association of future pain with X-ray features can be used to develop a prevention strategy for chronic pain. The public health systems can be benefit from the use of a radiological Biomarker.

### 480 SYNoviTIS IS ASSOCIATED WITH Bone MarROW AbNORMALITY IN PaTIENT WITH End-STAGE knee Osteoarthritis

A. Yusup¹, H. Kurokawa², E. Liu², R. Sadaoui², S. Hada³, M. Kinoshita¹, J. Futami¹, H. Kurosawa², Y. Shimura¹, Y. Saiita¹, Y. Takazawa¹, H. Ikeda¹, K. Kanoel¹, M. Ishijima¹,°,¹ ¹Dept. of Med. for Orthopaedics and Motor Organ, Juntendo Univ. Graduate Sch. of Med., Tokyo, Japan; ²Sportology Ctr., Juntendo Univ. Graduate Sch. of Med., Tokyo, Japan; ³Dept. of Orthopedics, Juntendo Tokyo Koto Geriatric Med. Ctr., Tokyo, Japan

**Purpose:** The degeneration and destruction of articular cartilage are associated with the progression of osteoarthritis (OA). However, the pain and a loss of joint function which are characteristics of OA are not correlated with the extent of degeneration and destruction of articular cartilage. Synovitis in OA may be a secondary phenomenon related to cartilage alterations induced by the release of degradative compounds from the extracellular matrix of articular cartilage and, presumably, bone. This could further stimulate cartilage damage. Recently, the role of synovitis in OA has attracted particular attention, as synovitis has been revealed to be one of the potential predictive factors for both structural and symptomatic progression of the disease, thus indicating its crucial role in the pathophysiology of OA. However, most of the studies focused on synovitis in OA were conducted to the patients with early to moderate stage of knee OA. We previously revealed the disability of patients with end-stage of knee OA who required TKA showed a significant correlation with the severity of synovitis in affected knee joint. However, it’s still remained unclear whether synovitis is also related to cartilage alterations in end-stage of knee OA, where articular cartilage is almost disappeared. The aim of our study was to investigate whether the joint abnormalities occurred in knee OA detected by MRI were associated with synovitis evaluated by histological analysis in patient with end-stage knee OA.

**Methods:** This study protocol was approved by the institutional review board of our university. Sixty patients with end-stage knee OA (female: 53, male: 7, 70.1y on average) who undergoing TKA were enrolled. All participants were performed with 1.5-Tesla MRI system, OA changes, such as (1) cartilage morphology, (2) BMAs, (3) bone cysts, (4) bone attrition, (5) meniscal pathology and (6) osteophytes, were scored using the whole-organ MRI scoring method (WORMS) as reported previously. The synovial samples were obtained during the operation from five regions of interest (ROIs). These ROIs included 3 in the suprapatellar recess (lateral recessROI 1, medial recess ROI 2), and just above the trochlear groove (ROI 5) and 1 each in the lateral and medial femoral gutters (ROIs 3 and 4, respectively). Six histological parameters were:

1. The thickness of synovial lining layer,
2. Subsynovial infiltration by lymphocytes and plasma cells,
3. Surface fibrin deposition,
4. Blood vessel vasodilation and blood vessel proliferation,
5. Fibrosis, and
6. Perivascular edema.

The parameters were graded as follows: 0 = none; 1 = mild; 2 = moderate; 3 = severe.

**Results:** A simple regression analysis was performed between each histological total scores and WORMS scores. While cartilage morphology scores, bone cyst scores, bone attrition scores, meniscal pathology, and osteophyte scores were not associated with histological total scores and its subcategory scores. On the other hand, BMA total score were significantly associated with histology total score (r = 0.641, p = 0.019). All patients showed BMA in medial femoro-tibial joint (MFTJ). On the other hand, twenty-six of sixty patients and sixteen of sixty patients did not show BMA in lateral femoro-tibial joint (LFTJ) and patella-femoral joint (PFJ), respectively. No significant differences of the MFTJ histology scores (ROI2 + ROI3) in patients with BMA in LFTJ in comparison to those in patients without BMA in LFTJ (p = 0.52). LFTJ histology scores (ROI1 + ROI3) of the patients with BMA in confronting LFTJ were significantly increased in comparison to those of patients without BMA in this lesion (p < 0.001). Similarly, PFJ histology score (ROI5) of the patients with BMA in confronting PFJ were also significantly increased in comparison to those of patients without BMA in this lesion (p < 0.001). Furthermore, total histological scores (SUM of ROI1 to ROI5) in patients with BMA in LFTJ were significantly increased in comparison to those in patients without BMA in LFTJ (p < 0.001).

**Conclusions:** Synovitis in OA is associated with the severity of pain in patients with primary through end-stage of knee OA. However, whether synovitis is related to cartilage alterations in end-stage of knee OA is unclear. BMAs are findings with a high signal intensity in the T2-weighted fat-suppressed images. BMAs have been also linked to pain, cartilage defects, and a progression of cartilage loss. However, the pathogenesis of BMA is still unknown. The present study indicates for the first time the association between the BMA and synovitis in patients with end-stage of knee OA.

