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One year change of knee cartilage morphology in the first release of participants from the Osteoarthritis Initiative progression subcohort: association with sex, body mass index, symptoms and radiographic osteoarthritis status

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Abstract

Objective—The Osteoarthritis Initiative (OAI) is a multicentre study targeted at identifying biomarkers for evaluating the progression and risk factors of symptomatic knee OA. Here cartilage loss using 3 Tesla (3 T) MRI is analysed over 1 year in a subset of the OAI, together with its association with various risk factors.

Methods—An age- and gender-stratified subsample of the OAI progression subcohort (79 women and 77 men, mean (SD) age 60.9 (9.9) years, body mass index (BMI) 30.3 (4.7)) with both frequent symptoms and radiographic OA in at least one knee was studied. Coronal FLASHwe (fast low angle shot with water excitation) MRIs of the right knee were acquired at 3 T. Seven readers segmented tibial and femoral cartilages blinded to order of acquisition. Segmentations were quality controlled by one expert.

Results—The reduction in mean cartilage thickness (ThC) was greater ($p = 0.004$) in the medial than in the lateral compartment, greater ($p = 0.001$) in the medial femur (−1.9%) than in the medial tibia (−0.5%) and greater ($p = 0.011$) in the lateral tibia (−0.7%) than in the lateral femur (0.1%). Multifactorial analysis of variance did not reveal significant differences in the rate of change in ThC by sex, BMI, symptoms and radiographic knee OA status. Knees with Kellgren–Lawrence grade 2 or 3 and with a BMI >30 tended to display greater changes.

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Competing interests: FE is CEO of Chondometrics GmbH, a company providing MR image analysis services. He provides consulting services to Pfizer, MerckSerono, Wyeth and Novo Nordisk. SM, WM and MH have part-time appointments with Chondometrics GmbH. BW and M-PH are employed by Pfizer Inc.

Ethics approval: The study was conducted in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with local Institutional Review Board, informed consent regulations and International Conference on Harmonization Good Clinical Practices Guidelines.

Conclusions—In this sample of the OAI progression subcohort, the greatest, but overall very modest, rate of cartilage loss was observed in the weight-bearing medial femoral condyle. Knees with radiographic OA in obese participants showed trends towards higher rates of change than those of other participants, but these trends did not reach statistical significance.

MRI at 1.5 Tesla (T) can provide valuable information on articular cartilage loss and other structural changes in knee osteoarthritis (OA). The rate and SD of change over time reported, however, has varied substantially between studies.[1–12] These variations may be partly due to differences in study populations, with different profiles of risk factors for progression. The rate and SD of change to be expected for a certain cohort has, however, major implications for powering epidemiological, clinical and pharmacological studies in OA. It is therefore important to identify the factors that drive cartilage loss in OA.

Methodologically, it has been shown that 3 T MRI provides a higher signal- and contrast-to-noise ratio[13] and higher test–retest precision of cartilage morphology measurements than 1.5 T MRI.[14] Previous longitudinal studies, have, however, relied on 1.5 T MRI.[1–12] There is thus the hope that 3 T MRI may provide a higher sensitivity to change of cartilage morphometry than 1.5 T MRI.

The Osteoarthritis Initiative (OAI) is targeted at identifying sensitive biomarkers of symptomatic knee OA, and at characterising risk factors associated with its onset and progression. A total of 4796 participants were recruited between 2004 and 2006: 1389 participants had frequent symptoms and radiographic OA (symptomatic knee OA) in at least one knee at baseline, and were assigned to a “progression subcohort”. The first longitudinal (year 1) 3 T MRI data from an age- and gender-stratified subsample of the progression subcohort has been recently released for public use (www.oai.ucsf.edu).

The objective of the current study was to analyse the rate and SD of change over 1 year for different measures of cartilage morphology (volume, thickness and surface areas) at 3 T in this OAI subcohort, and to determine their association with sex, body mass index (BMI), symptoms and radiographic knee OA status.

