Table 1
Different mediators produced by healthy and OA osteoblasts measured by LUMINEX

Osteoblasts	TSLP pg/ml	PAI-1 ng/ml	MCP-1 ng/ml	Leptin pg/ml	Resitin ng/ml	IL-6 ng/ml	IL-8 ng/ml	IL-21 ng/ml	Il-1a pg/ml	GM-CSF pg/ml	Cathepsin S pg/ml
Healthy	13±9	184±130	7±9	366±151	20±32	6±6	6±5	21±2	24±5	19±14	447±235
OA	19±13	91±32	20±12	452±145	5±3	3±3	18±9	23±1	29±6	43±26	1114±630
p	0.088	0.016	0.003	0.029	0.084	0.055	<0.001	0.034	0.028	<0.001	0.002

processes in OA. Importantly, these data are supportive to target osteoarthritic bone in OA to modulate cartilage repair.

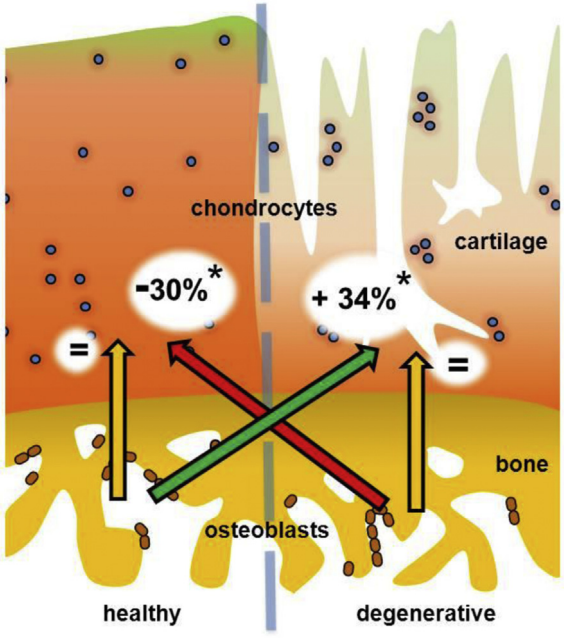

Figure 1. Biochemical effects of bone on cartilage. Human knee subchondral osteoblasts were isolated form healthy donors (n=14) and OA patients (n=16). Osteoblast culture supernatants were subsequently tested on both healthy and osteoarthritic cartilage and changes in proteoglycan (PG) synthesis were studied (mean % change are given).

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MICROSTRUCTURAL OBSERVATION OF COLLAGEN FIBRILS IN THE ARTICULAR CARTILAGE REVEALS A STRUCTURAL DIVERGENCE DEPENDING ON ITS LOCAL MECHANICAL ENVIRONMENT IN HUMAN FEMORAL HEAD

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Purpose: This study analyzed the pattern of collagen deposition in normal and degenerative human articular cartilage of the femoral head by a scanning electron microscope (SEM).
Methods: The femoral heads were obtained from the patients who received the operation of the total hip arthroplasty or the hemiarthroplasty due to osteoarthritis ($n = 7$), avascular osteonecrosis ($n = 5$), femoral neck fracture, and bone tumor ($n = 1$) with informed consent. Small pieces of the articular cartilage were dissected from the femoral head and were stored in Ringer's lactate. The cartilage was kept in the beaker with Ringer's lactate and was replaced in the ultrasonic bath (42,000 Hz) for 15 min to remove proteoglycans from the articular surface. The cartilage was fixed with 2% glutaraldehyde and 2% paraformaldehyde, and then with 1% OsO4. The tissue was dehydrated and was sputter-coated with Au/Pd. The articular cartilage was examined under a SEM. A split-line technique was used, in which a dissecting needle dipped in India ink was inserted in to the cartilage to identify the surface collagen orientations of the femoral head.
Results: Ultrasonic removed amorphous mucinous deposition on the articular surface effectively and enabled the observation for fine architecture of the cartilage. SEM study under low magnification revealed that the orientation of collagen fibrils in the superficial layer was radial from the fovea of the femoral head to the head-neck junction. This orientation of collagen fibrils corresponded with the split-line on the femoral head. Hip joint is a ball and socket joint and the direction of collagen fibrils correlated strongly with preferred alignment of fibrils suitable for joint motion. Under higher magnification, collagen fibrils in the superficial layer ran parallel to the articular surface, oriented randomly from layer to layer, and formed a compact network in the normal cartilage, The density of collagen fibrils was higher in the superior aspect of the femoral head (weight bearing surface) and lower in the inferior aspect (non-weight bearing surface). Chondrocytes, which were buried in collagen fibrils, could be observed only after shaving the articular surface. Fractured surface perpendicular to the articular surface showed that collagen fibrils arose in the subchondral bone then passed towards the surface and arched over to run tangential to the surface like Benninghoff's arcade model. In the degenerative cartilage, derangement and rupture of the collagen network were observed and those changes developed progressively in accordance with the macroscopic severity of osteoarthritis. Chondrocytes in the superficial layer emerged between the disrupted collagen fibrils. Collagen fibrils in the superficial layer were swollen and their diameter was thicker than that of normal cartilage. Vertically oriented collagen fibrils with large diameter were exposed in the area with macroscopic fibrillation. In the specimen from the patients with avascular osteonecrosis, collagen fibrils were almost normal in the early stage of the disease. Breakage of collagen network was seen in the femoral head with collapse.
Conclusions: Collagen fibrils were deposited parallel to the articular surface in the superficial zone, and were aligned radially from the fovea to the margin of the articular cartilage in accordance with the distribution of the split-line. Collagen meshwork was well preserved in normal cartilage and was more meticulous in the weight bearing area, but it was disappeared in the degenerative cartilage. Vertically oriented collagen fibrils with large diameter and exposed chondrocytes were the characteristics in degenerative articular cartilage.

