A comparative study of calcium phosphate bone cement enriched with strontium on enhancing tendon-bone osteointegration in a rabbit anterior cruciate ligament reconstruction model

INTRODUCTION:
Recent studies have shown that the healing of soft tissue tendon graft within the bone tunnels can be enhanced by the use of injectable calcium phosphate bone cements (CPC) in anterior cruciate ligament (ACL) reconstruction animal models.[1,2]. The mechanism lies in CPC not only biologically compatible, but also osteoconductive in vivo. Furthermore, the biological properties of CPC can be apparently enhanced by incorporation of strontium (Sr), which not only increases osteoblast-related gene expression and alkaline phosphatase (ALP) activity in mesenchymal stem cells (MSCs), but also inhibits the differentiation of osteoclasts. Therefore, it is in the present study hypothesized that tendon-bone osteointegration in the bone tunnels is better by the use of Strontium enriched calcium phosphate (Sr-CPC), compared with conventional CPC free of Sr. This hypothesis was tested in the rabbit in the present study.

MATERIALS AND METHODS:
30 New Zealand White rabbits at an age of 5 months were used. They were divided into two groups. One stage bilateral ACL Reconstruction using Achilles tendon allograft was performed in each animal. One group was for comparison of the Sr-CPC treated graft with non-treated graft (Negative control). Another group was for comparison of the Sr-CPC treated graft with the CPC treated graft (Positive control). 3 animals were sacrificed in each group at the time point 3, 6, 9, 12 and 24 weeks after the index operation. Histological examination was carried out to examine the degree of osteointegration of the tendon graft within the bone tunnels.

RESULTS:
Better healing of the graft within the bone tunnel was noted in the Sr-CPC treated group compared with CPC treated limb group at 6, 9 and 12 weeks. At 6 weeks, the tendon-bone interface in the negative control limb was only filled with fibrovascular tissue. However, new bone formation was apparently observed in positive control groups. In particular, the gap had already been obliterated by new bone formation with evidence of early Sharpey fiber formation and more cartilaginous tissues formation in Sr-CPC group (Figure 1). At 12 weeks, Sharpey like fibers started to appear in the negative control limb. The gap in the positive control group was filled by more matured bone and well organized cartilaginous tissue. In the Sr-CPC limb, apparent transitional zones consisting of bone, mineralized fibrocartilage to unmineralized fibrocartilage to tendon were observed in most of the samples. Safranin-O staining showed production of proteoglycan in the transitional zones (Figure 2). At 24 weeks, the tendon graft was connected to bone wall by well structured Sharpey fibers in the control sides. However, complete remodeling of the graft bone junction into normal ligament-bone insertion was found in the positive control group and Sr treated limbs (Figure 3).

DISCUSSION:
The present study showed that better healing of the soft tissue tendon graft within the bone tunnel was noted in the Sr-CPC treated group, compared with conventional CPC treated limb group, in a rabbit ACL reconstruction model using Achilles tendon allograft. Consistent with previous reports, [1, 2] tendon-bone healing was improved in the conventional CPC treated group due to the osteoconductivity of CPC. Moreover, CPC has been addressed as a delivery vehicle of various osteoinductive factors. The incorporation of Sr, which is a special osteogenic factor, will gradually release from CPC, resulting in osteogenic effects on the surrounding tissues. Therefore, better healing effects in terms of more new bone formation, more cartilaginous tissue formation, and earlier regeneration of direct tendon-bone insertion were observed in Sr enriched CPC group.

SIGNIFICANCE:
The findings in the present study may provide a potential way to enhance the tendon healing within the bone tunnels after ACL reconstruction in clinical practice.

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REFERENCES:

Figure 1: Representative images of the tendon-bone interface at six weeks after operation.

Figure 2: Representative images of the tendon-bone interface at twelve weeks after operation.

Figure 3: Representative images of the tendon-bone interface at twenty-four weeks after operation.