METHODS

An age- and gender-stratified subsample (OAI public-use data sets 0.1.1, 0.B.1 and 1.B.1) of the OAI progression subcohort was studied. Patients had been recruited at four clinical sites: the University of Maryland School of Medicine (Baltimore), the Ohio State University (Columbus), the University of Pittsburgh and the Memorial Hospital of Rhode Island (Pawtucket). The subsample included 79 women with a mean (SD) age of 60.3 (9.5) years, weight 79.6 (15.6) kg, BMI 30.3 (5.5); and 77 men, age 62.0 (10.2) years, weight 94.6 (13.6) kg, BMI 30.1 (3.7). The BMI for 18 participants was <25, for 59 it was 25–30, for 58 it was 30–35 and for 21 it was >35. The participants included a diversity of ethnic minorities, were 45–79 years old, and had both frequent knee symptoms (pain, aching or stiffness on most days of a month in the past year) and radiographic OA (definite osteophytes in the postero-anterior fixed flexion radiographs15 16) in at least one of their knees, based upon initial radiograph reading at the clinical sites. In this analysis, however, we used the results of independent readings by a musculoskeletal radiologist and a rheumatologist at Boston University for Kellgren–Lawrence (K-L) grade, which in the case of discrepancy were adjudicated by consensus with a third reader.

The MRI sequence used to quantify cartilage morphology (see below) was only available in the right knees, whereas some participants displayed symptoms and radiographic OA in their left knee. Therefore, and because the adjudicated central radiographic readings may have differed from the initial screening readings at the imaging sites, not all knees analysed had

symptomatic knee OA. Of the 156 knees analysed, 108 had frequent symptoms, 110 had definite radiographic OA (56 knees with K-L grade = 2, 47 with K-L grade = 3, and 7 with K-L grade = 4), and 87 had symptomatic and radiographic OA. Seventeen knees showed K-L grade = 0, and 29 K-L grade = 1. 87 knees had both frequent symptoms and radiographic OA. Exclusion criteria were rheumatoid or inflammatory arthritis, bilateral end-stage knee OA, inability to walk without aids and 3 T MRI contraindications.

Double oblique coronal 3D fast low angle shot (FLASH) MRIs with water excitation, a slice thickness of 1.5 mm and an in-plane resolution of 0.31 mm × 0.31 mm of the right knees were available, which had been acquired at 3 T (Siemens Magnetom Trio, Erlangen, Germany) using quadrature transmit–receive knee coils (USA Instruments, Aurora, Ohio, USA). Further technical details on this imaging sequence have been provided for the OAI pilot studies.[17–19] Additionally, a sagittal 3D double echo steady-state (DESS) sequence with 0.7 mm slice thickness was available for both knees,[17–19] but was not analysed in this study. The reasons for analysing the FLASH rather than the DESS were that: (1) published reports on the rate and SD of change of cartilage morphology have been based on spoiled gradient recalled echo sequences (FLASH or SPGR); (2) FLASH or SPGR are currently available for all scanner manufacturers and are therefore easier to implement in multicentre studies; (3) the double oblique coronal FLASH displays minimal partial volume effects in the weight-bearing femoro-tibial compartment of the knee,[20] with the OAI being targeted to (radiographic) femoro-tibial OA); (4) the FLASH has a high and isotropic in-plane resolution (0.31 mm × 0.31 mm vs DESS: 0.37 mm × 0.46 mm); (5) segmentation and quality control of the segmentations are less time consuming and more efficient for the FLASH (1.5 mm slice thickness), as it has fewer slices than DESS (0.7 mm); and (6) the OAI pilot analyses have shown similar test–retest precision for both sequences.[17–19 21] Limitations of the FLASH include the relatively long acquisition time, and inferior contrast between the cartilage and the joint capsule at the posterior femoral condyle and at the trochlea (in the region of Hoffa's fat pad).[17] However, these limitations are less important when investigating only the weight-bearing region of the femoro-tibial joint using coronal acquisitions.

