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Magnetic Resonance Imaging based Cartilage Loss in Painful Contra-Lateral Knees with and without Radiographic Joint Space Narrowing – Data from the Osteoarthritis Initiative (OAI)

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Abstract

Objective—Magnetic resonance imaging (MRI) was used to assess whether knees with advanced radiographic disease (medial joint space narrowing = mJSN) encounter greater longitudinal cartilage loss than contra-lateral knees with earlier disease (no or less mJSN).

Methods—Participants were selected from 2678 cases in the Osteoarthritis Initiative, based on exhibition of bilateral pain, BMI>25, mJSN in one knee, no or less mJSN in the contra-lateral knee, and no lateral JSN in both knees. 80 participants (age 60.6±9.1 yrs) fulfilled these criteria. Medial tibial and femoral cartilage morphology was analyzed from baseline and 1-year follow-up sagittal DESSwe 3 Tesla MRI of both knees, by experienced readers blinded to the timepoint and mJSN status.

Results—Knees with more radiographic mJSN displayed greater medial cartilage loss (-80 µm), assessed by MRI, than contra-lateral knees with less mJSN (-57µm). The difference reached statistical significance in participants with mJSN grade 2 or 3 (p=0.005 to p=0.08), but not in participants with mJSN grade 1 (p=0.28 to 0.98). In knees with more mJSN, cartilage loss increased with higher grades of mJSN (p=0.003 in the medial femur). Knees with mJSN grade 2 or 3 displayed greater cartilage loss in the weight-bearing medial femur than in the posterior femur or in the medial tibia (p=0.048).

Conclusion—Knees with advanced mJSN displayed greater cartilage loss than contra-lateral knees with less mJSN. These data suggest that radiography can be used to stratify fast structural progressors, and that MRI cartilage thickness loss is more pronounced at advanced radiographic disease stage.

Keywords

Progression; Joint Space Narrowing; Radiographic osteoarthritis; Cartilage loss; Magnetic Resonance Imaging

Introduction

Radiography has been used for decades to identify structural changes of joints and to diagnose osteoarthritis (OA) (1-5). Surprisingly, however, little is known about the rate of cartilage loss in different (radiographic) stages of the disease, and whether distinct radiographic features of OA predict the rate of cartilage loss. Felson et al. (6) reported that osteophyte scores were modestly associated with joint space narrowing (JSN) in the same knee compartment over a period of 30 months, but the relationship became weaker and non-significant, when adjusting for knee alignment. Wolfe and Lane (7) found that JSN was a strong predictor of further radiographic JSN, whereas body mass index (BMI) and osteophytes were less predictive, contributing significant information only among participants with no JSN at baseline. Mazzuca et al. (8) and Le Graverand et al. (9) also observed that progression of JSN was greater in knees with JSN than in knees without JSN by using fluoroscopically standardized knee radiographs. However, Bruyere et al. (10) reported that patients in the highest quartile of baseline joint space width experience more severe cartilage loss than those in the lowest quartile.

Few studies have investigated the relationship of cartilage loss measured quantitatively with magnetic resonance imaging (MRI) and radiographic features of OA at baseline. Raynauld et al. (11) found no significant association between radiographic joint space width at baseline and cartilage loss over 24 months, but another study from the same group (12) reported that cartilage loss in the central aspects of femorotibial cartilage plates was associated with smaller joint space width and higher grades of JSN at baseline. Wluka et al. (13) reported that participants with greater baseline cartilage volume encountered significantly greater cartilage loss over 24 months than those with smaller cartilage volumes. Therefore, it is currently unclear whether study participants can be successfully identified as “fast progressors” based on joint space narrowing in baseline radiographs or cartilage thickness volume in MRI, for instance to test the effect of a structure modifying, cartilage-protective drug in a relatively small cohort.

One difficulty in establishing the relationship between baseline JSN and OA progression is the variability in cartilage loss between subjects, and the potential large impact of inter-subject confounding factors, such as age, sex, race, BMI, etc. To compare cartilage loss in knees with and without medial JSN (mJSN), we therefore examined progression of JSN in contra-lateral knees, where one knee displayed mJSN at baseline and the other displayed no or less mJSN. This study design made it possible to directly compare rates of cartilage loss in early and more advanced radiographic disease within the same participants while controlling for other covariants between subjects. We assessed whether cartilage loss, as measured with MRI, is greater in knees with advanced medial radiographic OA (mJSN grades 1 to 3) than in contra-lateral knees with early disease (no or less mJSN).

