Comparison Of Hydroxyapatite And Beta-tricalcium Phosphate For Osteochondral Repair Using The Hybrid Implant Of Artificial Bone With A Scaffold-free Tissue Engineered Construct Derived From Mesenchymal Stem Cells

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Disclosures:

Introduction: For an ideal osteochondral repair, it is important to restore subchondral bone and cartilage layer-by-layer (1). Specifically, restoration of osteochondral junction, cartilage repair with secure integration with adjacent cartilage, and initial stabilization of subchondral bone could be the key to determine the treatment outcome. We have developed the hybrid implant made of hydroxyapatite (HA)-based artificial bone coupled with a scaffold-free tissue engineered construct (TEC) derived from synovial mesenchymal stem cells (MSCs), and demonstrated that the hybrid implant significantly improved osteochondral repair in a rabbit osteochondral defect model, which exhibited the formation of hyaline-line cartilage, secure good tissue integration to adjacent host tissue, and advanced repair of subchondral bone (2).

On the other hand, beta-tricalcium phosphate (βTCP) is highly bio compatible material that provides a resorbable interlocking network to implant within a bone defect and is resorbed more rapidly than HA in vivo (3). Therefore, the use of βTCP might be advantageous in more efficient subchondral bone remodeling. We hypothesized that a βTCP-based hybrid implant coupled with synovial MSC derived TEC would show a superior osteochondral repair, compared with a HA-based hybrid implant, and tested this hypothesis using a rabbit osteochondral defect model.

Methods: All animals (skeletally mature New Zealand White rabbits) were handled in accordance with a protocol approved by the institutional ethical committee.

Cell expansion and development of the TEC:
MSCs were isolated enzymatically from rabbit synovial membranes and the adherent cells were expanded until passage 4 to 7 according to our previous methods (4). The cultured cells were plated on a culture dish at a density of 400,000/cm² (9.6cm²) with 0.2mM ascorbic acid 2-phosphate. After additional culture duration, a complex of the cultured cells and the extracellular matrix synthesized by the cells was detached from the substratum to develop a three dimensional form (TEC) by active tissue contraction.

Implantation of the hybrid material to a osteochondral defect in vivo:
TEC was detached from culture dishes just before implanted surgery, and bind to artificial bone (5mm diameter, 4mm deep) of HA (NEOBONE®) or βTCP (OSferion®) without any glue to create the osteochondral hybrid. Under anesthesia, 5mm diameter, 6mm deep osteochondral defect was created on the femoral groove of skeletally mature rabbits. The hybridization of the TEC and artificial bone was done just before implantation and the hybrid implant was then implanted in the defect without suture for 29 right knees (TEC/HA; 18 knees, TEC/βTCP; 11 knees).

Histological evaluation:
Histology was stained with H&E and Toluidine Blue staining, and then histological scores were evaluated by modified O’Driscoll score (5) at 1, 2 and 6 months after surgery.

Results: The osteochondral defect treated with TEC/βTCP showed rapid subchondral bone repair at 1 month, but the degeneration of repair cartilage was progressed at 6 months. The osteochondral defect treated with TEC/HA showed the delayed subchondral bone repair at 1 month, but similar quality of subchondral bone repair to TEC/βTCP at 2 months. Notably, the repair osteochondral bone tissue maintained good quality until 6 months. Likewise our previous study (2), the repaired tissue exhibited good tissue integration to adjacent host tissue in both groups (Fig. 1, 2).

In the histological scores for cartilage layer, there were no significant differences detected between both groups. The histological scores for subchondral bone layer in TEC/βTCP group at 1 month showed significantly higher than that in TEC/HA group (Fig. 3).
Discussion: In the present study, the TEC/HA hybrid implant exhibited better histological findings in osteochondral repair than the TEC/βTCP hybrid implant, contrary to our hypothesis. We demonstrated that the TEC/HA hybrid implant could warrant longer-term durability of subchondral bone and prevent the degeneration of repair cartilage, although the TEC/βTCP hybrid implant showed an advanced subchondral bone repair at 1 month. These results may imply that the repaired subchondral bone with βTCP would be mechanically weaker than that with HA, similar to a previous study (3), and such mechanical weakness of subchondral bone might result in the cartilage degeneration. Longer follow-up with biomechanical analyses would be necessary to draw a specific conclusion.

Significance: The elucidation of material-specific differences in healing response of cartilage and subchondral bone by a hybrid implant of stem-cell-based tissue engineered construct (TEC) and artificial bone would be important for optimization of osteochondral repair and regeneration towards clinical application.

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Fig. 2
Toluidine Blue staining (6 months)

TEC/HA

TEC/βTCP

Bar=1mm
Fig. 3
O’Driscoll score

Cartilage

Subchondral bone

*; p<0.05

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