The image data were made available on an external hard drive by the OAI coordinating centre and were quality controlled and converted to a proprietary format at the image analysis centre (Chondrometrics GmbH, Ainring, Germany). Segmentation of the femoro-tibial cartilages was performed by seven technicians with formal training and at least 3 years experience in cartilage segmentation. Images were read in pairs, with blinding to the order of acquisition. The total subchondral bone area (tAB) and the cartilage joint surface area (AC) of the medial tibia (MT), the lateral tibia (LT), the central (weight-bearing) medial femoral condyle (cMF) and the central lateral femoral condyle (cLF) were traced manually.[22] The weight-bearing region of the femoral condyles was analysed between the intercondylar notch and 60% of the distance to the posterior end of the femoral condyles.[17 18] Quality control of all segmentations was performed by a single person (SM), reviewing all segmented slices of all data sets.[14 17] Computations of the tAB, the AC, the part of the subchondral bone covered with cartilage (cAB), the denuded subchondral bone area (dAB), the cartilage volume (VC), the mean cartilage thickness over the cAB (ThCcAB, not including denuded areas) and the mean cartilage thickness over the entire subchondral bone area (ThCtAB, including denuded areas as 0 mm cartilage thickness) were then performed.[22] Changes were also described for the medial (MFTC) and lateral (LFTC) femoro-tibial compartments, by comparing the summed values of MT and cMF, and LT and cLF, respectively, between baseline and follow-up.[18 19] Since changes in VC and ThCtAB may differ from one another under conditions where the tAB is not constant over time,[23 24] both variables were reported. We also compared changes in ThCcAB (actual cartilage thickness) or changes in cAB (cartilaginous area), since both may contribute differently to cartilage loss (changes in ThCtAB).[22]

The mean change, SD of change, standardised response mean (SRM = mean change/SD of change) and the significance of change (two-sided paired t test, without correction for multiple testing) were calculated for each parameter and cartilage plate. The mean percentage change (MC%) was calculated by relating the mean change (in µl, mm or cm^2) in all knees to the mean baseline values of all knees. Negative values indicate a decrease over time in the parameters. Differences in the rate of change between femoro-tibial cartilage plates (MFTC vs LFTC, MT vs cMF and LT vs cLF), and between different morphological parameters (ThCtAB vs VC and ThCcAB vs cAB) were tested using two-sided paired t tests. These tests were performed on the individual percentage changes in each parameter and plate/compartment, without correcting for multiple comparisons. Multifactorial analysis of variance (ANOVA) was used for categorical variables (sex, frequent symptoms (yes/no), radiographic OA (K-L grade 2–4 vs 0–1) and obesity (BMI <30 vs >30)), and general linear models (Statistica 6.1) for continuous variables (age, BMI), to test main and interaction effects and to identify risk factors of cartilage loss. The model was also used to evaluate whether estimates of loss were affected by confounders and needed adjustment.

RESULTS

The annual reductions in VC ranged from −1.5% (cMF; 95% CI −2.6% to −0.35%, p = 0.008) to 0.0% (cLF; −0.7% to 0.7%, p = 0.95), and those for ThCtAB from −1.9% (cMF; −2.9% to −0.9%, p = 0.0002) to +0.1% (cLF; −0.5% to 0.7%, p = 0.76) (table 1). The rate (MC%) and sensitivity (SRM) to change was higher for ThCtAB than for VC, the difference attaining significance (p<0.05) in cMF, but not in MT, LT or cLF. The SRM was highest for cMF.ThCtAB (−0.30) and for MFTC.ThCtAB (−0.31). The tAB of cMF displayed a significant increase (0.4% (SD 1.8%); p<0.01) over 1 year, whereas in MT (+0.1% (1.2%); p = 0.57), LT (+0.1% (1.3%); p = 0.15) and cLF (0.0% (1.5%); p = 0.91), only trends were observed.

The reduction in ThCtAB was significantly greater (p = 0.004) in the medial (MFTC) than in the lateral compartment (LFTC). Comparing plates within each compartment, the change was greater (p = 0.001) in cMF than in MT, and greater (p = 0.011) in LT than in cLF (table 1).

In all cartilage plates, the reduction in ThCcAB was greater than that in cAB (table 1), the differences being significant in cMF (p<0.05) and LT (p<0.01), but not in MT or cLF.

