group compared to those in a control group for radiological OA (ROA) incidence; and 2) to determine if cartilage T2-relaxation-parameters can predict which subjects will develop ROA.

Methods: In the Osteoarthritis Initiative (OAI), only right knees were imaged with T2. Cases were knees with X-ray KL scores at baseline that were either zero or one and that developed incident ROA (KL≥2) at the 12 through 48 month visits. Control knees were KL = 0 or 1 at baseline and that did not develop ROA by the 48 Mo. visit. Controls contained about 50% gender-age-KL exact matches to cases supplemented with roughly similar non-matches to the remaining cases. The MESE T2 series at the time of incidence of ROA (P0), the 1 year prior to incidence (P-1) and the BL were segmented and T2 maps were computed at the femur, tibia, cMF, cLF, MT, LT, medial trochlea and lateral trochlea using atlas-based segmentation software (Qmetrics, Rochester, NY). Descriptive T2 parameters (mean, variance, skewness, top 5% value) and Gray-Level Co-Occurrence Matrix (GLCM) texture parameters (entropy, mutual information, ASM, and contrast) were extracted for each cartilage region at three cartilage layers: superficial, medial and deep. All T2 features were adjusted by gender, BMI and age, and then standardized using a rank-inverse-normal procedure. Finally, each parameter was categorized as being low (<10%), high (>90%) or mid-range (10% to 90%) based on the control group values. A forward parameter selection algorithm based on Integrated Discriminant Improvement (IDI) on logistic regression models was used to select internally cross-validated multivariable models that characterized the differences between cases and controls at BL, P-1 and P0. All logistic models included height and baseline KL status as covariates.

Results: 179 incident ROA right knees with T2 Map series developed ROA, and 175 control subjects did not. Cases and controls had similar age and gender (60.7 ± 8.7 and 60.0 ± 8.7, respectively, and 62% and 64% females, respectively.) At baseline, there were 139 that were KL zero and 215 knees that were KL one. Table 1 shows the T2 parameters that discriminate between cases and controls at BL, P-1 and P0. At baseline, abnormal T2 texture parameters at tibia and trochlea separated cases and controls with odd ratios ranging from 1.73 to 2.47. At P-1 adjusted odds ratios (aORs) ranged from 1.74 to 2.44, and were from the lateral femur, lateral trochlea and the entire femur. At P0 the heterogeneity of T2 values at medial trochlea, lateral tibia, and entire tibia separated cases and controls (aOR 2.37, 2.44, 2.04, respectively). Detailed analysis of the predictive power of the P1 model indicated that T2 parameters can only be used to identify 22% of the subjects that will develop ROA with a 95% specificity. At P0, 34%, of the case subjects have a different T2 behavior than controls.

Table 1
Discriminant T2 parameters at BL, PI and PO. (−) Low 10% Category. (+) Top 10% Category. Adjusted odds-ratios in multivariable logistic regression models