Methods

The subsample studied was drawn from the first half (2678 cases) of the Osteoarthritis Initiative (OAI) cohort (public-use data sets 1.2.1 for the clinical data and 1.B.1 for the imaging data). The OAI is a multi-center, population-based longitudinal cohort study designed to identify biomarkers for the development and/or progression of symptomatic

knee OA (<http://www.oai.ucsf.edu/datarelease/>). Participants in the OAI cohort are between 45 and 79 years old and span across a diversity of ethnic backgrounds. Participants with rheumatoid or other inflammatory arthritis, bilateral end stage knee OA, inability to walk without aids, or 3 Tesla (T) MRI contra-indications were excluded from the OAI cohort.

The target population for the current study was a selection of approximately 80 participants fulfilling the following criteria:

- BMI >30
- chronic frequent pain in both knees (grade 2 = most days of a month within the past 12 months)
- mJSN (OARSI grade 1-2) in one knee
- no mJSN (grade 0) in the contra-lateral knee
- lack of JSN in the lateral femoro-tibial compartment of either knee.

However, the number of eligible participants based on the selection criteria above fell short of the targeted 80 participants. Thus, the criteria were modified to:

- BMI >25
- preferably chronic frequent pain (as defined above), alternatively “occasional” pain (grade 1 = pain in past 12 months, but not most days of a month) in knees with less mJSN. Knees with “occasional” pain were only included, however, if the knee displayed definite (OARSI grade ≥ 2) osteophytes (2 of the 80 cases)
- mJSN grade 1, 2 or 3 in one knee (JSN grade 3 = 8 cases)
- preferably no mJSN in one knee, alternatively less mJSN (for example grade 1) than in the contra-lateral knee (7 cases)
- preferably no lateral JSN in both knees, alternatively some lateral JSN in the knee with more mJSN, but lower grade of lateral JSN than mJSN in the same knee (3 cases)

In a first step, we used the files of 160 participants from the OAI progression subcohort (OAI public-use datasets 0.1.1, 0.B.1 and 1.B.1), for which readings of fixed flexion radiographs (JSN and osteophyte status) at the 4 imaging sites as well as central readings and adjudicated readings were available (14,15). Based on the adjudicated readings, 19 (of the 160) cases fulfilled the modified selection criteria described above. Another 61 cases were selected by using the radiographic readings from the 4 imaging sites of all 2678 cases (OAI public-use data sets 1.2.1 and 1.B.1) less the 160 cases mentioned above (public-use datasets 0.1.1, 0.B.1 and 1.B.1). Central radiographic readings were performed within the context of the current study, and participants were only included, if the selection criteria were confirmed based on central readings by an experienced musculoskeletal radiologist (A.G.) and adjudication by a rheumatologist (D.H.) in case of disagreement between site and central reading. Finally, 80 participants were included.

As part of the OAI, baseline and 1-year follow-up MRI of both knees were acquired for each of the 80 participants at one of 4 imaging sites, using 3 Tesla MRI systems (Siemens Magnetom Trio, Erlangen, Germany) and quadrature transmit-receive knee coils (USA Instruments, Aurora, OH). Sagittal double echo at steady state (DESS) images (Fig. 1) with 0.7 mm slice thickness (160 slices, in-plane resolution = 0.37 mm $\times$ 0.46 mm, interpolated to 0.37 mm $\times$ 0.37 mm; 140 mm field of view, 512 $\times$ 512 matrix; repetition time 16.3 ms, echo time 4.7 ms, flip angle 25°) were acquired with water excitation (16). The sagittal DESS has been shown (16) to produce cartilage thickness data consistent with that of

previously validated spoiled gradient recalled (SPGR) sequences with water excitation or fat suppression (17,18) and to display a similar test-retest precision (reproducibility) (16,19,20). Additional details on MRI procedures are available in the recently published OAI imaging protocol (21). The OAI study protocol, amendments, and informed consent documentation were reviewed and approved by the local institutional review boards.

