintegration in the early phase. We have already applied beta-TCP block to 150 or more patients in the clinical field and recognize this bioceramic to be reliable. In addition, a complex of beta-TCP and hyaluronate is a paste-like material, easy to handle, and injectable. It has good osteoconductive properties and may be an alternative to autograft. Thus, it could be useful in a variety of clinical application or a carrier of growth factors as high resorbable property and scaffolding for new bone.

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