could be a relative increase in trabecular bone volume, which decrease in advance OA. For the tibias, only the SMI was increased in the ACLT knees versus the controls. It might be that 12 weeks is not sufficient time to detect OA trabecular bone microarchitecture changes in the tibia after the Pond-Nuki surgically induced secondary OA in the canine model. This study quantitatively analyzed the trabecular bone in the anterior cruciate ligament transection (ACLT) Pond-Nuki dog model. The results may help establish the standard characteristics of the knee joint trabecular bone microarchitecture upon development of OA, and to provide a greater understanding of OA from the clinical viewpoint and to aid in its treatment.
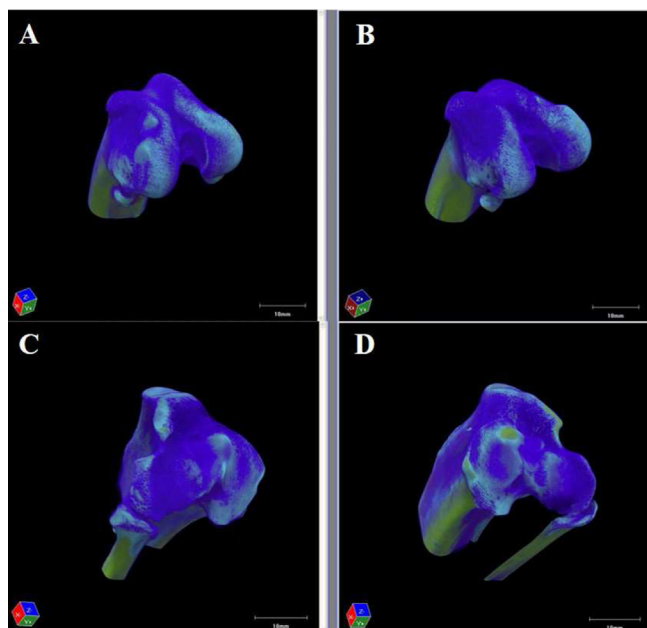

Figure 1. showing 3D BMD color maps for the control femur (A) and tibia (B) and the ACLT femur (B) and tibia (D). The ACLT femur (B) shows lower BMD than the control (A).

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MAPPING ARTICULAR CARTILAGE BIOMECHANICAL PROPERTIES OF NORMAL AND OSTEOARTHRITIS MICE USING INDENTATION

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Purpose: Due to their size (~1mm), mouse models pose significant challenges to map biomechanical properties over their articular surfaces. The purpose of this study was to determine if an automated indentation technique could be used to map the biomechanical properties of the articular surfaces in murine knees and to identify early alterations of the articular cartilage of a mouse strain (STR/ort) that spontaneously develops osteoarthritis (OA) on the medial side of their knees.

Methods: The biomechanical measurements were performed ex vivo, on the left femoral condyles and tibial plateaus of five healthy Balb/c males (age of 12-15 weeks) and five age- and sex-matched STR/ort mice, using a 3-axis mechanical tester (Mach-1 v500css, Biomomentum, Laval) equipped with a multiple-axis load cell. Indentation measurements (30-42/surfaces) were performed using a 0.35 mm diameter spherical indenter (30 μm indentation in 1 second with 20 seconds relaxation). Following biomechanical testing, the articular surfaces were fixed in 4% paraformaldehyde for histological assessment. Data reported is the structural stiffness at an indentation depth of 10μm. To compare the structural stiffness between healthy and OA-developing animals each articular surface were divided into 4 regions, exterior medial (I), inner medial (II), inner lateral (III) and exterior lateral (IV). Data is reported as the mean ± SE (n= 5) for each of these regions. Statistical analysis was performed by ANOVA.

Results: In healthy animals, mapping of the structural stiffness at an indentation depth of 10 μm showed a spatial distribution similar to that of larger animals (Figure 1A,B, inserts). The structural stiffness of the lateral and inner half of the medial condyles (Figure 1A) was similar in OA and healthy mice. The stiffness of the exterior lateral plateau was also not significantly different OA and healthy mice. In contrast, the stiffness of the exterior half of the medial condyle in OA mice (5.9±0.7 N/mm) was significantly lower than that of the healthy mice (10.2±1.1 N/mm, ANOVA, p<0.05). The structural stiffness of the exterior medial condyle and the inner half of the lateral plateaus in OA mice was inferior to that of healthy mice (ANOVA, p<0.05).