Multifactorial ANOVA did not indicate significant differences in the rate of change in any of the cartilage parameters by sex, frequent symptoms, radiographic OA status or obesity as categorical variables, or by age and BMI as continuous variables. No significant interactions between these factors and cartilage loss were found. The general linear models showed that the estimate adjusted for potential confounders did not differ relevantly from the non-adjusted values given in tables 1–5.

Although not statistically significant, some interesting trends were observed: men tended to show a somewhat greater rate of change than women (table 1), and knees with frequent knee symptoms a somewhat lower rate than those without symptoms (table 2). Knees with definite radiographic OA (K-L grade ≥2) tended to display a greater rate of change than those with KL grade 0–1 (tables 2 and 3), but knees without radiographic OA also displayed a significant (p<0.05) cartilage loss in MFTC. Knees with K-L grade 3 tended to display a higher rate than those with K-L grade 2 in cMF and LT, and KL grade 4 knees (n = 7) did not show any trend for cartilage loss (table 3). Participants with a BMI >30 tended to display a higher rate of change than those with a BMI <30, but those with a BMI >35 did not show trends towards a greater loss than those with a BMI of 30–35 (table 4). Amongst different subgroups defined by baseline characteristics, the highest rate of change (−5.1%) and SRM (−0.52) was observed for cMF.ThCtAB in a group with K-L grade 3, obesity and frequent symptoms (table 5).

DISCUSSION

This is the first study to present the rate and sensitivity of longitudinal change in cartilage morphology from the Osteoarthritis Initiative progression subcohort based on the coronal FLASHwe (FLASH with water excitation) sequence at 3 T. The reliability (test–retest reproducibility) has been tested and reported previously on the same MRI acquisition protocol (OAI pilot studies) and with the same team of readers, both using "unpaired"[17] and "paired" reading designs.18 19 The advantage of the FLASH/SPGR sequence family is that it is universally available on all MRI vendor platforms. The advantage of the double oblique coronal acquisition is that it is subject to only minimal partial volume effects in the weight-bearing femoro-tibial compartment and can be acquired with a high isotropic in-plane resolution.14 [20] Also, FLASH/SPGR sequences have been extensively validated versus external standards for accurate measurement of cartilage volume and thickness,[11 14 25–31] and their test–retest precision has been thoroughly documented by several groups (reviewed in Eckstein *et al*11 12). Furthermore, previous reports on longitudinal change in cartilage morphology have relied on this[1–4 8 10 19] or the technically similar FISP sequence (fast imaging at steady-state precision).[5–7 9] On the other hand, sagittal DESS images (which were also acquired as part of the protocol) display a broader range of tissue contrast and better delineation of cartilage–fluid interfaces, and may thus reveal structural features within the cartilage that are not visualised by FLASH.

A limitation of the current study is that FLASHwe was only available for right knees, but not necessarily for the knee that met the inclusion criteria for the OAI progression subcohort. This protocol decision had been made to accommodate also the broader scientific objectives of the OAI without exceeding subject tolerance limits. The inclusion of knees without frequent symptoms and without definite radiographic OA in this study, however, made it possible to compare the rate and sensitivity of change across knees with a wide range of these features.

The rate of cartilage loss reported here was very modest and at the lower end of that observed in previous studies,[1–12 19] despite the use of 3 T MRI. The highest annual rates of change have been reported by Cicuttini *et al*[4] (7.4% (7.8%) in MT and 8.7% (9.7%) in cLF) in a 2-year observational study, using coronal reconstructions of sagittal SPGR images at 1.5 T. A potential reason for the relatively low rate of change in our analysis, despite the use of 3 T MRI, is the heterogeneity of the cohort examined and the fact that the observation period was only 12 months. In a subgroup with radiographic OA and obesity, we observed a 4.0% change in ThCtAB of cMF, and in one with K-L grade 3, obesity and frequent symptoms a 5.1% change.

