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Longitudinal analysis of cartilage T2 relaxation times and joint degeneration in African American and Caucasian American women over an observation period of 6 years – data from the Osteoarthritis Initiative

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SUMMARY

Objectives: To investigate the change in cartilage T2 values and structural degeneration in knee joints over 72 months in women of African American (AA) vs Caucasian American (CA) ethnicity.
Methods: Knee 3T magnetic resonance imaging (MRIs) from baseline, 24, 48 and 72 months visits of 100 AA and 100 CA women from the Osteoarthritis Initiative (OAI) were assessed for cartilage T2 values and whole-organ magnetic resonance imaging (WORMS) score. Subjects were pair-matched by age, body mass index (BMI), Kellgren–Lawrence (KL) score, clinical site and subcohort within the OAI. We compared the rate of change in whole knee cartilage T2 values and WORMS cartilage, bone marrow edema pattern (BMEP) and meniscus scores between the two ethnic groups using mixed random effects models.
Results: At 24 and 48 months 60 subjects and at 72 months 45 subjects per group were available for analysis resulting in 38 complete pairs with data of all time points. Compared to CA, cartilage T2 values in AA increased at a significantly faster rate at baseline (AA: 0.45 ms/y, CA: 0.35 ms/y, $P = 0.029$) and averaged over 6 years (AA: 0.36 ms/y, CA: 0.27 ms/y, $P = 0.039$) with changes in both groups reaching a plateau by 48 months. Cartilage, meniscus and BMEP scores tended to increase in both groups during follow up, but rates of change did not differ by ethnicity.
Conclusion: Cartilage T2 values increased faster over 72 months in AA than CA, however changes in WORMS cartilage, meniscus and BMEP scores did not differ. T2 values may be able to distinguish ethnicity-related differences of cartilage degeneration at an early stage before differences in structural joint degeneration appear.

Introduction

Osteoarthritis (OA) is a chronic degenerative form of arthritis; it is a complex entity evolving as a collection of multiple etiologies. These etiologies can be categorized by local factors such as joint injury and joint instability, constitutional factors such as muscle weakness, misalignment and obesity as well as systemic factors such as sex, age, hormonal status, bone mineral density, inflammatory, metabolic and genetic factors, all of which contribute to the onset and development of the disease[1]. Genetic factors may be responsible for up to 65% of the variance of OA in women[2] and

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there is evidence that the prevalence and degree of OA varies between ethnic groups with a higher prevalence of knee OA among African American women[3] and a higher prevalence of hip OA in African American men[4]. While these ethnic differences may in part be explained by behavioral, socioeconomic and constitutional factors, genetic differences have to be considered as a contributing factor.

A recent study on ethnic differences in cartilage composition showed that MRI T2 relaxation times of the knee cartilage in African American women were significantly lower compared to Caucasian women[5]. In the context of a higher prevalence of knee OA in African American as reported in several studies[3,4] the finding of lower T2 values in this group was surprising since degradation of the cartilage matrix[6] and progression of structural changes with knee OA[7] have been shown to be associated with increased T2 values raising the question of whether the natural history of cartilage degeneration is different in African Americans.

To further explore differences in joint degeneration and cartilage biochemical composition over 6 years we performed a longitudinal study using 3T MRI for the measurement of cartilage T2 and the WORMS scoring system for the assessment of structural joint degeneration in African American and Caucasian American women.

Materials and methods

Subjects

Subjects for this study were from the Osteoarthritis Initiative (OAI), a multi center cohort study consisting of 4796 participants divided into a progression cohort (subjects with symptomatic knee OA), an incidence cohort (subjects without symptomatic knee OA but risk factors for OA) and a normal cohort without knee OA or risk factors[8]. We used the same sample as our recent study of 200 African-American and Caucasian-American women selected from the OAI incidence and progression subcohorts[5] [Fig. 1].

The inclusion criteria for that study were: females who were either of African-American or Caucasian-American ethnicity, age 45–69 and a body mass index (BMI) of 22.5–39.5 kg/m^2. Subjects also had to have low Kellgren–Lawrence (KL) scores of 0 (definitively radiographically absent OA), and 1 (doubtful radiographic OA) to ensure that only participants with low cartilage lesion load were included and were suitable for T2 relaxation time measurements. Exclusion criteria were history of inflammatory arthritis and knee surgery at the right knee. The resulting selection of 140 African-American and 609 Caucasian American women was matched pairwise by KL grade (0 or 1), baseline age (5 year strata from 45 to 69 years) and BMI (5 point strata from 22 to 40 kg/m^2), subcohort and clinical site. For each stratum Caucasian subjects were randomly selected. A total of 100 Caucasian American women could be identified to fulfill the matching criteria, thus 38 African American women had to be excluded. Two subjects had to be excluded because of incomplete data sets resulting in a total of 100 pairs at baseline.

For the present study, 60 pairs (120 subjects) had follow-up MRI data in both members of the pair at both 24 and 48 months. At month 72, the data of 45 individuals was available in each group including 38 complete pairs and seven individuals each, who lost their matching partner. These individuals were kept in the study groups to maintain a sufficient sample size. A retrospective analysis of the demographic data showed that both groups remained balanced [Fig. 1, Table I].