The images were shipped from the OAI coordinating center to the image analysis center (Chondrometrics GmbH, Ainring, Germany) using hard drives and were quality controlled. The images were then analyzed in pairs (baseline and 1-year follow-up per participant) by 7 readers, each with more than 3 years experience in cartilage segmentation and with previous experience in segmenting sagittal DESS images from the OAI pilot studies (16,19,20). The readers were blinded to the timepoint of image acquisition and to the mJSN status of the knee. Manual segmentation of the cartilage surface and of the bone interface of the medial femoro-tibial cartilage plates, specifically the medial tibia (MT) and medial femoral condyle (MF), was performed using custom software (Chondrometrics GmbH, Ainring, Germany). All segmentations were quality controlled by a single reader (S.M.).

As an outcome measure, the mean cartilage thickness over the entire subchondral bone area (ThCtAB) was computed, including denuded areas of subchondral bone with zero millimeter cartilage thickness (22). The MF was separated into a weight-bearing part (cMF) and a posterior part (pMF) (16,19,20,22) by a plane parallel to the femoral shaft, cutting through the condyle at 75% of the distance between the trochlear notch and the posterior ends of both the medial and lateral femoral condyles (Fig. 1). To achieve this, the readers marked a vector running parallel to the shaft through the most posterior point of the trochlear notch (Fig. 1a) and the most posterior points of the medial and lateral femoral condyles (Figs. 1b and 1c). To obtain a single integral measure for the weight-bearing part of the femorotibial joint (MFTC), ThCtAB of MT and cMF were added at baseline and follow up (14,19,20).

As a measure of progression, the mean change in ThCtAB (in mm) was determined in the knees with and without mJSN as well as in subgroups with different mJSN grades (1 to 3). Additionally, the standard deviation (SD) of the change, and the standardized response mean (SRM = mean change / SD of the change) was calculated, as a measure of the sensitivity to change.

To determine whether the rate of cartilage loss was affected by mJSN, we compared the mean change in ThCtAB (over one year) in knees with mJSN (grades 1 to 3) to the mean change in contra-lateral knees with less mJSN (n=80), using a Wilcoxon signed rank test. In a further step, the analysis was restricted to participants with mJSN in one knee and no mJSN (grade 0) in the contra-lateral knee (n=73).

To determine whether the baseline grade of mJSN was an important predictor of cartilage loss, Wilcoxon signed rank tests were performed in mJSN grade 1 knees versus contra-lateral knees (n=47), and in mJSN grade 2 or 3 versus contra-lateral knees (n=33), respectively. Kruskal-Wallis tests were used to study the effect of mJSN on the mean change of ThCtAB in the knees with more mJSN.

To determine whether the rate of cartilage loss differed between regions of the medial femoro-tibial compartment, we compared the mean change of ThCtAB in the MT, cMF and pMF using an ANOVA of repeated measures. The test was applied to knees with more mJSN (n=80), knees with less mJSN (n=80), and knees with mJSN grades 2 and 3 (n=33), respectively.

Results

The sub-sample studied included 32 men and 48 women, aged 60.9 ± 9.1 [mean $\pm$ SD] with an age range of 45 to 78 years (BMI 31.1 ± 4.0 kg/m², range 25.1 to 42.3 kg/m²; weight 87 ± 13.4 kg, range 56 to 121 kg; height 167 ± 10.1 cm, range 142 to 192 cm). In the knees with less mJSN, 73 of the 80 subjects had no mJSN (grade 0; 22% with and 78% without definite [$\geq$ OARSI grade 2] medial femoro-tibial osteophytes), and 7 subjects had mJSN grade 1 (29% with and 71% without definite osteophytes). In the knees with more mJSN, 47 displayed mJSN grade 1 (47% with and 53% without definite medial femoro-tibial osteophytes), 25 displayed mJSN grade 2 (64% with and 36% without definite osteophytes), and 8 displayed mJSN grade 3 (all with definite osteophytes). Subjects with mJSN grade 1 (more mJSN knees) did not show significant differences in sex distribution (44.7% versus 33.3% male; Chi-square $p=0.31$), age (58.3 ± 8.5 y versus 57.4 ± 10.0 y; unpaired t-test $p=0.91$), or BMI (30.5 ± 3.7 versus 32.1 ± 4.3 SD; unpaired t-test $p=0.08$) compared with subjects with mJSN grade 2 and 3 (more mJSN knees).

Baseline values, mean change in ThCtAB over 12 months, and the SD of the change in the knees with less mJSN are shown in Table 1, and those with more mJSN in Table 2. The SRMs for different mJSN grades are displayed in Figure 2.

