three cases from each groups one year after the surgery and revealed that cartilage damage deteriorated in all three cases of BCL (+).

**Conclusions:** Fleming et al. reported that dGEMRIC index decreased especially at medial femoral condyle after ACL rupture. This means that cartilage compositional change is already there after ACL injury. The present results showed that the longer the interval between the initial traumatic episode and the reconstruction surgery becomes the more likely meniscal damage is, leading to cartilage damage described here as the “Barcode-like lesion” at the medial femoral condyle. This cartilage damage did not essentially improve one year after the surgery.

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**PREVALENCE OF IMPINGEMENTS SIGN IN 1992 HIPS FROM THE MROS COHORT: PRELIMINARY RESULTS.**

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**Background and aims:** Femoroacetabular impingement (FAI) is a recently appreciated cause of hip pain and early, rapidly progressive osteoarthritis (OA). The purposes of this study are to evaluate the prevalence of FAI in elderly men and to correlate radiographic FAI with radiographic hip OA and hip pain.

**Material and methods:** Pelvic radiographs were obtained at visit 2 of MrOS. At this time 1992 hip radiographs have been evaluated. Each hip was assessed for cam type FAI by measurement of the caput-collum-diaphysis (CCD) angle and impingement slope as well as for pincer type FAI by measurement of the impingement angle and lateral center-edge angle (CE). Radiographic hip OA was assessed by expert readers and summary grades (modified Croft) 0-4 were recorded. Pain variables and covariates were collected at study visit 2. Logistic regression was used to evaluate the association of FAI and prevalent radiographic hip OA, adjusted for age, race, and body mass index.

**Results:** The cohort ages ranged from 69 and 93 years with a mean of 76.5 years. Reliability for radiographic endpoint assessments by Cohen’s kappa values for intra-observer agreement on categorical classification was calculated: 0.62, 0.78, 0.84, and 0.86 for impingement slope, impingement angle, CE and CCD angles, respectively. The Cohen’s kappa values for inter-observer agreement on categorical classification were 0.60, 0.60, 0.85, and 0.65 for impingement slope, impingement angle, CE and CCD angles, respectively. The prevalence of FAI pincer and cam or mixed types were respectively. The prevalence of FAI pincer and cam or mixed types were

**Discussion:** FAI is prevalent in elderly men and is associated with radiographic hip OA. We determined that the radiographic criteria for the pincer type of FAI is associated with the prevalence and severity of hip OA, and that the CCD angle is associated with radiographic hip OA.

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**LARGE-SCALE ANALYSIS OF THE TRANSCRIPTIONAL RESPONSE OF CHONDROCYTES TO MECHANICAL STRESS**

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**Purpose:** Mechanical stress (stretch) is one of the main actors of cartilage homeostasis and osteoarthritis pathogenesis. Little is known about the underlying molecular mechanisms involved in the response of articular chondrocytes to mechanical stress. Several studies have described the precise signaling pathways of stretch stress applied on chondrocytes, but they focused on only a few previously chosen molecular targets. We aimed to screen, using a large-scale approach, the global gene expression profiles of articular chondrocytes submitted to stretch stress.

**Methods:** Primary rabbit articular chondrocytes from 4-week-old female New Zealand white rabbits cultured in monolayer at high density were subjected or not to equibiaxial stretching (5%, 1 Hz) for 20 hours, applied by using the Flexcell® system (FX-3000™) and total RNA was extracted. Seven independent experiments were done. RNA from stretched and static chondrocytes underwent microarray assay using Rabbit Genome Oligonucleotides Micro-arrays 4X4K (Agilent Technologies). A gene was considered differentially regulated between stretch and static conditions if the ratio between these two conditions was more than two-fold with a P value less than 0.05 (n = 7). Gene expression was also examined by real-time quantitative RT-PCR and protein expression by western blot analysis.

**Results:** We identified 95 up-regulated genes and 169 down-regulated genes in response to stretch stress, among which 31 and 50, respectively, were known genes in the rabbit genome. Eight of the up-regulated genes and eleven of the down-regulated genes showed greater than four-fold change in expression between stretch and static conditions. The validity of our micro-array analysis was confirmed by qRT-PCR and western blot. Some of the modulated genes are involved in inflammation, cell death and extracellular matrix degradation in normal and osteoarthritis cartilage, so their modulation by mechanical stress was not surprising. However, some identified targets with unknown function in cartilage may have a role in cartilage homeostasis and osteoarthritis pathogenesis.

**Conclusions:** Large-scale analysis of the transcriptional response of chondrocytes to mechanical stress highlighted new molecules possibly implicated in osteoarthritis pathogenesis.

