location of mJSW) there is a steep change in the JSN profile for KL3 subjects and a crossing of the Non OA and KL2 plots. The Std Dev of the measurements, are relatively consistent from 50 to 100%.

<table>
<thead>
<tr>
<th>mJSW narrowing</th>
<th>aJSN 51–90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Std Dev</td>
</tr>
<tr>
<td>KL0</td>
<td>−0.07</td>
</tr>
<tr>
<td>KL2</td>
<td>−0.14</td>
</tr>
<tr>
<td>KL3</td>
<td>−0.43</td>
</tr>
</tbody>
</table>

Conclusions: This study is unique in that it measured the JSN profile from Lyon schuss X-rays. The range of 51%–90% for the aJSN measurements was chosen because it was an area of fairly consistent narrowing as well as low Std Dev for the measurements. For KL3, both mJSN and aJSN 51–90% showed significant change but the latter had a higher SRM and hence is potentially more sensitive. While the Non-OA had a significant and unexpected change in JSN 51–90% it should be noted that direct comparisons between the two methods were not significantly different. The aJSN measures may provide additional information regarding OA progression in the medial compartment to mJSN narrowing alone and further investigation is warranted to determine how these measures reflect the complicated underlying biological progression of OA.

**383** ASSESSMENT OF CARTILAGE UNLOADING BY QUANTITATIVE T2 MAPPING OF KNEE CARTILAGE: INITIAL RESULTS ON THE DIFFERENTIATION OF HEALTHY AND ALTERED ARTICULAR CARTILAGE

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**Purpose:** Biomechanical behaviour of articular cartilage in-vivo is hardly to assess. However, taking into consideration that walking and standing is loading, hence deformation of collagen structure and water content changes after rest. T2 mapping is an adequate approach for the evaluation of collagen structure and water content. The goal was to use T2 mapping and its zonal assessment for evaluation of unloading during a one hour MR scan in healthy volunteers, patients with cartilage defect and in the follow-up after cartilage repair (MACT).

**Methods:** 3T MRI was performed using a multi-echo spin-echo (SE) in 10 volunteers and Twenty-five patients: Eight patients pre-operatively with a single partial thickness cartilage defect on the femoral condyle and 17 patients 20.7±16.9 months after MACT. T2 relaxation times were obtained using a pixel wise, mono-exponential (NNLS) fit analysis. T2 sequence was obtained at the beginning (pre-scan) and at the end (post-scan) of the clinical MR examination, including high resolution morphological scan. The time gap between both T2 measurements was 45 minutes. The patients were required to rest before the MR scan, so daily activity and walking to the scanner was used as loading. were enrolled in this study. Within the knee. Regions of interest (ROI) analysis were manually done in consensus and areas of cartilage damage/cartilage repair and healthy control cartilage were identified using the morphological images as well as surgical reports. All areas were located within the weight bearing zone of the femoral cartilage. For further evaluation on the zonal variation, the ROIs were divided into two equal sized deep and superficial regions.

**Results:** For healthy seen cartilage quantitative T2 values for the pre-unloading evaluation were 50.9±13.1 ms for the deep zone and 58.0±10.9 ms for the superficial zone. After 45 minutes T2 values showed not significant increase to 51.2±13.3 ms for the deep aspects and 57.7±12.8 ms for the superficial aspect. The increase between deep and superficial T2 values was significant. Pre-operative patients show initial significant lower T2 values with 41.5±6.0 ms for the deep zone and 50.4±6.4 ms for the superficial zone, however after unloading, values increased up to 52.6±14.3 for the deep and 58.5±14.3 for the superficial aspect. The cartilage repair tissue after MACT showed pre values of 51.9±11.6 ms for the deep cartilage zone and 55.9±14.1 for the superficial (Pre and Post T2 and Substraction Image shown in Figure 1).

Thus there was no significant difference from the healthy seen cartilage sites, the post-unloading scan showed a significant increase in T2 values for deep (56.3±14.1 ms) and even clearer for superficial (90.8±18.5 ms) aspects of cartilage repair tissue.

**Conclusions:** Quantitative T2 relaxation can be used to assess pre- and post unloading values of articular cartilage in a clinical setup. Furthermore the presented approach of two SE-T2 scans at the beginning and the end of an MR scan might give additional information on the constitution of cartilage and might help to differentiate between healthy and affected articular cartilage. However it appears that changes in water content and anisotropy over time are different in healthy cartilage compared to altered cartilage. Larger patient groups have to elucidate a potential clinical impact of the presented approach.