Generally, the knees with more mJSN displayed a greater mean change of ThCtAB than those with less mJSN (Tables 1 and 2). However, the difference in the mean change between both knees did not reach statistical significance ($n=80$; range of p-values [Wilcoxon signed rank test] for different regions 0.11 to 0.23; Table 3). This was similar when restricting the analysis to participants who displayed no mJSN (grade 0) in one knee, and mJSN grade 1 to 3 in the contra-lateral knee ($n=73$; range $p=0.12$ to 0.29; Table 3). When stratifying for mJSN grades, participants with mJSN grade 1 in one knee and no mJSN in the contra-lateral knee did not display any difference in the mean change of ThCtAB between knees ($n=47$; range $p=0.28$ to 0.98; Table 3). The knees with mJSN grades 2 or 3 in one knee and less mJSN in the contra-lateral knee, however, displayed significant differences in the rate of cartilage loss in MF, cMF, pMF and MFTC ($n=33$; range $p=0.005$ to 0.04; Table 3). The difference reached borderline significance in MT ($p=0.08$).

In knees with less mJSN, those with mJSN grade 1 ($n=7$) displayed relatively large changes of ThCtAB compared to those with mJSN grade 0 (Table 1, Fig. 2). In knees with more mJSN, the mean change and SRM tended to increase with higher mJSN grade (Table 2, Fig. 2). The Kruskal-Wallis test among knees with more mJSN (mJSN grades 1 to 3) identified significant differences among the mean changes of ThCtAB in cMF ($p=0.003$), MFTC ($p=0.005$), and MF ($p=0.005$), but not in MT ($p=0.34$) or pMF ($p=0.11$). The greatest SRM was observed in the cMF of the mJSN grade 3 knees (Fig. 2).

The mean change of ThCtAB in cMF was higher than in pMF in most subgroups, but the difference in cartilage loss between MT, cMF and pMF was not statistically significant in the knees with less mJSN ($p=0.19$) or in those with more mJSN ($p=0.58$). In the mJSN grade 2 or 3 knees ($n=33$), however, the mean change of ThCtAB significantly differed between the three regions ($p=0.048$), with the change in cMF being greater than in pMF or MT (Fig. 3).

Discussion

In this study, we assessed whether knees with advanced radiographic disease, specifically with medial joint space narrowing (mJSN), encounter greater longitudinal cartilage loss than contra-lateral knees with no or less mJSN. In knees with advanced (grade 2 or 3) mJSN, but

not in knees with mJSN grade 1, we found a significantly greater longitudinal cartilage loss over 12 months compared to contra-lateral knees with no or less mJSN.

A limitation of the study is the relatively small sample size, and that a significant difference in cartilage loss between knees with and without mJSN was only confirmed in the subgroup of 33 mJSN grade 2 or 3, but not in the 47 mJSN grade 1 (versus grade 0) knees. The strength of this design approach, however, was the ability to study the question of interest across subjects with different grades of mJSN, but based on examining contra-lateral knees such that one knee displayed mJSN and the other knee displayed no or less mJSN. This allowed us to remove confounding by inter-subject differences in sex, age, race, BMI, etc. The main analyses for this paper focused upon within person differences in MR cartilage thickness loss and attributed these to differences in radiographic JSN. There is potential for residual unmeasured confounding in more severely radiographically damaged knees that may be at the knee level, as opposed to the person level that could also account for these differences.

Despite a substantial cohort of 2678 cases to choose from, relatively few subjects (n=80) fulfilled the specific selection criteria for the current study after confirmation of mJSN grades by central radiographic reading. This suggests that a large cohort, such as the OAI cohort, is required to support this specific approach. The extensive size and public nature of the OAI data enabled the study of targeted questions that might have been difficult or even impossible to address in smaller cohorts. Other strengths of the current analysis are that 3 Tesla MRI and validated imaging sequences were used for determining structural progression (cartilage loss), and that radiographic readings at the imaging sites were confirmed by central radiographic readings.