Time Point	Description	Control mean (std)	Case mean (std)	Odds ratio
	Lateral tibia texture ASM	0.004 (0.002)	0.004 (0.002)	2.47 (1.25-3.57) (−)
BL: Sensitivity 19% ± 1.5% at 95% ± 0.7% specificity	Lateral Trochlea Texture Correlation	0.58(0.029)	0.58(0.04)	2.50(1.59–4.00)(−)
	Medial Trochlea Texture Entropy	9.73(0.31)	9.81(0.37)	1.73(1.14-2.62)(+)
	Texture Contrast at Tibia	389.62(118.94)	404.13(152.23)	0.53(0.35-0.79)
	High Signal Value at cLF	116.81(27.63)	109.00(23.44)	2.44(1.59-3.70)(-)
P-1: Specificity 22% ± 1.3 at 95% ± 0.8 Specificity	Texture MI at Lateral Trochlea	0.21(0.06)	0.20(0.05)	2.13(1.37-2.33)(−)
	Texture Energy at cLF	0.014(0.001)	0.014(0.001)	1.89(1.25-2.86)
	T2 Mean of the Femur Superficial Layer	54.38(4.41)	65.17(5.05)	1.74(1 17-2.60)(+)
At P-1 T2 Analysis (AUC = .69.95% CI .64 to .75)				
	Medial Trochlea MI	0.61(0.11)	0.65(0.14)	2.37(1.56-3.58)(+)
	Medial Trochlea Skevness.	1.46(1.13)	1.17(0.99)	0.49(0.31-0.79)
P0: Sensitivity 34% ± 1.1% at 95% ± 0.7% Specificity	Superficial Layer T2 STD value at cMF	19.44(3.57)	20.53(4.01)	2.08(1.36-3.17)
	Texture ASM at LT	0.009(0.066)	0.004 (0.001)	2.44(1.54-3.85)(−)
	Entire Tibia MI	0.22(0.06)	0.23 (0.07)	2.04 (1.29–3.23)
	Superficial Layer T2 at cLF	54.78 (5.93)	53.33 (6.22)	0.53 (0.35–0.81)

Conclusions: A combination of various T2 map parameters from different parts of the TF cartilage was able to distinguish between those that developed incident ROA at time of incident ROA and the year prior to developing incident ROA.

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RELATIONSHIP BETWEEEN SUBREGIONAL LONGITUDINAL CARTILAGE LOSS AND MENISCUS POSITION IN KNEES WITH AND WITHOUT JOINT SPACE NARROWING – DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: It is well known that meniscus extrusion is associated with structural progression of knee OA. However, it is unknown whether medial meniscus extrusion promotes cartilage loss in specific femorotibial subregions, or whether it is associated with a general increase in cartilage thickness loss throughout the entire medial femorotibial compartment. We applied quantitative MRI-based measurement technology of subregional cartilage thickness (change) and meniscus position (relative to the tibial surface), to address the above question in knees with and without radiographic joint space narrowing (JSN)

Methods: 60 participants with unilateral medial (but not lateral) OARSI JSN grade 1-3, and with contralateral knee OARSI JSN grade 0 were drawn from the Osteoarthritis Initiative. Manual segmentation of the medial tibial (MT) and weight-bearing medial femoral (cMF) cartilage was performed, using baseline and 1-year follow-up sagittal double echo steady-state (DESS) MRI, and proprietary software (Chondrometrics GmbH, Ainring, Germany). Segmentation of the entire medial meniscus was performed with the same software, using baseline coronal reconstructions of the DESS images. Longitudinal cartilage loss was computed for 5 tibial (central, external, internal, anterior, posterior) and for 3 femoral (central, external, internal) subregions. Meniscus position was determined as a) the % area of the entire meniscus that extrudes over the tibial plateau medially; b) the distance between the medial border of the meniscus and the tibial cartilage in an image located 4 mm posterior to the central image (i.e. a location commonly used for semi-quantitative scoring of meniscus extrusion). The relationship between meniscus position and cartilage loss was assessed using Pearson (r) correlation coefficients, stratifying between knees with JSN and contralateral knees without JSN.

Results: The percentage of knees showing a quantitative value of >3 mm for medial meniscus extrusion was 50% in JSN knees, and only 12% in no-JSN knees. The 1-year cartilage loss in the medial femorotibial compartment was 74 ± 182 μm (2.0%) in JSN knees, and 26 ± 120μm (0.8%) in no-JSN knees. There was a significant (negative)

Pearson coefficients (r) for med meniscus position + subregional (1 y) med cartilage loss (CI 95; *sign)