Radiographs

Standing postero-anterior fixed flexion knee radiographs were acquired as described in detail in the OAI Radiographic Procedure Manual freely accessible at http://www.oai.ucsf.edu. All knee radiographs were analyzed centrally and graded with regard to the degree of joint degeneration using the KL score[9,10].

MR imaging protocol

MR images of the right knee were obtained using four identical 3.0 T scanners (Trio, Siemens) and quadrature transmit–receive coils (USA Instruments, Aurora, OH, USA) at one of four sites (Ohio State University, Columbus, OH; University of Maryland, School of Medicine, Baltimore, MD; University of Pittsburgh, Pittsburgh, PA; and Memorial Hospital of Rhode Island, Pawtucket, RI). Details of the acquisition protocol have been published[11] and included the following sequences: (1) coronal proton density-weighted fast spin-echo (FSE); (2) sagittal 3-D dual echo in the steady state (DESS) with selective water excitation; (3) sagittal intermediate-weighted FSE with fat suppression; and (4) sagittal T2-weighted multi-echo spin-echo (SE) for quantitative T2 relaxation time measurements.

Quantitative T2 relaxation time measurements

The sagittal 2-D multi-echo SE of the right knee was used for segmentation and quantification of T2 relaxation time using an in-house developed spline-based, semi-automated software segmentation algorithm in MATLAB (Mathworks Inc., El Segundo, CA)[12,13]. Segmentation of the cartilage was performed on the first echo sequence to maximize signal-to-noise ratio. All segmentations were performed by four individuals (MK, AY, UH, MS) in the following compartments: patella, medial/lateral femoral condyle, medial/lateral tibia. The trochlea was not segmented because of interfering flow artifacts from the popliteal artery. Inter-reader (1.57%) and intra-reader reproducibility errors of the (1.46%) of this technique were minimal as reported in a prior study[14].

Whole-organ magnetic resonance imaging score (WORMS) grading

MR images were evaluated for the grade of cartilage, meniscal and bone marrow edema pattern (BMEP) lesions using WORMS[15], modified as previously described[16]. Two radiologists (MK with 11 and AY with 9 years of experience) who were blinded to the ethnicity of subjects analyzed separately an equal number of subjects (AA and CA subjects all time points). Problematic cases were reviewed with TML (24 years of experience) and a final consensus diagnosis was obtained. Inter- and intra-observer agreement data of the UCSF modified WORMS score were published previously[16]. Meniscus lesions were graded 0–4 in each of six regions (medial/lateral and anterior/body/posterior). Cartilage grades (0–6) and BMEP grades (0–3) were also scored in six regions (patella, trochlea, medial/lateral femur, and medial/lateral tibia). BMEP was defined as areas of poorly marginated increases in T2 signal intensity in the fat suppressed imaging sequences. For each type of lesion (meniscus, cartilage, BMEP), a sum score per knee was defined as the sum of scores in all regions. We also calculated a total score (WORMS sum) by summing scores for menisci, cartilage, ligaments, BMEP, cysts, effusion and baker cysts for each knee over all regions.

Statistical analysis

Statistical analysis was performed using JMP version 11 (SAS Institute, Cary, NC, USA) and STATA version 12 software (StataCorp LP, College Station, TX, USA). In addition to descriptive statistics, differences of demographic variables between ethnic