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**LOW-INTENSITY PULSED ULTRASOUND INHIBITS MESSENGER RNA EXPRESSION OF MATRIX METALLOPROTEINASE-13 INDUCED BY INTERLEUKIN-1 β IN INTENSITY-DEPENDENT MANNER ON CHONDROCYTES**

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**Purpose:** Low-intensity pulsed ultrasound (LIPUS) has been studied about its ability which promotes anabolic reactions like collagen and aggrecan synthesis on the articular cartilage. However, it is still unknown about the effective intensity of LIPUS on articular cartilage degradation factors, and the effect of LIPUS on the articular cartilage with the inflammatory symptoms of several levels. The purpose of this study is to investigate the immediate effect of LIPUS using several intensities on chondrocytes accompanied by the inflammatory reaction induced by IL-1β.

**Methods:** Chondrocytes were aseptically isolated from rat knee joints (Wistar, 12 week-old). All procedures were approved from Institutional Animal Care and Use Committee in Kyoto University (Kyoto, Japan). After
expanding chondrocytes, the chondrocytes were subcultured into 6 well culturing dishes at $4 \times 10^5$ cells/well. When cells grew into 80-90% confluent, the culture medium was changed for serum free medium or serum free medium with IL-1β (100pg/ml or 1ng/ml concentration). LIPUS treatment at 0, 7.5, 30, 120mW/cm$^2$ intensity was applied for 20 minutes. Total RNA was extracted immediately after 1 hour incubation. To elucidate the inhibitory effect of LIPUS on the articular degradation, the mRNA expression of MMP13 was analyzed by real-time PCR method. The condition of 0mW/cm$^2$ intensity without IL-1β was set as 1, and each of other conditions was shown as the relative amount. To compare any significant differences between control sample (LIPUS intensity 0mW/cm$^2$ without IL-1β) and LIPUS-stimulated sample, the test results were statistically analyzed using the Student’s t-test. The difference observed was considered to be significant when p value is lower than 0.05.

**Results:** LIPUS stimulation inhibited the mRNA expression of MMP13 induced by IL-1β of 100pg/ml concentration in intensity-dependent manner (0mW/cm$^2$: 4.67±1.60, 7.5mW/cm$^2$: 3.20±0.24, 30mW/cm$^2$: 2.06±0.55, 120mW/cm$^2$: 1.30±0.29). However, there were no significant differences when expression of MMP13 was induced by IL-1β of 1ng/ml concentration.

**Conclusions:** Our results indicate that LIPUS has a possibility to inhibit IL-1β induced mRNA expression of MMP13 in intensity-dependent manner on rat chondrocytes. Therefore, we may be able to use LIPUS as a daily useful modality to protect articular cartilage.

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**Meniscus, Muscle, Tendon & Ligament Biology**

THE MICRO-STRUCTURAL RESPONSE OF TENDON FASCICLES TO APPLIED STRAIN IS ALTERED WITH AGEING

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**Purpose:** The objectives of this study were to investigate the microstructural strain response and cell strain environment in the injury prone equine superficial digital flexor tendon (SDFT) and to determine if this response alters with increasing age. We hypothesise that the fibre level response to applied strain is heterogeneous and varies with ageing, with the result that cells within aged tendon are exposed to an altered strain environment.

**Methods:** Fascicles were dissected from the SDFT of 4 horses aged 4 to 6 years, and 4 horses aged 18 to 20 years (n=8 from each tendon). Fascicles were incubated in the collagen stain 5-dichlorotriazynyl fluorescein, washed in PBS and secured in a tensile straining rig. Each fascicle was viewed under a confocal microscope using a x20 objective, and a grid was photobleached onto the fascicle (Fig. 1 A). Images of the fascicle were taken at 2% strain increments up to 10% (Fig. 1 B) and deformation of the grid at each strain increment quantified (Fig 1. C) by measuring changes in longitudinal strain ($x + \Delta x$), perpendicular strain ($y + \Delta y$), deviation from the vertical gridline ($d_1 + d_2$) and angle of the horizontal gridline ($\Delta \gamma$). Statistical significance was set at $p<0.05$ and is indicated by *. Data is displayed as mean ± SEM.

**Results:** Local longitudinal strains were heterogeneous, consistently smaller than applied strain, and did not alter with increasing age (Fig. 2). Large compressive strains were measured perpendicular to the direction of applied strain; the magnitude of these strains decreased with increasing subject age ($p<0.016$, Fig. 3).

Deviation from the vertical gridline increased with each strain increment (Fig. 4), indicating some sliding between adjacent fibres.

The amount of fibre sliding did not change with increasing horse age. However, rotation of the horizontal gridline, which increased with each strain increment, did decrease significantly with age, at and above 8% strain ($p<0.033$, Fig. 5).