	% Meniscus extruded		Extrusion distance 4 mm posterior to central	
	JSN knees	No JSN knees	JSN knees	No JSN knees
MFTC	−0.30 [−0.51; −0.05]*	−0.09 [−0.32; 0.16]	−0.20 [−0.43; 0.05]	−0.10 [−0.34; 0.16]
cMT	−0.20 [−0.43/0.06]	−0.004 [−0.25/0.25]	−0.11 [−0.35/0.15]	0.06 [−0.19/0.31]
eMT	−0.36 [−0.56/−0.12]*	−0.26 [−0.48/−0.02]*	−0.28 [−0.49/−0.03]*	−0.30 [−0.51/−0.05]*
iMT	−0.18 [−0.41/0.08]	−0.01 [−0.26/0.24]	−0.12 [−0.36/0.14]	0.11 [−0.15/0.35]
aMT	−0.27 [−0.49/−0.02]*	−0.01 [−0.26/0.24]	−0.16 [−0.39/0.10]	0.03 [−0.22/0.28]
pMT	−0.23 [−0.45/0.02]	0.09 [−0.16/0.33]	−0.08 [−0.32/0.17]	0.10 [−0.15/0.35]
ccMF	−0.20 [−0.43/0.06]	−0.09 [−0.33/0.17]	−0.16 [−0.40/0.09]	−0.15 [−0.38/0.11]
ecMF	−0.06 [−0.30/0.20]	−0.12 [−0.36/0.13]	0.03 [−0.22/0.28]	−0.18 [−0.41/0.07]
icMF	−0.26 [−0.48/−0.01]*	−0.04 [−0.29/0.21]	−0.26 [−0.47/−0.01]*	0.03 [−0.22/0.28]

correlation between cartilage loss throughout the entire femorotibial compartment (MFTC) with extrusion area in JSN knees; however, the correlation did not attain statistical significance in no-JSN knees (Table 1). Also, the extrusion distance measured 4 mm posterior to the central slice was not significantly correlated with MFTC cartilage loss. The strongest (negative) correlation between meniscus position and subregional femorotibial cartilage loss ($r = -0.36$) was observed for the external medial tibia (eMT; Table 1). In contrast, no significant relationship was seen in the central tibia (cMT; Table 1). No significant relationship was found in other tibial subregions, except for the anterior medial tibia, but only in JSN knees ($r = -0.27$; Table 1). Correlation coefficients for the femoral subregions were generally smaller than those for tibial subregions, with only the internal medial weight-bearing femur (icMF) attaining statistical significance ($r = -0.26$; Table 1).

Conclusions: The current results show that the relationship between meniscus extrusion and cartilage loss differs substantially between femorotibial subregions. The correlation was strongest for the external medial tibia (eMT), a region that is physiologically covered by the medial meniscus. It was less for other tibial and femoral subregions, including the central medial tibia (cMT), a region that exhibited similar rates of cartilage loss as eMT (data not shown). The findings suggest that external tibia may be particularly vulnerable to cartilage tissue loss once the meniscus extrudes and the surface is "exposed" to direct, non-physiological, cartilage-cartilage contact.

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DO SCORES ON WOMAC PAIN AND FUNCTION SUBSCALES VARY WITH DIFFERENT DEFINITIONS OF KNEE OSTEOARTHRITIS?

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Purpose: The MRI definition for knee osteoarthritis, developed in 2011, has not yet been validated in other populations. In previous work, we showed that if this MRI definition of tibiofemoral (TF) OA (TFOAMRI) is applied, more cases of knee OA are detected than with the radiographic Kellgren and Lawrence grading (K&L). With a better content validity and at least equal construct validity, we concluded that the TFOAMRI is more sensitive in detecting structural knee OA. However, it is unknown whether women defined with TFOAMRI differ in pain and disability from those who are not, or those who have a radiographic K&L grade ≥2. Furthermore, with the available MRI definitions, a distinction between patellofemoral (PF) OA and TFOA can be made, and the debated contribution to pain and disability by PFOA can be assessed. Therefore the aim of the present study was to investigate if women with knee OA defined with PF- or TFOAMRI report different pain and function scores measured with The Western Ontario and McMaster Universities Arthritis Index (WOMAC), or report different scores than women with knee OA defined by K&L-grading.