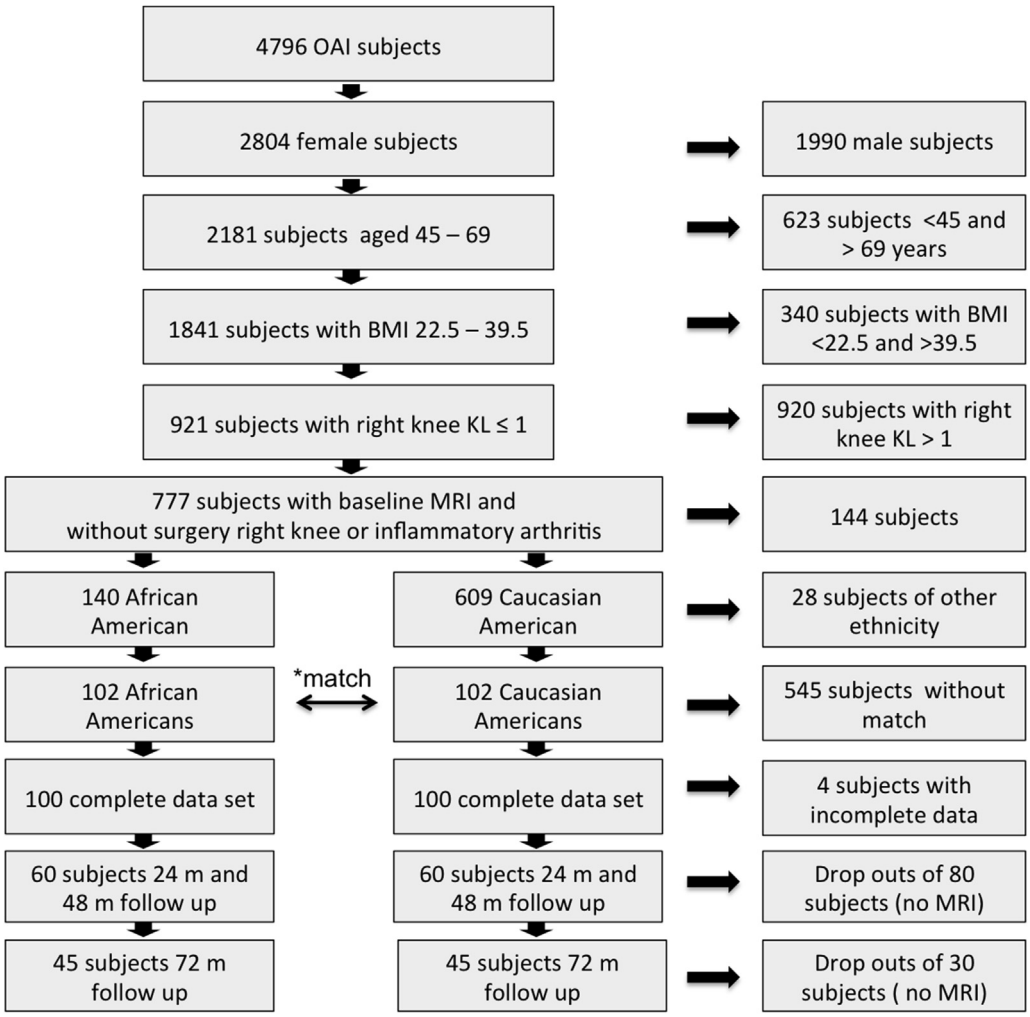

Fig. 1. Selection of subjects. *Pairwise matching by age, BMI, KL grade, subcohort and clinical site. Overall 200 subjects in 100 matched pairs were included in the analysis. Due to dropouts the data set contained 38 matched pairs with a complete MRIs at all time points. At month 72, the data of 45 individuals was available in each group including 38 complete pairs and seven individuals each, who lost their matching partner.

groups were determined using the Kruskal–Wallis test. Based on the previously published significant differences in baseline cartilage T2 values[5] we wanted to investigate the development of T2 values and WORMS grades in the two different ethnic groups. Mean T2 values and WORMS scores of AA and CA subjects were compared at each time point using paired *t*-test. Significance of differences of mean T2 values and WORMS scores from baseline to 72 months follow-up was tested using analysis of variance (ANOVA), level of confidence was set to $P < 0.05$. Mixed models were used to assess the differences in the rates of change of (1) cartilage T2 and (2) WORMS scores (using all four time points) between the AA and CA subjects. We assumed a nonlinear increment of T2 values and found a significant quadratic relationship with time while WORMS changes followed a significant linear pattern. We controlled for random effects with multiple measurements per subjects in adding the identification code for the individual subject as a covariate. Pairs were identified with a numerical code and included as a covariate. Since the T2 increments followed a non-linear quadratic relationship, we reported the (1) difference in the baseline rate of change in T2 between both groups and (2) difference in the average annual rate of change averaged over 6 years between both groups.

Results

Subject characteristics

Subject characteristics at baseline are summarized in Table I. Although drop out changed group composition slightly at the different follow up time points, there were no significant differences in BMI, age, KL grade or physical activity scale for the elderly (PASE) physical activity scores including the subscore for occupational physical activity between AA and CA at any of the time points.

T2 relaxation time and ethnicity

AA cartilage T2 values remained lower at all time points. However, the significance of differences disappeared after 24 months ($P = 0.617$), which was mainly due to the increase of T2 values in AA cartilage (Tables II and IV, Fig. 2(A)). There was a significant increase of T2 values averaged over the joint in both groups over the 6 years [Table III, Fig. 2(A)] ($P < 0.0001$). The slope followed a non-linear pattern and gradually decreased with time building a plateau after 4th year [Fig. 2(A)]. Compared to the Caucasian Americans the

Table I
Subject characteristics

	Ethnicity		*P*-value
	African American	Caucasian American	
Baseline			
N	100	100	
Age	55.89 (6.02)	55.32 (6.46)	0.138
BMI*	29.20 (4.02)	29.16 (3.81)	0.816
KL*	0.29	0.29	1.000
PASE*	151.2 (80.4)	167.1 (78.7)	0.160
Occupational act. level	2.17	2.16	0.888
24 months follow up			
N	60	60	
Age*	57.7 (5.8)	57.2 (6.3)	0.690
BMI*	29.6 (0.56)	29.0 (0.53)	0.393
KL*	0.54 (0.7)	0.48 (0.74)	0.658
PASE*	154.4 (73.0)	164.7 (87.8)	0.491
PASE occupational act. level	2.26	2.17	0.685
48 months follow up			
N	60	60	
Age*	59.4 (6.0)	59.0 (6.2)	0.733
BMI*	29.5 (0.53)	29.3 (0.51)	0.832
KL*	0.55 (0.77)	0.63 (0.96)	0.619
PASE*	159.0 (79.2)	164.2 (80.1)	0.727
PASE occupational act. level†	2.24	2.26	0.905
72 months follow up			
N	45	45	
Age*	61.1 (5.5)	60.3 (6.2)	0.388
BMI*	30.0 (3.7)	29.3 (4.1)	0.360
KL*	0.5 (0.68)	0.66 (0.77)	0.348
PASE*	156.2 (76.4)	170.1 (81.4)	0.407
PASE occupational act. level	2.38	2.34	0.796