**384** MAGNETIC RESONANCE IMAGING FOR THE MEASUREMENT OF STRUCTURE MODIFICATION IN KNEE OSTEOARTHRITIS

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**Purpose:** The objective of this pilot study was to explore the structure modifying effect of Structure® (Chondroitin Sulfate) in knee osteoarthritis (KOA) using quantitative and qualitative magnetic resonance imaging (MRI).

**Methods:** Multicenter, double-blind, placebo-controlled, parallel-group study. Forty-three patients over 50 years with KOA (ACR criteria), graded II or III on Kellgren-Lawrence scale, were randomized to receive either Structure® 500 mg (N=22) or placebo (N=21) twice daily for 48 weeks. Clinical symptomatology was assessed throughout the Lequesne index and VAS for pain during daily activities, at baseline 24 and 48 weeks. In parallel 3D MRI imaging was acquired at baseline, 24 and 48 weeks. Global and compartments cartilage volume was quantified as well as other MRI features such as joint cartilage abnormalities, meniscal lesions, ligaments abnormalities, synovials, synovial effusion, osteophytes, subchondral cysts, popliteal cysts and subchondral oedema. Intra- and inter-reproductibility of MRI was tested by the Spearman correlation coefficient for quantitative assessments and by the kappa coefficient for qualitative assessments. Treatment groups were compared by an analysis of covariance (ANCOVA) with baseline value as a covariate.

**Results:** Demographic data for the Structure® and placebo groups were as follow: mean (SD) age 63.6 (8.2) and 66.5 (8.1) respectively, female 72.7% and 57.1%. At baseline clinical signs and total volume of cartilage were comparable in both groups: Mean Lequesne index was 9.6 (3.4) in the Structure® group and 10.4 (3.6) in the placebo, pain VAS 50.9 (15.0) and 55.4 (14.5) and mean total cartilage volume was 12969.8 mm³ (3657.7) and 13916.9 mm³ (4439.2). At baseline we observed a highly significant correlation for the assessment of cartilage volumes, number of cysts and osteophytes, the Spearman coefficients ranging from 0.951 to 0.980 for the within investigator and from 0.714 to 0.957 for the between investigator. Between investigator reproducibility.
was slightly lower, but still acceptable, for the assessment of synovial effusion, cartilage abnormalities, ligaments abnormalities and meniscus fissure grade. A correlation was observed between pain VAS score at baseline and the subchondral oedema \( r = 0.24 \). However, due to the very high variability of measurements, no significant treatment effect could be shown.

No statistically significant differences between groups were observed for subchondral oedema, osteophytes, subchondral cysts, meniscus fissure grade, cartilage abnormalities, synovitis or synovial effusion. No correlations were evidenced between key MRI parameters changes after 48 weeks and clinical symptomatology.

Conclusions: Despite the weak correlation between clinical symptoms and MRI, the observed difference in the evolution of cartilage volume between the 2 groups could reflect a structure modifying effect of Structum®. Hence, a larger and longer longitudinal study will be needed to confirm MRI findings.

This pilot study confirm the usefulness of quantitative and qualitative MRI as a sensitive tool to assess a structure modifying drugs in KOA.

### 385 IDENTIFICATION OF PRE-CLINICAL OSTEOARTHRITIS: A SUBCOHORT IN THE ROTTERDAM STUDY


**Purpose:** The major risk factors for osteoarthritis (OA) are known, allowing to identify high-risk groups. Several biochemical markers and imaging techniques are available that may identify early signs of OA. Because of the progressive character of OA and severe disability and pain to which it can lead, early treatment in a pre-clinical stage should be explored. This can be achieved if we can easily identify: (a) people in pre-clinical stage of OA, (b) people at extreme high risk, and (c) determinants for a deterioration into a clinically manifest OA.

Therefore, the present study has two major aims: (1) to identify early predictive signs of clinically manifest OA of the knee in predefined high-risk groups, and (2) to identify extremely high-risk groups to develop knee OA, by establishing what additional factors determine a clinically manifest OA in a pre-defined high-risk group.