Methods: Of 891 females (aged 45-60) from a random subpopulation of the Rotterdam Study, radiographs and MRI of both knees were assessed for knee OA; radiographs with the K&L-grading (K&L≥2 was defined as OA) and MRIs with a comprehensive semi-quantitative scoring system. Based on these scored features we applied the proposed MRI definition. We distinguished a PFOAMRI-definition from a TFOAMRI-definition. All women filled in the WOMAC questionnaire. With multivariable regression analysis we tested if the definitions (K&L≥2, PFOAMRI or TFOAMRI) reported different WOMAC pain and function scores independently from each other. Analyses were adjusted for BMI, age and bilaterality (if women had knee OA in one or both knees).

Results: Data of 871 women were analyzed. Of 20 women data was missing due to insufficient quality of images (radiographs or MRIs). Table 1 shows the mean and the standard deviation (sd) of age, BMI, WOMAC pain and function scores per definition. 21 women met the K&L≥2 and TFOAMRI definition in one or both knees; 3 women met the K&L≥2 and PFOAMRI definitions; 35 women met the TF- and PFOAMRI definitions; 17 women met all three definitions of knee OA in one or both knees. All three definition contributed significantly ($p < 0.001$) to higher WOMAC pain scores (K&L≥2: $\beta = 1.61$; (95% confidence interval (95% CI) 0.79–2.44), PFOAMRI: $\beta = 1.32$ (95% CI: 0.69–1.95) or TFOAMRI: $\beta = 1.15$ (95% CI: 0.52–1.77)) and to WOMAC function score (K&L≥2: $\beta = 5.21$ (95% CI:2.56–7.86), $p < 0.001$; TFOAMRI ($\beta = 2.75$ (95% CI:0.74–4.75), $p = 0.007$; PFOAMRI: $\beta = 4.06$ (2.02–6.10), $p < 0.001$).

Conclusions: The MRI definitions show differences in WOMAC pain and function scores between women with and without knee OA. Those women with all definitions positive had the highest pain and disability scores, and those with alone K&L≥2 the lowest. The TF- and PFOAMRI definitions, but also the K&L-definition, all contributed significantly and independently from each other, to the higher pain and disability scores.

Table 1
Mean (sd) of age, BMI, WOMAC pain (0-20) and function subscale (0-68)

	Women met the definition (n)	Age mean (sd)	BMI mean (sd)	Uni-/bilateral n/n	WOMAC pain mean (sd)	WOMAC function mean (sd)
No OA	676	54.6 (3.8)	26.3 (4.3)	-	1.0 (2.4)	3.0 (7.5)
K&L≥2	61	56.2 (3.3)	30.1 (6.3)	25/36	4.2 (4.7)	12.9 (16.1)
- Only K&L≥2	17	56.1 (3.8)	27.1 (3.3)	11/6	1.8 (2.3)	5.7 (8.2)
- K&L≥2 + TFOAMRI	21	55.7 (3.4)	30.1 (7.2)	7/14	3.8 (4.9)	11.8 (17.6)
- K&L≥2 + PFOAMRI	3	57.5 (1.3)	34.8 (7.7)	0/3	5.7 (6.4)	21.3 (25.3)
TFOAMRI	125	56.6 (3.3)	29.4 (6.2)	69/56	3.5 (4.7)	10.3 (14.7)
- Only TFOAMRI	51	55.9 (3.6)	27.7 (6.2)	42/9	2.2 (3.4)	7.0 (11.2)
PFOAMRI	106	56.9 (2.9)	30.1 (4.1)	59/47	3.5 (4.6)	10.6 (14.4)
- Only PFOAMRI	51	56.1 (2.9)	29.2 (4.1)	40/11	2.3 (3.4)	8.2 (11.7)
- TF- + PFOAMRI	35	57.7 (2.8)	29. (5.8)	15/20	3.5 (5.1)	8.9 (14.0)
K&L≥2	17	57.3 (2.6)	32.4 (6.6)	4/13	6.7 (5.2)	19.2 (17.6)