A recent clinical multicentre study at 3 T in 61 OA participants (1 mm coronal FLASHwe acquisitions) also reported relatively small rates of changes and SRM values at 12 months, although only obese women (BMI >30) were studied.32 Another study of the same OAI participants investigated here was based on the sagittal DESSwe.33 Because the DESSwe acquisitions were available in both knees, the investigators selected the study knee to be preferably symptomatic and display radiographic OA. Nevertheless, 16% of the knees investigated in their study were K-L grade 0 or 1 (because final classification was based on the central and not on the initial site readings), whereas in our study these were 30%. Despite this difference in knee selection, the different MRI sequence and the different image analysis platform, the observations were surprisingly similar to those made here.33 The mean and SD of change were similar, and the greatest changes were also observed in cMF. We have no plausible explanation as to why changes might have been higher in cMF than in MT (and higher in LT than in cLF), as this pattern of cartilage loss has not been consistently reported in other cohorts.11 12

Previous studies have reported an increase in tAB over time in subjects with,[23] 24 and without knee OA,34 probably because metaphyseal growth continues throughout adulthood.35 [36] In the current study, a significant increase of the tAB was observed in cMF and there were trends towards increases in the other cartilage plates. Because an increase in tAB may be associated with an increase in cartilage volume, the reduction in ThCtAB may have been greater and less variable than that in volume, and thus more sensitive to change. In the present cohort, the reduction in ThCtAB was primarily due to a reduction in actual cartilage thickness (ThCcAB) rather than a decrease in cartilaginous area (cAB) or an increase in denuded area, and, to our knowledge, this pattern has not been described previously.

No significant differences in the rate of change by age, sex, BMI, frequent symptoms or radiographic knee OA status (KL grade) were detected, probably because the differences in structural progression between these subgroups were too small to be significant in this size of cohort over a 1-year period. Given that a total of >1400 participants and longer observation periods (up to 4 years) will be available for the progression subcohort, there will be ample opportunity to test for differences in structural progression of cartilage morphology between these groups with higher statistical power. Because of the lack of statistical significance, all interpretations with regard to trends must remain speculative and should thus be viewed with caution: previous studies reported that women have a higher rate of progression of knee OA, [5] 9 but we were unable to confirm this finding in our current study. Also, we did not find symptomatic knees to display higher rates of change than those without symptoms, potentially because frequent symptoms reduce the level of physical activity and thus the mechanical forces that drive cartilage loss. A higher cartilage loss in subjects with high BMI has been reported previously in the literature5 9 [37] and was therefore expected. The same was expected for knees with radiographic OA. Although some knees with early OA may progress before radiographic changes become apparent, the likelihood of progression in a knee that has already undergone substantial structural changes may be expected to be higher than in one without, and these assumptions were confirmed here.

In conclusion, only a modest rate of cartilage loss was observed in this first subsample of the OAI progression subcohort, despite the use of 3 T MRI. The greatest changes were observed in the weight-bearing medial femoral condyle, and changes in the medial compartment were significantly greater than those in the lateral femoro-tibial compartment. Changes in cartilage thickness (over the tAB) were greater than those in cartilage volume, and changes in thickness (over the cAB) greater than the reduction in cartilage-covered areas. Knees with radiographic OA in obese persons tended to display higher rates of change than those of the other participants, but these trends did not reach statistical significance.

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Table 1

Change in cartilage morphology (in the right knee) over 1 year for the total subcohort, and for women and men, respectively

