Table 1
Details of the new synovitis scoring system.

Score	Synovitis Score Parameters			
	Hoffa Synovitis	Joint Effusion	Synovial Thickening (measured when JE > 0)	Synovial Proliferation (measured when JE > 0)
0	Normal	< 2mm	Normal, almost invisible	(NA)
1	Mild hyperintensity	≥ 2mm and < 5mm	< 2mm	Smooth
2	Moderate hyperintensity	≥ 5mm and < 10mm	≥ 2mm and < 4mm	Mild irregularity, bands, small bodies
3	Severe hyperintensity	≥ 10mm	≥ 4mm	Irregular villonodular proliferation, bands, large bodies

Table 2
Prevalence of each score (# of patients).

Score	Prevalence			
	Hoffa Synovitis	Joint Effusion	Synovial Thickening	Synovial Proliferation
0	3	18	2	(NA)
1	22	14	24	4
2	18	11	4	22
3	5	5	0	4

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EFFECTS OF TISSUE CALCIFICATION DURING OSTEOARTHRITIS ON EXTRACELLULAR MATRIX AND CARTILAGE STIFFNESS

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Purpose: In a previous study we showed that osteoarthritic changes of human articular cartilage are accompanied by tissue calcification, which correlates with disease severity. During this pathological process, chondrocytes undergo phenotypic changes from a resting state towards hypertrophy, recapitulating endochondral ossification. Here, we investigated, if the calcified osteoarthritic tissue exhibits altered biomechanical properties compared to the non calcified osteoarthritic samples, which might contribute to disease severity.
Methods: Formalin-fixed, paraffin-embedded sections of human articular knee cartilage from eight different donors with variable grades of osteoarthritis (ranging from OARSI grade 0-6) and varying grades of calcification (0-2% of total articular cartilage) were analyzed via histology and immunohistochemistry. Total calcification was measured via digital-contact radiography (DCR) to detect macro-calcification, whereas micro-calcification was evaluated via von-Kossa staining. Alcian blue (pH1.0)/PAS staining was performed to visualize the negatively charged proteoglycan content and antibodies against certain subspecies of chondroitin sulfate disaccharide units (ΔC0S, ΔC4S and ΔC6S, respectively) were used to further analyze alterations of the glycosaminoglycan chains. In addition, unfixed cartilage samples were examined for their compressive stiffness using atomic force microscopy and the results were correlated with disease state and grade of calcification.
Results: With increasing disease severity, but without signs of calcification, the negative charge of the tissue decreases, as indicated by a decreased Alcian blue staining. Intriguingly, we found an enhanced Alcian blue staining in samples, if osteoarthritic changes were accompanied by calcification of the matrix. Therefore, we investigated the sulfation pattern of proteoglycans. In all samples, no staining for ΔC0S was detectable, regardless of disease state and grade of calcification. Articular cartilage without calcification and no signs of osteoarthritis showed a homogenous staining for ΔC4S within the superficial layer and the upper part of the middle zone, but no staining in the deeper parts of the tissue, whereas almost no staining for ΔC6S could be observed. Upon increasing disease severity (OARSI ≤2) but without calcification, ΔC4S staining showed no striking differences compared to OARSI grade 0 tissue, but a slight increase in ΔC6S staining was visible. These samples showed a decrease in mean compressive stiffness (down to 60 kPa) compared to non calcified OARSI grade 0 tissue (100 kPa). In osteoarthritic samples (OARSI ≥2) accompanied by increasing tissue calcification, the staining for ΔC4S increased and also extended into the deeper cartilage zones, together with a distinct increase in ΔC6S staining. Interestingly, the compressive stiffness in these samples was much higher (up to 190 kPa) compared to the non-calcified osteoarthritic cartilage samples or the control cartilage.
Conclusions: We could confirm in this study, that due to enhanced catabolic processes and the resulting matrix degradation during osteoarthritis, the compressive stiffness of osteoarthritic tissue decreases with increasing disease severity. Interestingly, osteoarthritic tissue with increasing calcification exhibits increased compressive stiffness and increased extracellular matrix sulfation. If the increase in compressive stiffness is a direct consequence of calcification or an indirect, because of enhanced sulfation of the tissue, has to be further investigated.

[1] The first two authors contributed equally to this work.

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A REFERENCE DATABASE OF CARTILAGE T2 VALUES IN KNEES WITHOUT CARTILAGE DEGENERATION, AND DIFFERENCES IN CARTILAGE T2 BY DEMOGRAPHICS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: The purpose of this study was 1) to establish a gender- and BMI-specific reference database of cartilage T2 values, and 2) to assess the associations between cartilage T2 values and gender, BMI and age in knees without radiographic Osteoarthritis (OA) (Kellgren-Lawrence (KL) 0/1) and without morphological evidence of degeneration on 3T MRI.
Methods: 481 subjects between the ages of 45-65 years with KL 0/1 at baseline in the study knee were selected from the Osteoarthritis Initiative database. Baseline morphologic cartilage MRI readings whole-organ magnetic resonance imaging scores (WORMS) and T2 measurements were performed in the medial femur, lateral femur, medial tibia, lateral tibia, and patella compartments. We analyzed joint compartments with WORMS cartilage scores of 0-1 and applied a logarithmic transformation to obtain the 5th–95th percentile values for cartilage T2. Linear regression models were used to assess the relationship between (1) cartilage T2 and age (adjusted for gender, BMI, WOMAC pain score, and clinical site), (2) cartilage T2 and gender (adjusted for age, BMI, WOMAC pain score, and clinical site), and (3) cartilage T2 and BMI (adjusted for age, gender, WOMAC pain score, and clinical site) after log transformation.
Results: Within each compartment, there was substantial T2 variability among subjects (~10ms range between the 5th and 95th percentiles) (Table 1). Overall, a positive association between cartilage T2 and both age and BMI was observed (Table 1, Fig. 1). The association between age and T2 was most pronounced in the medial femur (1.40% increase in median T2/10 years, p=0.050,) and the patella (3.27% increase in median T2/10 years, p=0.009) (Fig. 1). A positive association between BMI and cartilage T2 was evident in all cartilage compartments and was most pronounced in the lateral tibia (5.33% increase in median T2/5 kg/m^2 increase in BMI, p<0.0001). Obese subjects (BMI=30-45 kg/m^2) had significantly higher (p<0.02) mean T2 values than subjects with a "normal" BMI" (BMI=18-24.9 kg/m^2) and subjects that were "overweight" (BMI=25-29.9 kg/m^2) in the lateral tibia, medial femur, and medial tibia compartments. When investigating the association between gender and cartilage T2, we observed that females had slightly higher cartilage T2 values than males in a majority of compartments; however, the differences were only significant in the medial femur (p<0.0001) (Table 1).
Conclusions: This study established the first reference database of cartilage T2 values in a large sample of morphologically normal cartilage plates in knees without radiographic OA. While higher BMI was most significantly associated with higher knee cartilage T2, we also observed