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THREE DIMENSIONAL DISTRIBUTION OF HIP CARTILAGE T2 MAPPING ASSESSED BY RADIAL MR IMAGING: COMPARISON BETWEEN HEALTHY VOLUNTEERS AND PATIENTS WITH HIP DYSPLASIA

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Purpose: Hip dysplasia is one of the main causes for developing hip osteoarthritis, and sensitive and accurate detection of early cartilage lesions is important to estimate disease prognosis and plan conservative or surgical treatments. Several quantitative magnetic resonance (MR) imaging techniques have been developed for assessment of early cartilage degeneration. Though previous hip arthroscopic studies showed frequent involvement of acetabular cartilage degeneration predominantly at anterosuperior limited regions before appearance of radiographic osteoarthritic changes in patients with hip dysplasia, few studies have reported on three-dimensional evaluation with quantitative cartilage MR imaging in the hip joint. The purpose of this study was to investigate 3D distribution of cartilage T2 mapping over the whole acetabular cartilage using radial MRI techniques, and to examine association between cartilage T2 and adjacent labral lesions in healthy volunteers and patients with hip dysplasia.
Methods: Nine symptomatic patients with hip dysplasia (dysplasia group; all female, mean age; 33 ±10 years) and eight asymptomatic healthy volunteers (control group; all female, mean age; 28±2 years) were evaluated with 3.0-T MR imaging system. Patients in the dysplasia group had mean lateral center edge angle of 5.3° (range; -18° to 17°) with no osteoarthritic changes on plain radiographs. Radial T2 map images of the unilateral hip were obtained at 30° intervals passing through the center of

the acetabular dome and perpendicular to the acetabular rims (Plane A90 to P90, Fig 1) for evaluation of the acetabular cartilage. Radial fast spin-echo T2-weighted images on matched planes were also obtained for evaluation of the acetabular labrum. In each radial image, the acetabular cartilage area on the weight bearing was defined manually, which was further subdivided into medial (Zone M) and lateral zones (Zone L) of equal length using our custom-made software (Fig 2). Average cartilage T2 values in each zone, and lateral-medial (LM) ratio, which was defined as cartilage T2 value in Zone L divided by that in Zone M, was calculated. LM ratio was employed due to adjust physiological variations of cartilage T2 among individuals. Labral tear was defined as abnormal internal signal or exhibiting effusion extending into labrum. Relationships between labral tear and cartilageT2 value or LM ratio at the adjacent cartilage zones were evaluated.

Results: Acetabular cartilage T2 values at Zone L were significantly greater in the dysplasia group than the control group on all planes, while T2 values at Zone M were significantly greater only on the S and P90 planes in the dysplasia group ($p<0.05$, Fig 3). The LM ratios on all planes except the P30 and P60 plane were significantly greater in the dysplasia group ($p<0.05$, Fig 4). Labral tear was observed in seven of nine joints (24/63 planes) in the dysplasia group and in two of eight joints (3/56 planes) in the control group. In the dysplasia group, labrum tear was found most frequently in the A90 and A60 planes, followed in the A30, S, and P30 plane. Cartilage T2 values at Zone L and LM ratios were significantly higher in cartilage with adjacent labral tear than cartilage without labral tear. ($p<0.01$)

Conclusions: Distribution of cartilage T2 value in dysplastic hips without radiological osteoarthritis was different from that in healthy volunteers. After adjusting individual variations of cartilage T2 using LM ratios, T2 values at lateral zones were significantly greater in almost planes in patients with dysplastic hips, especially anterosuperior planes. Cartilage T2 values at lateral zones were significantly higher in cartilage with adjacent labral tear than cartilage without labral tear. These results were supported by significant associations between labral tear and T2 increase at the adjacent cartilage, and were in accordance with previous arthroscopic findings in patients with hip dysplasia. In further studies, it is important to investigate associations between degree and location of degeneration in acetabular and femoral cartilage, and clinical symptom among patients with hip dysplasia and femoroacetabular impingements.