* Numbers are mean (SD).
† Graded with 1 = sitting, 2 = sitting/standing/walking, 3 = walking/handling <50 lbs., 4 = walking/handling >50 lbs.

Table II
Differences in T2 values and WORMS scores at time points baseline to 6 years

	Ethnicity				*P*
	African Americans		Caucasian Americans		
	Mean	95% CI	Mean	95% CI	
Baseline					
Average T2 (ms)	32.07	31.7–32.4	32.85	32.5–33.2	**<0.0001**
WORMS sum	7.79	6.47–9.12	7.57	6.58–8.56	0.755
WORMS medial compartment	1.22	0.90–1.53	1.16	0.84–1.47	0.774
WORMS lateral compartment	1.83	1.38–2.26	1.74	1.29–2.17	0.775
Cartilage sum	3.61	2.97–4.23	3.62	2.96–4.28	0.969
BMEP sum	1.81	1.37–2.24	1.35	0.99–1.71	*0.069*
Meniscus sum	0.9	0.54–1.26	1.36	0.89–1.83	*0.065*
Medial meniscus sum	0.34	0.16–0.52	0.61	0.38–0.84	**0.031**
Lateral meniscus sum	0.56	0.25–0.87	0.75	0.33–1.16	0.379
24 months					
Average T2 (ms)	33.49	33.2–33.8	33.97	33.8–34.4	0.617
WORMS sum	8.66	6.91–10.39	8.91	7.44–10.38	0.687
WORMS medial compartment	1.37	0.73–2.00	1.66	1.04–2.27	0.5516
WORMS lateral compartment	2.08	1.42–2.73	2.16	1.52–2.79	0.857
Cartilage sum	4.29	3.47–5.11	4.54	3.69–5.38	0.556
BMEP sum	2.17	1.60–2.74	1.71	1.25–2.16	0.231
Meniscus sum	0.66	0.18–1.13	1.42	0.82–2.02	**0.003**
Medial meniscus sum	0.26	0.02–0.49	0.55	0.26–0.84	**0.017**
Lateral meniscus sum	0.4	−0.01–0.8	0.87	0.34–1.40	**0.034**
48 months					
Average T2 (ms)	34.16	33.8–34.5	34.43	34.2–34.9	0.259
WORMS sum	12.15	10.48–13.82	10.93	8.98–12.89	0.268
Medial meniscus sum	2.21	1.41–3.02	2.15	1.33–2.96	0.908
Lateral meniscus sum	3.39	2.33–4.45	3.02	1.95–4.09	0.633
Cartilage sum	5.88	5.09–6.67	5.75	4.90–6.60	0.749
BMEP sum	2.83	0.28–3.38	2.02	1.56–2.48	**0.024**
Meniscus sum	1.39	0.94–1.85	1.85	1.25–2.45	0.252
Medial meniscus sum	0.49	0.27–0.71	0.74	0.44–1.03	0.287
Lateral meniscus sum	0.9	0.52–1.29	1.11	0.58–1.65	0.506
72 months					
Average T2 (ms)	34.08	33.7–34.5	34.23	33.9–34.7	0.386
WORMS sum	13.84	11.88–15.79	12.38	9.57–15.19	0.251
Medial meniscus sum	2.90	1.64–4.16	2.49	1.21–3.76	0.648
Lateral meniscus sum	3.91	2.49–5.34	3.67	2.22–5.11	0.810
Cartilage sum	6.79	5.87–7.71	6.44	5.45–7.43	0.866
BMEP sum	3.09	2.44–3.73	2.11	1.58–2.65	*0.065*
Meniscus sum	1.54	1.01–2.08	2.02	1.32–2.72	0.639
Medial meniscus sum	0.63	0.37–0.89	0.87	0.52–1.21	0.216
Lateral meniscus sum	0.91	0.46–1.37	1.15	0.54–1.78	0.871

Significance of differences was tested with the paired *t* test. Bold numbers indicate significant differences ($P < 0.05$), italic numbers indicate trends ($P > 0.05 < 0.1$). Part of baseline data were reported in Yu et al. 2015[5].

baseline rate of increase in the African Americans was significantly higher in the total cartilage per joint (AA 0.45 ms/y [CI 0.38–0.5], CA 0.35 ms/y [CI 0.29–0.41], $P = 0.029$). Also the average annual rate of change of the total cartilage T2 was significantly higher in AA (AA 0.36, [CI 0.30–0.43], CA 0.27 [CI 0.20–0.33], $P = 0.039$, Table IV), so that while total cartilage T2 values were lower in AA at baseline the values converged over time. In addition, baseline and overall annual rates of change were greater in AA in the medial femoral condyle (baseline rate $P = 0.025$, average annual rate $P = 0.030$) and there were trends for a greater baseline and average annual rates of change in the medial and lateral tibia in the African Americans subjects [Table IV, Fig. 2(A)].