**Methods:** A nested prospective cohort of 800 women aged 45–60 years will be studied. These women were part of the participants who were invited from 2006 onwards to extend the Rotterdam Study. We included the following high-risk groups: middle-aged females without OA, but with known risk factors for knee OA like overweight (400 women), malalignment (100 women), and history of knee trauma (100 women).

Furthermore, we include a group with unilateral knee OA (100 women), and 100 female controls (without OA and risk factors). At baseline all participants of the Rotterdam Study had x-rays and whole-body dexa scans, blood and urine was collected and a questionnaire was administered.

Participants are identified based on data from baseline measurement of the Rotterdam Study and their knee x-rays, which are scored for OA with Kellgren and Lawrence classification system. After identification of women at high risk a telephonic screening for pain and contraindications for MRI is done. If eligible, they are asked to visit the research centre for an additional questionnaire and a MRI scan and physical examination of both knees. MRI will be scored for OA with Knee Osteoarthritis Scoring System (KOSS), and shape modeling based on x-rays will be done as well as quantitative scoring of cartilage on MRI. Physical examination contains the SQUASH and KOOS among other things. Every 1.5 year a questionnaire will be send to the participants and first follow-up will be after 3 years, with in principal unlimited follow up every 3 years.

**Results:** We started in August 2007, and included 344 women so far, of which 205 in the overweight group, 98 in the group with malalignment, 25 in the group with unilateral knee OA, 15 in the history of trauma group and invited 46 controls. The only high-risk group in which women can have pain is the high-risk group with unilateral knee OA. We aim to fulfill the inclusion in April 2009.

**Conclusions:** Our cohort is more or less comparable with the Incidence subcohort of the Osteoarthritis Initiative (OAI). A difference is that all our participants in high-risk groups will not have knee pain, except the unilateral knee OA group. All participants in the Incidence subcohort of OAI in age category of 45–49 will have knee pain and all in age-category 50–69 can have knee pain. Furthermore, we have another risk group with malalignment in our study. Therefore, our study can give important information in addition to the OAI incidence subcohort as well as essential replication data.

### 386 NEW MICROCT METHODOLOGY TO EXAMINE ARTICULAR CARTILAGE AND UNDERLYING BONE TISSUE IN THE HUMAN TEMPOROMANDIBULAR JOINT

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**Purpose:** The cause of primary osteoarthritis/osteoarthrosis (OA) has a mechanical background. Excessive joint loading is suspected to initiate a sequence of events that may eventually lead to joint degradation. One of these events is the thickening and stiffening of the subchondral bone (SCB). SCB and the overlying articular cartilage perform as a functional unit. Presently, little is known about the mechanical interaction between cartilage and bone in the etiology of OA.

OA is one of the most common arthritis forms affecting the temporomandibular joint (TMJ). Micro-computed tomography (μCT) can be used to detect OA-related bone abnormalities like erosion and osteophytosis of the TMJ components (i.e., condyle, fossa, and tubercle) and to assess the complete bone structure. The articular cartilage covering the condyle, fossa and tubercle, as well as the cartilaginous articular disc, may also be affected by OA-associated degenerative changes. It is difficult to visualize these structures directly with μCT. However, assessment of cartilage can be facilitated by applying a hydrophilic contrast agent. The aim of this study was to test the application of a hydrophilic, tri-iodinated contrast medium (Optiray) for in vitro assessment of bone and cartilage components with μCT in the human TMJ.

**Methods:** Three human TMJ samples (1 healthy, 2 OA-classified) were treated with contrast medium Optiray (Tyco Healthcare Nederland BV, the Netherlands) to enhance cartilage contrast. The samples were submerged for two hours in Optiray (51% isosolent). Before and after this treatment, the samples were scanned and evaluated with a μCT system (μCT 40, Scanco medical AG, Switzerland, resolution: 18 μm). During scanning, the samples were submerged in a hydrophilic fluid to prevent diffusion of Optiray out of the soft tissues. From the images, the thickness of the cartilage layers was determined in three regions (i.e., medial, midsagittal, and lateral). Furthermore, the images were segmented and 3D reconstructions could be made to visualize bone and cartilage tissue separately.

![Figure 1](a) Midsagittal cross-section of a healthy TMJ after Optiray treatment. (b) Enlargement of articular cartilage (AC). (c) Superior view of OA-classified condyle and (d) overlying articular cartilage.