Conclusions: This study shows that this automated indentation technique can map the biomechanical properties of murine knee joints. The mapping of mechanical properties shows similar distribution patterns to those previously observed for larger species (human, sheep and rat). The identification of cartilage regions with lower structural stiffness, at sites known to develop OA in the STR/ort strain, suggests this method can be used to identify and characterize OA affected articular surfaces. Studies are ongoing to validate, by histology, the cartilage quality of the affected areas. These results show that indentation mapping could be used in mouse models to test the efficacy of drugs aiming to inhibit cartilage degradation or improving its healing in OA or following a joint injury.
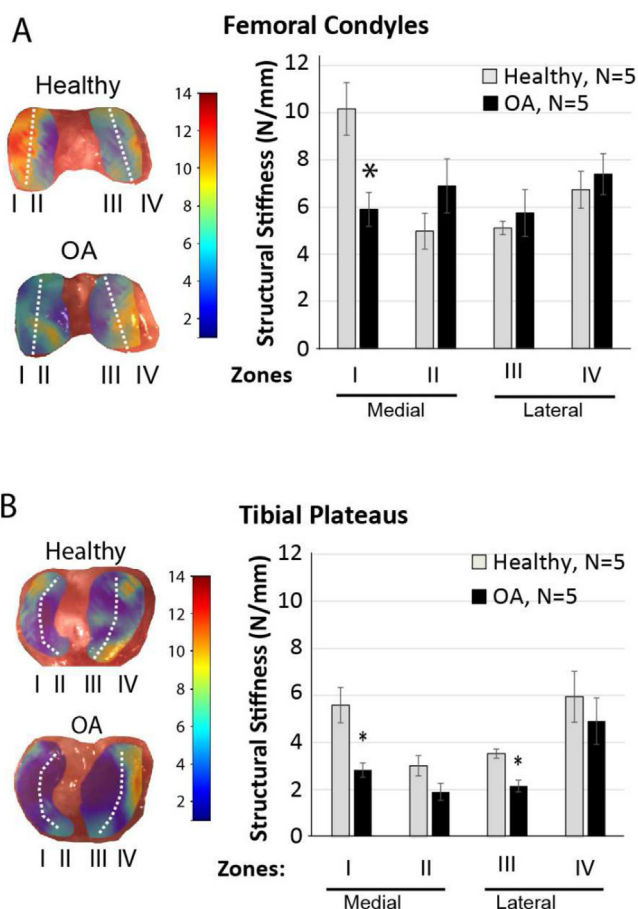

Figure 1. **Quantification of the structural stiffness at 10 μm indentation for the left (A) Condyles and (B) tibial plateaus**. Asterisk indicates p<0.05, ANOVA.

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A 3D MRI STUDY OF CHANGES IN THE MENISCI OF THE OA KNEE: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: The meniscus is crucial to the normal functioning of the knee, and damage or compromise to the meniscus is an important component in the development of knee osteoarthritis (OA). Quantitative

measurement of the damage to the meniscus is likely to serve as a useful biomarker of OA progression. In principle, the meniscus is a simple shape; however damage to the meniscus may appear as loss of meniscal volume, extrusion of the meniscus, or a general failure of meniscal competence, resulting in the spreading of the surface.

This study employed statistical shape modelling to study a number of potential measures of meniscal deterioration within a one-year period. Additionally, statistical models were used to visualise the areas of the menisci which underwent most change.

Methods: 88 subjects with medial OA were identified from the NIH-OAI dataset. Subjects had K-L scores of 2 or 3; medial JSN > lateral JSN, medial osteophytes and ≥1° of varus mal-alignment: 43 were female. Baseline and 12 month DESS images were manually segmented for the white meniscus of the medial and lateral menisci. Segmenters were blinded to time point but not to subject, using EndPoint software (Imorphics, UK). Segmented contours were converted to 3-D surfaces using a marching quads algorithm, followed by quadratic smoothing. Bone surfaces in the tibia were identified by automated segmentation using active appearance models (AAMs). A dense set of anatomically corresponded points was automatically identified on the tibia bone surfaces, allowing mapping of meniscal change both within and across subjects, by using the tibia as a reference surface.

Several measurements were taken (see Figure 1): (a) the total volume of the entire meniscus including the meniscal attachment, (b) the trimmed menisci: the volume of the meniscus, after the attachments are systematically removed, (c) the height (thickness) of the meniscus above the tibia in the anterior, central and posterior sections of meniscal contact, (d) the volume of medial meniscal extrusion beyond the edge of the medial plateau, performed on medial side only, (e) the area of the meniscal window, and the proportion of that window to the area normally covered by cartilage (tAB). Change from baseline for each measure was measured using a paired students t-test.

Population maps of the average height of the menisci above the tibia were prepared, and areas of most significant change identified.

Results: Measures of meniscal volume change were mostly not significant, with the exception of the trimmed lateral meniscus. Change in the extruded volume of medial meniscus was also not significant. (Table 1).

Change in the size of the medial meniscal window, either measured in mm^2 or as a percentage of tAB were highly significant; the lateral meniscal window showed no change.

Change in meniscal height above the tibia (meniscal thickness) was significant in the posterior regions of both the lateral and medial menisci, and is visualised in Figure 2. The area which showed the most significant change in height was at the posterior of the medial meniscus.