Progression of WORMS lesions and ethnicity

Both the African and the Caucasian American group started with a nearly identical total WORMS score of 7.57 and 7.79 ($P = 0.755$, Table II) and increased significantly in a linear pattern over the time interval of 6 years ($P < 0.0001$ and $P = 0.0003$ in the two groups, respectively, Table III, Fig. 2(D)). However, there were no significant differences in the rate of change over 6 years between the two groups (AA 0.99/y [CI 0.79–1.19], CA 0.81/y [CI 0.61–1.01], $P = 0.193$) (Table V). The WORMS sum of the medial and lateral compartment did not significantly differ between AA and CA at all time points (Table II). WORMS sum of both compartments increased significantly in both ethic groups (Table III). While the sum of WORMS cartilage lesions increased significantly during follow up in both groups ($P < 0.0001$ in both groups) the slope of increase was not significantly different between the groups (AA 0.54/y [CI 0.41–0.66], CA 0.48/y [CI 0.35–0.61], $P = 0.526$) [Table V, Fig. 2(B)].

There was a non-significant trend for BMEP lesion scores to increase faster in the African American group (AA 0.17/y [CI 0.12–0.22], CA 0.11/y [CI 0.06–0.16], $P = 0.11$). The rate of change was significantly higher in the medial femoral condyle of the African Americans (AA 0.037/y [CI 0.02–0.05], CA 0.003/y [CI −0.01 to 0.02], $P = 0.006$). In contrast, in the lateral femoral condyle the BMEP score decreased in the African Americans while it slightly increased in the Caucasian Americans ($P = 0.009$) [Table V, Fig. 2(C)]. CA subjects showed higher mean meniscus lesions scores form baseline to 48 m follow up. The difference was predominantly found and significant in the medial meniscus. There was only a slight progression of meniscus lesions that was not significant in either group. Also the rates of change were not significantly different ($P = 0.41$) [Table V, Fig. 2(D)].

Discussion

The results of this study show that compared to CA, AA cartilage T2 relaxation times averaged over the whole joint and in the medial femoral condyle increased at a significantly faster rate per year, so that while T2 values in the latter were lower at baseline the T2 values of the two groups converged slowly within the observation period. In contrast, the rate of progression of WORMS cartilage

Table III
Development of T2 values and WORMS scores over 6 years

	Follow up								
	Baseline		24 months		48 months		72 months		*P*
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	
African Americans									
Average T2 ms	32.07	31.7–32.4	33.49	33.2–33.8	34.16	33.8–34.5	34.08	33.7–34.5	**<0.0001**
WORMS sum	7.79	6.47–9.12	8.66	6.91–10.39	12.15	10.48–13.82	13.84	11.88–15.79	**<0.0001**
WORMS medial compartment	1.22	0.69–1.75	1.37	0.68–2.06	2.21	1.55–2.88	2.90	2.13–3.67	**0.001**
WORMS lateral compartment	1.83	1.99–2.45	2.07	1.25–2.89	3.39	2.60–4.17	3.91	2.99–4.83	**0.0003**
WORMS Cartilage sum	3.61	2.97–4.23	4.29	3.47–5.11	5.88	5.09–6.67	6.79	5.87–7.71	**<0.0001**
WORMS BMEP sum	1.81	1.37–2.24	2.17	1.60–2.74	2.83	0.28–3.38	3.09	2.44–3.73	**0.003**
Meniscus sum	0.9	0.54–1.26	0.66	0.18–1.13	1.39	0.94–1.85	1.54	1.01–2.08	**0.033**
Medial meniscus	0.34	0.16–0.52	0.26	0.02–0.49	0.49	0.27–0.71	0.63	0.37–0.89	0.148
Lateral meniscus	0.56	0.25–0.87	0.4	−0.01–0.8	0.9	0.52–1.29	0.91	0.46–1.37	0.191
Ligament sum	0.22	0.10–0.34	0.12	−0.02–0.26	0.16	0.02–0.30	0.04	−0.04–0.13	0.396
Cyst sum	0.63	0.31–0.94	0.57	0.15–0.98	0.95	0.56–1.35	1.35	0.88–1.81	**0.043**
Effusion	0.12	0.04–0.19	0.05	−0.04–0.14	0.11	0.02–0.19	0.13	0.03–0.23	0.629
Baker cyst	0.65	0.42–0.87	0.79	0.53–1.06	0.83	0.57–1.08	0.89	0.59–1.18	0.563
Caucasian Americans									
Average T2 ms	32.85	32.5–33.2	33.97	33.8–34.4	34.43	34.2–34.9	34.23	33.9–34.7	**<0.0001**
WORMS sum	7.57	6.58–8.56	8.91	7.44–10.38	10.93	8.98–12.89	12.38	9.57–15.19	**0.0003**
WORMS medial compartment	1.15	0.57–1.73	1.66	0.93–2.39	2.14	1.41–2.88	2.49	1.63–3.34	**0.044**
WORMS lateral compartment	1.74	1.03–2.44	2.16	1.26–3.05	3.02	2.12–3.92	3.67	2.61–4.71	**0.012**
WORMS cartilage sum	3.62	2.96–4.28	4.54	3.69–5.38	5.75	4.90–6.60	6.44	5.45–7.43	**<0.0001**
WORMS BMEP sum	1.35	0.99–1.71	1.71	1.25–2.16	2.02	1.56–2.48	2.11	1.58–2.65	*0.052*
Meniscus sum	1.36	0.89–1.83	1.42	0.82–2.02	1.85	1.25–2.45	2.02	1.32–2.72	0.328
Medial meniscus	0.61	0.38–0.84	0.55	0.26–0.84	0.74	0.44–1.03	0.87	0.52–1.21	0.494
Lateral meniscus	0.75	0.33–1.16	0.87	0.34–1.40	1.11	0.58–1.65	1.15	0.54–1.78	0.626
Ligament sum	0.28	0.17–0.39	0.08	−0.07–0.23	0.15	0.00–0.29	0.09	−0.08–0.26	0.117
Cyst sum	0.29	0.05–0.53	0.42	0.11–0.72	0.48	0.17–0.78	0.82	0.46–1.18	0.119
Effusion	0.06	0.03–0.09	0.00	−0.04–0.04	0.00	−0.04–0.04	0.00	−0.05–0.05	**0.042**
Baker cyst	0.66	0.43–0.88	0.77	0.48–1.05	0.69	0.41–0.97	0.89	0.56–1.21	0.68