### 481 CT Arthrography of the Human Knee to Quantitatively Measure Cartilage Biochemical Composition: Preliminary Results of an In Vitro Validation Study using Ex-Vivo Reference Standards for Cartilage Composition


**Purpose:** To non-invasively diagnose knee osteoarthritis (OA) in an early stage of disease, to follow subtle disease progression over time and to assess the efficacy of potential novel treatment strategies for OA, quantitative radiological measurements of cartilage composition have become of interest. Delayed gadolinium-enhanced MRI of cartilage, T1rho- T2-mapping, sodium imaging and gacEST are examples of MRI based techniques to measure cartilage sulphated glycosaminoglycan (sGAG) or collagen content. Recently, the ability of CT arthrography (CTa) to quantitatively measure knee cartilage composition in terms of its sGAG content has been demonstrated in an ex-vivo study using human cadaveric knee joints. Since a validation study comparing in-vivo acquired CTa outcomes against ex-vivo reference standards for cartilage composition has not yet been performed, the aim of the present study was to perform such a validation in humans with knee OA.

**Methods:** We analyzed data of 12 patients from an ongoing study in which knee OA patients (Kellgren and Lawrence grade 2-4) undergo CTa before total knee replacement (TKR). Mean X-ray attenuation values were calculated in 6 regions of interest (ROI) of the articular cartilage (medial and lateral weight-bearing (WB) femoral condyles and tibial plateau and non-WB cartilage of the condyles) (Fig. 1). Femoral and tibial cartilage was harvested during TKR and rescanned with contrast-enhanced microCT (CE-uCT). Mean CE-uCT X-ray attenuation values served as surrogate reference standard for cartilage sGAG content since it has been shown to accurately measure sGAG content compared to a reference standard for cartilage composition. We analyzed the correlation between mean CTa X-ray attenuation and mean CE-uCT X-ray attenuation with linear regression.

**Results:** Mean X-ray attenuation values of the different ROIs in the medial tibiofemoral joint ranged from 177 to 455 Hounsfield Units and from 151 to 454 Hounsfield Units in the lateral tibiofemoral compartment. Outcomes of CTa had a strong correlation with reference CE-uCT X-ray attenuation, representing sGAG content of articular cartilage in the femoral cartilage (r = 0.79; p < 0.0001; r^2 = 0.63) (Fig. 2A), in the tibial cartilage (r = 0.75; p < 0.0001; r^2 = 0.58) (Fig. 2B) and in the tibiofemoral cartilage (r = 0.78; p < 0.0001; r^2 = 0.61) (Fig. 2C).
DEGENERATION AND DESTRUCTION FOR FEMORAL ARTICULAR CARTILAGE IS PRECEDED THAN THOSE FOR CONFRONTING TIBIAL AND PATELLAR ARTICULAR CARTILAGE IN EARLY STAGE OF KNEE OSTEOARTHRITIS: A CROSS-SECTIONAL STUDY

S. Hada 1, H. Kaneko 1, R. Sadatsu 1, L. Liz 1, A. Yusup 1, M. Kinoshita 1, I. Futami 2, Y. Shimura 3, M. Tsuchiya 4, Y. Saita 1, Y. Takazawa 1, I. Ikeda 1, K. Kaneko 1, M. Ishii 1, 1 Dept. of Med. for Orthopaedics and Motor Organ, Juntendo Univ. Graduate Sch. of Med., Tokyo, Japan; 2 Sportology Ctr., Juntendo Univ. Graduate Sch. of Med., Tokyo, Japan; 3 Dept. of Orthopedics, Juntendo Tokyo Koto Geriatric Med. Ctr., Tokyo, Japan, Tokyo, Japan

Purpose: Osteoarthritis (OA) is a slowly but progressively degenerative joint disease, which is characterized by cartilage degeneration, attrition by the loss of cartilage, subchondral sclerosis, and degradation of the meniscus and bone marrow abnormality. In the initial stage of knee OA, OA changes are started in a molecular level of the articular cartilage, such as loss of proteoglycan, increased water content, and disorganization of the collagen network, probably before a morphologic change of the articular cartilage. The morphologic changes can be visualized and semi-quantified by Magnetic Resonance Imaging (MRI) and the Whole Organ Magnetic Resonance Imaging Score (WORMS), respectively. T2 mapping sequence on MRI is a technique that is sensitive to detect the early biochemical changes of water content and the disorganization of the collagen network in articular cartilage. These techniques enable us to understand a very early stage of knee OA. It is still remained unclear whether OA-induced qualitative and morphological changes of articular cartilage are simultaneously and equally occurred in the confronting femoral and tibial articular cartilage in both tibio-femoral joint (TFJ) and patello-femoral joint (PFJ). The aim of the present study was to figure out this question by qualitatively and morphologically evaluating the OA-induced articular cartilage changes using T2 mapping and WORMS technique.