		All (n = 156)			Women (n = 79)			Men (n = 77)		
		MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value
MT	VC	−0.42	−0.12	0.13	−0.40	−0.13	0.25	−0.44	−0.12	0.28
	ThCtAB	−0.52	−0.16	0.04*	−0.46	−0.14	0.22	−0.58	−0.18	0.11
	ThCcAB	−0.34	−0.12	0.14	−0.23	−0.08	0.47	−0.44	−0.15	0.19
	cAB	−0.19	−0.11	0.19	−0.31	−0.14	0.22	−0.11	−0.07	0.56
cMF	VC	−1.49	−0.21	0.008*	−1.14	−0.18	0.12	−1.74	−0.25	0.03*
	ThCtAB	−1.92	−0.30	<0.001*	−1.69	−0.26	0.02*	−2.12	−0.34	0.004*
	ThCcAB	−1.46	−0.26	0.002*	−1.34	−0.23	0.047*	−1.56	−0.28	0.02*
	cAB	−0.47	−0.12	0.14	−0.20	−0.06	0.61	−0.69	−0.17	0.15
MFTC	VC	−0.79	−0.22	0.007*	−0.66	−0.19	0.10	−0.88	−0.25	0.03*
	ThCtAB	−1.23	−0.31	<0.001*	−1.08	−0.26	0.03*	−1.37	−0.37	0.002*
LT	VC	−0.55	−0.17	0.03*	−0.55	−0.14	0.21	−0.55	−0.20	0.08
	ThCtAB	−0.68	−0.23	0.005*	−0.76	−0.21	0.07	−0.60	−0.27	0.02*
	ThCcAB	−0.60	−0.21	0.009*	−0.68	−0.19	0.09	−0.52	−0.24	0.04*
	cAB	0.03	0.02	0.78	0.15	0.11	0.32	−0.06	−0.05	0.67
cLF	VC	0.02	0.01	0.95	0.67	0.13	0.27	−0.42	−0.11	0.33
	ThCtAB	0.09	0.02	0.77	0.60	0.13	0.26	−0.35	−0.11	0.35
	ThCcAB	0.13	0.03	0.67	0.70	0.15	0.18	−0.37	−0.12	0.30
	cAB	0.01	0.00	0.95	−0.06	−0.04	0.75	0.06	0.03	0.77
LFTC	VC	−0.33	−0.12	0.14	−0.09	−0.02	0.83	−0.50	−0.21	0.07
	ThCtAB	−0.30	−0.11	0.17	−0.10	−0.03	0.80	−0.48	−0.23	0.046*

cAB, cartilage-covered bone area; cLF, weight-bearing lateral femoral condyle; cMF, weight-bearing medial femoral condyle; LFTC, lateral femoro-tibial compartment; LT, lateral tibia; MC%, mean change (in %); MFTC, medial femoro-tibial compartment; MT, medial tibia; SRM, standardised response mean (mean change/SD of change); ThCcAB, thickness of the cartilage over the entire cAB; ThCtAB, thickness of the cartilage over the entire subchondral bone area; VC, volume of cartilage.

* p Values <0.05 for paired t test between baseline and 1 year, without correcting for multiple testing, showing that the rate of loss was significantly different from zero.

Table 2

Change in cartilage thickness over the entire subchondral bone area (ThCtAB) over 1 year for participants without and with frequent symptoms of the right knee, and without (Kellgren–Lawrence (K-L) grade = 0 or 1) and with radiographic osteoarthritis of the right knee (K-L grade = 2, 3 and 4)

	No freq. symp. (n = 48)			Freq. symp. (n = 108)			No ROA (n = 46)			ROA (n = 110)		
	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value
MT	−1.17	−0.45	0.003*	−0.25	−0.07	0.452	−0.45	−0.23	0.13	−0.55	−0.15	0.11
cMF	−1.50	−0.37	0.02*	−2.11	−0.30	0.003*	−0.97	−0.35	0.02*	−2.35	−0.32	0.001*
MFTC	−1.34	−0.47	0.002*	−1.18	−0.27	0.006*	−0.72	−0.36	0.02*	−1.45	−0.32	0.001*
LT	−0.70	−0.25	0.08	−0.66	−0.22	0.03*	−0.11	−0.04	0.77	−0.93	−0.30	0.002*
cLF	0.59	0.17	0.23	−0.12	−0.03	0.77	0.15	0.05	0.76	0.07	0.02	0.86
LFTC	−0.09	−0.04	0.81	−0.39	−0.14	0.15	0.01	0.00	0.98	−0.43	−0.15	0.12

* p Values <0.05 for paired t test between baseline and 1 year, without correcting for multiple testing, showing that the rate of loss was significantly different from zero.

Freq., frequent; ROA, radiographic osteoartritis; Symp, symptoms; for other abbreviations see the footnotes of table 1.