Significance of differences between groups was tested with ANOVA. Bold numbers indicate significant differences ($P < 0.05$), italic numbers indicate trends ($P > 0.05 < 0.1$). Part of baseline data were reported in Yu et al. 2015[5].

lesion scores was not significantly different between the two groups. There were also no differences between groups in the rate of progression in WORMS meniscus or total joint BMEP lesion scores, but BMEP lesions in the MFC increased more in the AA and BMEP lesions in the LFC increased more in the CA women.

To date there is limited knowledge on ethnic differences in cartilage composition with MRI and to the best of our knowledge only one study was performed[5]. This cross-sectional analysis of baseline data of AA and CA women in the OAI, a subset of whom were also included in this study, showed consistently lower T2 values in AA women in all compartments. Since the results were strictly controlled for the main confounders of age, BMI and KL grade and a sub analysis of compartments without cartilage lesions confirmed the results of lower T2 lesions in AA, the differences in cartilage T2 might reflect racial differences in cartilage composition. Interestingly data from our longitudinal study show that the initially different T2 values converged over time. This effect was due to both the significantly higher rate of increment at baseline and average change over 6 years in AA women and may be indicative for a faster progression of matrix degeneration.

The development of cartilage T2 followed a nonlinear quadratic relationship entering a plateau phase after 4 years while cartilage lesions measured with WORMS progressed constantly during follow up. This ceiling effect has been theorized in a prior study[17] that followed the development of cartilage T2 over 2 years and found an inverse relationship between baseline T2 and the slope of T2 progression. The authors hypothesized a saturation effect that might occur after a certain degree of cartilage matrix degeneration prior to the onset of a cartilage lesion. There are other studies supporting this finding e.g., Dunn *et al.*[18] found significantly elevated T2 values in subjects with mild knee OA while no significant further increment could be observed from mild to severe OA and a study with a pig model reported a ceiling effect with cartilage maturation followed by a decrease of T2 with further aging[19].

While cartilage T2 values increased faster in AA women the progression of structural knee degeneration as expressed with the WORMS score was comparable. This seems to be in contrast to the higher prevalence of knee OA (at least KL 2) in AA women found by Anderson *et al.*[3] However, our study cohort consisted of subjects without definite OA (KL0-1) thus the grade of knee joint degeneration may have been too low and the observation period too short to detect significant differences. A longer follow up observation with more subjects entering the stage of definite radiographic OA is needed to estimate the predictive value of cartilage T2 changes with regard to the onset of definite knee OA in these groups.

There was also a difference in the distribution of lesions within the joint. Meniscus lesions were found to be significantly more frequent in the Caucasian American group while BMEP lesion scores tended to be higher in African Americans. Since potential risk factors for meniscus lesions and higher BMEP such as high physical activity[20] (measured with PASE) or obesity[21,22] (no significant difference in BMI) were very similar in both groups these factors are not a likely explanation for these differences. Analyzing the distribution of degeneration according to medial and lateral disease we did not find a significant discrepancy between the ethnic groups. Particularly we did not find a predominance of lateral disease in African American knees as described in Braga *et al.*[23] who analyzed knee X-rays of more than 3187 participants of the Johnston County osteoarthritis project. The reason for this may be that we included only subjects with no or doubtful signs of radiographic knee OA.