Method: A total of 50 patients (mean age 59.7 years) who consulted our out-patient clinic for knee pain between May and December 2012 were enrolled in this study. The severity of knee OA was classified by Kellgren-Lawrence (K/L) grading scale based on standing extended-knee X-ray images. All patients showed either K/L grade 0, 1 or 2, and were also performed 3T MRI for the affected knee. Diagnosis of knee OA for the subjects with K/L 0 was conducted using 3T MRI according to the method by Shama et al (ARD 2013). Patients who showed less than 174° of femorotibial tibial angle (FTA) were excluded from the study. T2 mapping were calculated from a five multi-echo, spin-echo (MESE) sequence (TR = 1000ms, TE = 13.8, 27.6, 41.4, 55.2, 69 ms matrix = 384 × 384, slice thickness = 3.0mm, turbo-factor = 3.3), and the parameters were divided into 14 places of areas according to WORMS using sagittal and coronal two dimensional (2D) fat suppressed and T2 weighted image for measurement. T2 mapping sequence on MRI is a technique that is sensitive to detect the early biochemical changes of water content and the disorganization of the collagen network in articular cartilage. These techniques enable us to understand a very early stage of knee OA. It is still remained unclear whether OA-induced qualitative and morphological changes of articular cartilage are simultaneously and equally occurred in the confronting femoral and tibial articular cartilage in both tibio-femoral joint (TFJ) and patello-femoral joint (PFJ). The aim of the present study was to figure out this question by qualitatively and morphologically evaluating the OA-induced articular cartilage changes using T2 mapping and WORMS technique.

Method: A total of 50 patients (mean age 59.7 years) who consulted our out-patient clinic for knee pain between May and December 2012 were enrolled in this study. The severity of knee OA was classified by Kellgren-Lawrence (K/L) grading scale based on standing extended-knee X-ray images. All patients showed either K/L grade 0, 1 or 2, and were also performed 3T MRI for the affected knee. Diagnosis of knee OA for the subjects with K/L 0 was conducted using 3T MRI according to the method by Shama et al (ARD 2013). Patients who showed less than 174° of femorotibial tibial angle (FTA) were excluded from the study. T2 mapping were calculated from a five multi-echo, spin-echo (MESE) sequence (TR = 1000ms, TE = 13.8, 27.6, 41.4, 55.2, 69 ms matrix = 384 × 384, slice thickness = 3.0mm, turbo-factor = 3.3), and the parameters were divided into 14 places of areas according to WORMS using sagittal and coronal two dimensional (2D) fat suppressed and T2 weighted image for measurement. T2 mapping sequence on MRI is a technique that is sensitive to detect the early biochemical changes of water content and the disorganization of the collagen network in articular cartilage. These techniques enable us to understand a very early stage of knee OA. It is still remained unclear whether OA-induced qualitative and morphological changes of articular cartilage are simultaneously and equally occurred in the confronting femoral and tibial articular cartilage in both tibio-femoral joint (TFJ) and patello-femoral joint (PFJ). The aim of the present study was to figure out this question by qualitatively and morphologically evaluating the OA-induced articular cartilage changes using T2 mapping and WORMS technique.

Results: This study protocol was approved by the institutional review board of our university. Radiographic OA severities of the patients were K/L grade 0: 3, K/L grade 1: 27, K/L grade 2: 20. Twenty-three of fifty patients were male, while remaining twenty-seven patients were female. No significant differences of FTA were observed between the patients with three different K/L grades. T2 values of the femoral cartilage were significantly higher than those of the confronting tibial cartilage of the patients with early stage of knee OA (p < 0.001) [Odds ratio (OR) of T2 values in femoral cartilage was higher than that of tibial cartilage: infinity, p < 0.001]. T2 values of the femoral cartilage were significantly higher than those of the confronting patellar cartilage of the patients (p < 0.001) [OR: infinity, p < 0.001]. WORMS cartilage score of the femur were significantly higher than those of both the confronting tibia and patella of the patients with early stage of knee OA [TFJ: p < 0.001; OR: 4.8 (95% CI: 2.2-10.4), p < 0.001]; PFJ: p < 0.001; OR: 3.0 (95% CI: 1.5-6.1), p < 0.01]. WORMS osteophyte scores of the femur were significantly higher than those of both the confronting tibia and patella of the patients with early stage of knee OA [TFJ: p < 0.001; OR: 4.1 (95% CI: 1.9-8.9), p < 0.001]; PFJ: p = 0.011; OR: 2.1 (95% CI: 1.1-4.0), p < 0.01].

Conclusions: Our preliminary results suggest that CTa can accurately measure sGAG content of articular cartilage in human knee joints in vivo. The coefficient of determination, however, is only moderate and therefore CTa outcomes are likely to be also influenced by other composites of cartilage, e.g. collagen. Despite the use of intra-articular contrast agent and ionizing radiation, CTa might become a cheap and fast alternative to MRI based techniques to quantitative measure cartilage composition in patients with contra-indications to undergo MRI.