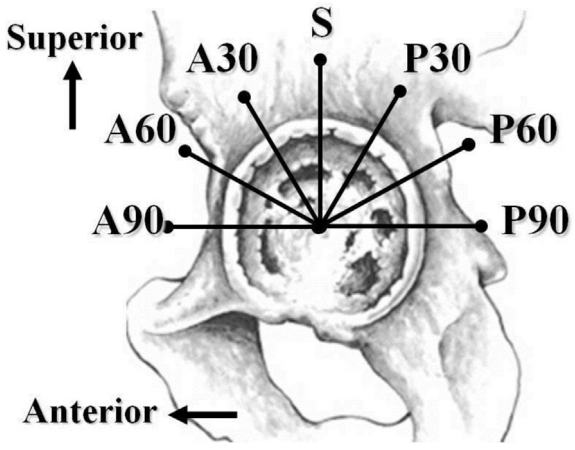

Fig.1. Definition or radial planes

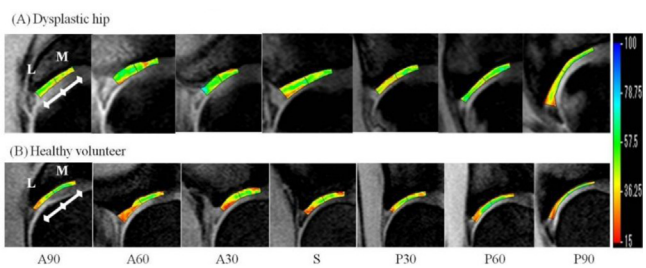

Fig.2. Radial T2 mapping in a patient with dysplastic hip (A) and a healthy volunteer (B) (L: lateral zone, M: medial zone)

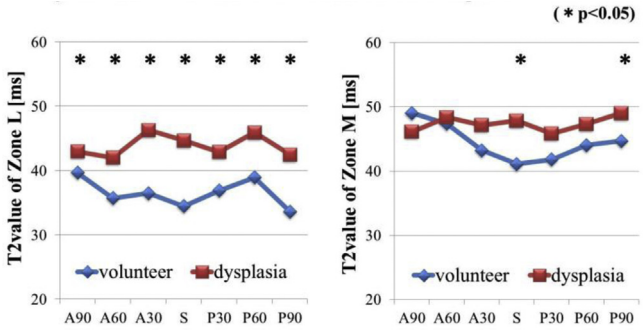

Fig.3. T2 values of lateral zones and medial zones in each plane

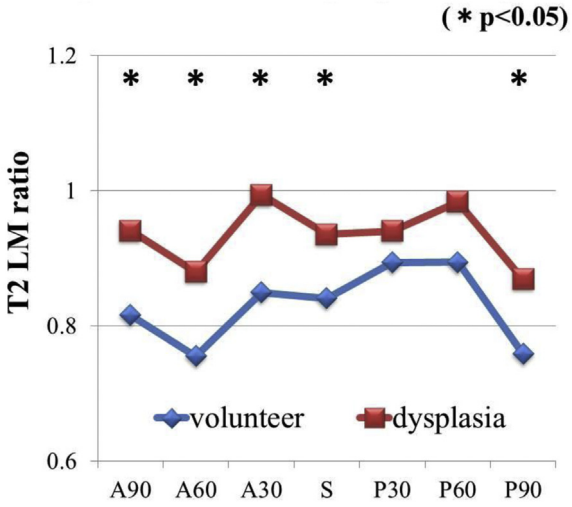

Fig.4. LM ratio of both groups in each plane (*p<0.05)

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THE RELATION BETWEEN SERUM COMP AND CILP CONCENTRATIONS AND MRI SUBREGIONAL CARTILAGE THICKNESS CHANGE OVER THE FIRST FIVE YEARS AFTER ACUTE ACL INJURY – DATA FROM THE KANON-TRIAL

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Purpose: In parallel abstracts, we report serum concentrations of Cartilage Oligomeric Matrix Protein (COMP) and Cartilage Intermediate Layer Protein (CILP) as well as MRI derived subregional changes in cartilage thickness over 2 and 5 years after ACL injury in the KANON cohort. The purpose of this study was to relate change in MRI cartilage thickness and the two above molecular serum biomarkers of cartilage remodeling.

Methods: 121 young active adults with an acute ACL tear were studied as part of the KANON randomized controlled trial. Sagittal MRIs (3D/WATSc) and serum samples were obtained within 5 weeks of the tear (BL), at Y2 and at Y5 follow-up; 107 (81men, 26 women; median age 25.6y; age range 18-36) had complete series of MR images. Subregional cartilage thickness was analyzed in 16 femorotibial subregions and change between BL and Y2 and between Y2 and Y5 was summarized by computing a cartilage thinning score (summarizing all negative subregion changes) and a cartilage thickening score (summarizing all positive subregion changes) in each knee, regardless of location. A total subregional femorotibial cartilage change score was also computed by summarizing magnitudes of all subregional changes, independent of their direction. Serum concentrations of biomarkers were measured with a commercially available COMP sandwich ELISA (AnaMar AB) and an in-house research competitive