Our study has several limitations: Many subjects were lost for the follow-up time points resulting in relatively small groups of 45 subjects per ethnic group at 72 months. This reduces the

Table IV
Rate of change in T2 values at baseline and over 6 years

Rate of change at baseline	Ethnicity				*P*
	African Americans		Caucasian Americans		
	Slope coeff.*	95% CI	Slope coeff.*	95% CI	
Average of all regions	0.45	0.38–0.51	0.35	0.29–0.41	**0.029**
LFC	0.62	0.53–0.72	0.55	0.45–0.65	0.238
LT	0.53	0.44–0.62	0.42	0.34–0.51	*0.058*
MFC	0.37	0.28–0.42	0.23	0.13–0.33	**0.025**
MT	0.37	0.28–0.45	0.26	0.18–0.34	*0.054*
P	0.33	0.19–0.47	0.32	0.18–0.45	0.835
Average change rate over 6 years	Rate/year*	95% CI	Rate/year*	95% CI	*P*
Average of all regions	0.36	0.30–0.43	0.27	0.20–0.33	**0.039**
LFC	0.51	0.41–0.61	0.43	0.33–0.53	0.269
LT	0.46	0.37–0.54	0.35	0.26–0.43	*0.067*
MFC	0.29	0.20–0.39	0.14	0.05–0.24	**0.030**
MT	0.29	0.21–0.37	0.18	0.10–0.26	*0.061*
P	0.27	0.15–0.40	0.25	0.13–0.38	0.821

Bold numbers indicate significant differences ($P < 0.05$), italic numbers indicate trends ($P > 0.05 < 0.1$).
* Numbers of slope coefficients at baseline and average rate/year are least square means adjusted for multiple measurements per ID and matched pairing between groups pairs using a mixed random effects model. Units are ms/year.