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Table 3

Change in cartilage thickness over the entire subchondral bone area (ThCtAB) over 1 year for participants with Kellgren–Lawrence (K-L) grade 0, 2, 3 and 4

	K-L grade 0 (n = 17)			K-L grade 2 (n = 56)			K-L grade 3 (n = 47)			K-L grade 4 (n = 7)		
	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value
MT	−0.70	−0.33	0.19	−0.58	−0.18	0.19	−0.58	−0.14	0.35	−0.13	−0.07	0.85
cMF	−1.12	−0.43	0.10	−1.82	−0.29	0.04*	−4.04	−0.51	0.001*	4.46	0.34	0.40
MFTC	−0.92	−0.46	0.07	−1.23	−0.30	0.03*	−2.24	−0.46	0.003*	2.07	0.33	0.42
LT	0.07	0.03	0.89	−0.80	−0.27	0.047*	−1.26	−0.37	0.01*	0.29	0.16	0.68
cLF	−0.16	−0.07	0.79	−0.19	−0.05	0.72	0.08	0.02	0.90	2.15	0.43	0.30
LFTC	−0.03	−0.02	0.92	−0.50	−0.18	0.18	−0.58	−0.19	0.20	1.28	0.42	0.31

* p Values <0.05 for paired t test between baseline and 1 year, without correcting for multiple testing, showing that the rate of loss was significantly different from zero.

For abbreviations see table 1.

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Table 4

Change in cartilage thickness over the entire subchondral bone area (ThCtAB) over 1 year for participants with normal weight (body mass index (BMI) <25), for overweight participants (BMI ≥25), for obese participants (BMI ≥30) and for participants with obesity grade 2 and 3 (BMI ≥35)

	BMI <25 (n = 18)			BMI 25–30 (n = 59)			BMI 30–35 (n = 58)			BMI ≥35 (n = 21)		
	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value
MT	−0.46	−0.14	0.56	−0.22	−0.08	0.53	−1.00	−0.27	0.04*	−0.08	−0.03	0.90
cMF	0.10	0.03	0.89	−1.38	−0.24	0.07	−3.28	−0.42	0.002*	−1.56	−0.30	0.18
MFTC	−0.17	−0.06	0.80	−0.81	−0.25	0.06	−2.14	−0.43	0.001*	−0.84	−0.25	0.26
LT	−0.43	−0.21	0.39	−0.38	−0.11	0.39	−0.97	−0.41	0.003*	−0.96	−0.29	0.21
cLF	−0.02	−0.01	0.98	0.17	0.05	0.71	−0.09	−0.02	0.87	0.48	0.09	0.68
LFTC	−0.23	−0.10	0.67	−0.12	−0.04	0.75	−0.53	−0.21	0.13	−0.25	−0.09	0.68

* p Values <0.05 for paired t test between baseline and 1 year, without correcting for multiple testing, showing that the rate of loss was significantly different from zero.

For abbreviations see the footnotes of table 1.

Table 5

Change in cartilage thickness over the entire subchondral bone area (ThCtAB) over 1 year for participants with radiographic OA (ROA: K-L grade ≥2) and frequent symptoms (FS), with ROA and obesity, with K-L grade 3 and obesity and with K-L grade 3, obesity and FS

	ROA+FS (n = 87)			ROA+obesity (n = 57)			K-L 3+obesity (n = 29)			K-L 3+obesity+FS (n = 23)		
	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value	MC%	SRM	p Value
MT	−0.52	−0.16	0.04*	−0.95	−0.24	0.08*	−0.81	−0.17	0.37	−0.35	−0.07	0.74
cMF	−1.92	−0.30	<0.001*	−3.98	−0.46	<0.001*	−4.38	−0.48	0.02*	−5.06	−0.52	0.02*
MFTC	−1.23	−0.31	<0.001*	−2.45	−0.45	0.001*	−2.48	−0.42	0.03*	−2.55	−0.40	0.07
LT	−0.68	−0.23	0.005*	−1.11	−0.39	0.005*	−1.27	−0.49	0.01*	−1.40	−0.51	0.02*
cLF	0.09	0.02	0.77	0.06	0.01	0.92	0.46	0.10	0.61	0.31	0.06	0.77
LFTC	−0.30	−0.11	0.17	−0.52	−0.18	0.17	−0.39	−0.13	0.50	−0.53	−0.16	0.44

* p Values <0.05 for paired t test between baseline and 1 year, without correcting for multiple testing, showing that the rate of loss was significantly different from zero.

For abbreviations see the footnotes of table 1.