Conclusions: Quantitative assessment of the menisci is desirable in studies of knee OA, and it is important to select a responsive measure which is biologically meaningful. Measures of meniscal volume and meniscal extrusion are very noisy, due to the many shapes which the damaged meniscus may adopt. Extrusion of menisci in this cohort, measured using careful 3D measurements did not show significant change, which is disappointing. The primary location of meniscal change in the posterior medial meniscus indicates that searching for meniscal extrusion at the most medial point of the tibia may not be the best approach.

The most promising measure of meniscal change from this study is the meniscal window, measured either as an area, or as a proportion of the cartilage plate. This measure is very responsive, and should be easier to perform for research groups without access to specialist 3D measurement. Additionally, measurements of meniscal height over the tibia, used in a similar manner to the method used for articular cartilage thickness measurement, appears to provide a promising measure of change.
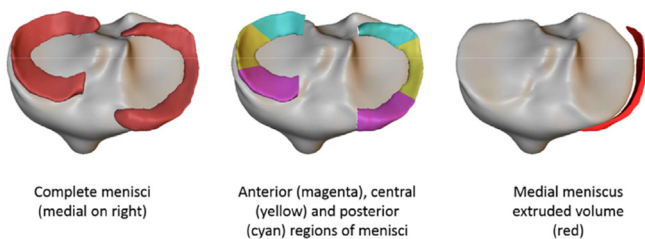

Figure 1. Meniscal measurement strategies: figure show (from left to right), total meniscus volume, sections used for meniscal height (thickness) and extruded volume.
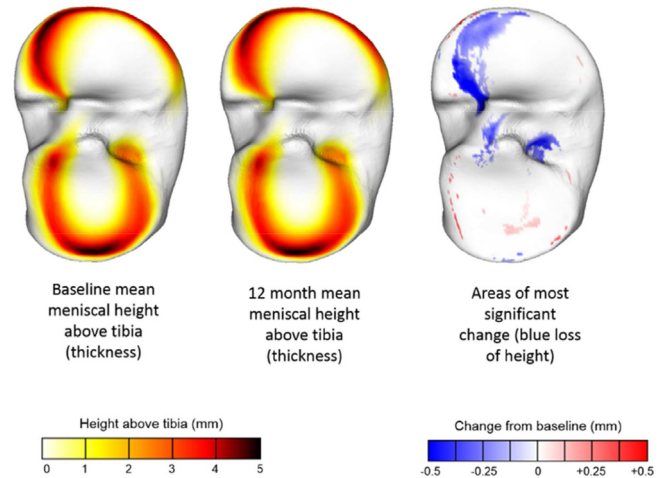

Figure 2. Change in meniscal height above the tibia at baseline and 12 months, with most significant area of change shown at right.

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ANTERIOR DOMINANT JOINT SPACE NARROWING IN THE DYSPLASTIC HIP OSTEOARTHRITIS

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Purpose: Hip osteoarthritis (OA) is mainly derived from developmental dysplasia of the hip in Japan. In daily clinical practice, a frontal radiograph of the hip joint is considered the most important image. However, this image only allows the observation of the joint from a single viewpoint. Sagittal CT images contain information that cannot be found by a frontal radiograph. We have investigated the characteristics of the joint space narrowing in a sagittal plane in the dysplastic hip OA.

Table 2
Change in various meniscal measures over 12-month period. Change for each measure was assessed using a pairwise Student's t-test. SRM = standardised response mean (mean change/SD of change).

Meniscus	Measure	0 months	12 months	Change	p value	SRM
Medial Meniscus	Total Volume (mm^3)	2566	2522	-43	0.223	-
Lateral Meniscus	Total Volume (mm^3)	2478	2476	-3	0.877	-
Medial Meniscus	Trimmed Volume (mm^3)	2345	2338	-7	0.815	-
Lateral Meniscus	Trimmed Volume (mm^3)	1582	1626	+46	0.002	0.34
Medial Meniscus	Extruded Volume (mm^3)	925	956	+34	0.130	-
Medial Meniscus	Meniscal Window Area (mm^2)	789	814	+25	$<10^{-4}$	-0.51
Lateral Meniscus	Meniscal Window Area (mm^2)	532	532	0	0.888	-
Medial Meniscus	Meniscal Window Area %	67.7	69.3	+1.66	$<10^4$	-0.45
Lateral Meniscus	Meniscal Window Area %	51.7	51.6	+0.1	0.725	-
Medial Meniscus	Anterior Thickness (mm)	0.69	0.70	+0.01	0.755	-
Medial Meniscus	Central Thickness (mm)	0.87	0.83	-0.04	0.050	-0.21
Medial Meniscus	Posterior Thickness (mm)	2.07	1.96	-0.10	0.002	-0.34
Lateral Meniscus	Anterior Thickness (mm)	1.72	1.76	+0.04	0.036	0.23
Lateral Meniscus	Central Thickness (mm)	1.84	1.86	+0.02	0.288	-
Lateral Meniscus	Posterior Thickness (mm)	1.40	1.46	+0.06	0.0005	0.38