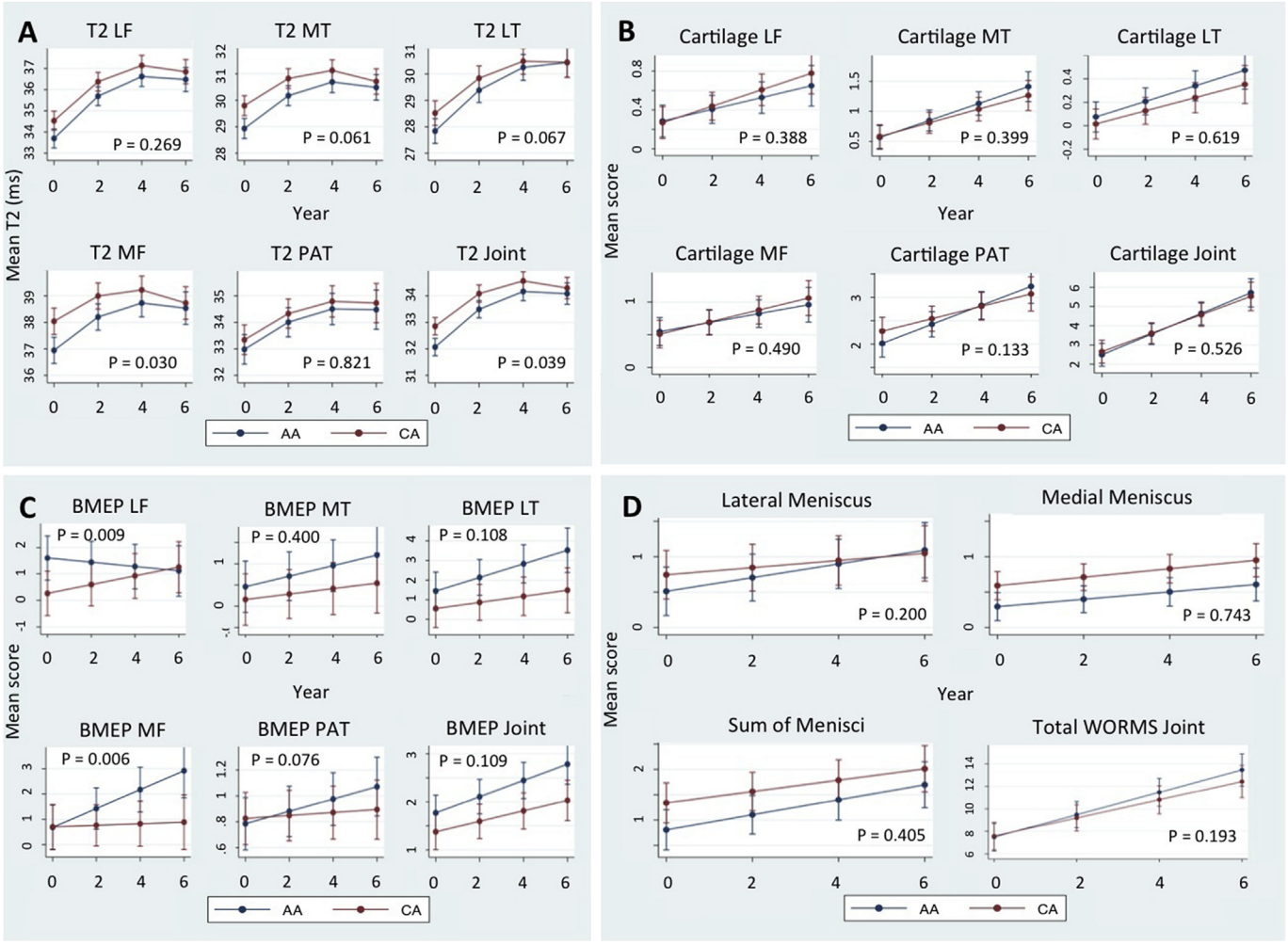

Fig. 2. Mean cartilage T2 (A) and the WORMS scores for cartilage (B), BMEP (C) menisci (D) and the sum of all WORMS scores (D) in African American (AA) and Caucasian American (CA) women over 6 years. Values are least square means adjusted for multiple measurements per ID and matched pairing between groups pairs using a mixed random effects model. Error bars indicate standard errors. *P* values indicate significance of differences of the rate of change (at baseline in non-linear increments). LF = lateral femur, MF = medial femur, LT = lateral tibia, MT = medial tibia, PAT = patella, Joint = mean of all compartments.

Table V
Rate of change of WORMS scores over 6 years

WORMS scores	Ethnicity				*P*
	African Americans		Caucasian Americans		
	Rate/year*	95% CI	Rate/year*	95% CI	
Total score	0.99	0.79–1.19	0.81	0.61–1.01	0.193
Cartilage					
Sum of all regions	0.54	0.41–0.66	0.48	0.35–0.61	0.526
LFC	0.06	0.02–0.89	0.08	0.04–0.12	0.388
LT	0.14	0.09–0.19	0.11	0.07–0.16	0.399
MFC	0.07	0.02–0.11	0.09	0.04–0.13	0.49
MT	0.07	0.04–0.09	0.06	0.03–0.08	0.619
P	0.2	0.14–0.26	0.13	0.07–0.19	0.133
BMEP					
Sum of all regions	0.17	0.12–0.22	0.11	0.06–0.16	0.109
LFC	−0.01	−0.02–0.04	0.02	0.003–0.03	**0.009**
LT	0.03	0.02–0.05	0.02	−0.001–0.03	0.108
MFC	0.037	0.02–0.05	0.003	−0.01–0.02	**0.006**
MT	0.01	0.003–0.02	0.006	−0.003–0.02	0.400
P	0.05	0.02–0.08	0.01	−0.02–0.04	*0.076*
Menisci					
Meniscus sum	0.15	0.09–0.21	0.11	0.05–0.17	0.405
Medial meniscus	0.05	0.02–0.08	0.06	0.03–0.09	0.743
Lateral meniscus	0.09	0.05–0.15	0.05	0–0.10	0.200

Bold numbers indicate significant differences ($P < 0.05$), italic numbers indicate trends ($P > 0.05 < 0.1$).
* Numbers of rate/year are least square means adjusted for multiple measurements per ID and matched pairing between groups pairs using a mixed random effects model.

generalizability of our findings and may have reduced the power of the study leading to significant differences of T2 values only in the average of compartments and the MFC and borderline significant results of T2 measures in the lateral and medial tibia. Moreover the high rate of dropouts could have introduced a selection bias, e.g., changing demographic data or improving T2 values due to potential dropout of the worst cases receiving TKR. However, demographic data were equally distributed among study groups at all time points and no subject of our study cohort received a TKR during the observation period. Moreover structural degeneration proceeded constantly over the four observation time points. We used the arithmetic average as a parameter for the T2 cartilage composition of the whole joint. This method gives equal weight to all compartments regardless the size of the cartilage segmentations, thus regions with smaller segmentation size may have been overrepresented in the average value. Since we used the same method in both ethnic groups it should not have biased the differences between groups. The strengths of this study are the one to one matching of the African and Caucasian subjects enabling a thorough comparison between the groups and the follow up regimen with four measurements over 6 years that allowed a precise monitoring of the cartilage composition and structural joint degeneration.

In conclusion, this study showed that in AA women without definite radiographic OA T2 values increased faster compared to CA women while the progress of cartilage degeneration and joint degeneration measured with WORMS was comparable. The results suggest that T2 values are able to distinguish ethnicity-related longitudinal cartilage changes in an early stage before differences of structural joint degeneration appear.

Authors' contributions

Study design: MK, UH, GBJ, MN, CEM, TML.
Subject selection: MK, UH, AY, MS, FL.
Image analysis: MK, AY, UH, MS.
Statistical analysis: GBJ, CEM, MK.
Interpretation of data: MK, GBJ, MN, CEM, TML.
Drafting of article: MK, TML.
Review/revision: MK, AY, UH, MS, FL, GBJ, MN, CEM, TML.
Final approval: MK, AY, UH, MS, FL, GBJ, MN, CEM, TML.

Conflict of interest

The authors declare that they have no conflict of interest.

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