Our findings agree with previous work (7-9,12) that the rate of progression towards higher grades of JSN or cartilage loss is greater in knees with JSN than in knees without JSN at baseline. Our findings, however, directly contradict those of Bruyere et al. (10) who reported that patients in the highest quartile of baseline joint space width experience more severe cartilage loss than those in the lowest quartile and therefore recommended the inclusion of participants with less severe OA in trials studying disease modifying OA drugs (DMOADs). These authors (10) used radiography and the measurement of joint space width may have been influenced by the meniscus (23), whereas the current study examined the articular cartilage independent of other tissues. Because our findings show that higher grades of mJSN are also reflected in lower medial baseline cartilage thickness values, our findings also indirectly contradict those of Wluka et al. (13) who reported that participants with greater baseline cartilage volume encountered significantly greater cartilage loss than those with smaller volumes. We have no explanation as to why our results deviate from their findings (13). Our results reinforce, however, previous observations that the rate of progression (reduction in joint space width) is higher in knees with established OA than in contra-lateral knees without established OA (24).

Our study not only confirms, but also extends previous findings since it highlights the importance of mJSN grade. The results suggest that only knees with higher grades of mJSN (2 or 3) are associated with accelerated cartilage loss, while knees with mJSN grade 1 display a rate of change and sensitivity similar to that of contra-lateral knees with no mJSN. Interestingly, baseline values in cartilage thickness (ThCtAB) varied only a little between mJSN grade 0 and mJSN grade 1 knees, but were clearly lower in mJSN grade 2 or 3 knees.

To assess the practical implications of our findings, we performed sample size calculations based on the assumption that a DMOAD will be able to reduce the cartilage thickness loss by 50% (i.e. from 80 μ m to 40 μ m per annum), that the SD of change in the treated group is

similar to that in the placebo group, and that the power to detect 1-tailed significance with a type 1 error rate of 5% between the DMOAD and placebo group is 90%. Using these assumptions and the observed rates of change in MFTC in this study, a DMOAD trial would require 1114 participants per group to show a significant reduction in cartilage thickness loss by the DMOAD when including only participants with mJSN grade 0, 326 participants per group when including knees with mJSN (grade 1, 2 and 3 proportional to the knees with more mJSN in this study), and 127 participants per group when including knees with mJSN grade 2 or 3 only. These represent considerable savings in sample size, but will require exclusion of considerable proportions of potential participants during screening: In the OAI cohort, of all knees with definite radiographic OA (definite osteophytes; n = 4346), 44% displayed JSN (OARSI grade 1, 2 or 3) and 56% displayed no mJSN (grade 0) according to the screening readings at the sites. Adjudicated central readings in 160 cases from the OAI progression cohort found that in those with mJSN, 47% were OARSI mJSN grade 1, 46% mJSN grade 2, and 7% mJSN grade 3 (53% mJSN grade 2 or 3). This translates to exclusion of approximately 56% of all knees with definite radiographic OA, when selecting only knees with any mJSN during screening, and to exclusion of approximately 75% of all knees when selecting only knees with mJSN grades 2 or 3 during screening.

Among knees with less mJSN (where the contra-lateral knee was mJSN grade 2 or 3), those with mJSN grade 1 showed relatively large changes in ThCtAB compared to knees with mJSN grade 1 where the contra-lateral knee had no mJSN. Potentially the participants with higher mJSN grade in the contralateral knee put greater loads on the mJSN grade 1 knee than those with no mJSN in the contralateral knee during gait and other activities. This finding must, however, be interpreted with caution because only 7 knees displayed mJSN grade 1 among the knees with less mJSN. It may be interesting for future studies to examine whether JSN grade of the contra-lateral knee significantly affects progression in a knee with a distinct JSN grade.

To our knowledge, this is one of the first studies to show that the rate and sensitivity to change is greater in cMF than in pMF and is most pronounced in knees with mJSN grades 2 or 3. This may result from the mechanical stress encountered during common activities, such as walking, which may accelerate cartilage loss in the cMF. In contrast, the pMF may encounter mechanical insults more rarely as it is only in contact with the MT during deep knee flexion, an activity likely avoided by people with symptomatic OA.

In conclusion, knees with advanced medial radiographic disease (mJSN 2 or 3, but not knees with mJSN 1) displayed significantly greater cartilage loss than contra-lateral knees with no or less mJSN. These findings suggest that advanced mJSN predicts MRI cartilage loss, that fixed flexion radiography can be used to stratify fast structural progressors by assessment of mJSN, and that cartilage thickness loss is more pronounced at advanced radiographic disease stage. Studies aiming to demonstrate reductions in cartilage loss by drugs (DMOADs) or other therapeutic measures over short time intervals may thus be enriched by inclusion of participants with advanced grades of radiographic JSN.

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Figure 1.

Sagittal DESS images with water excitation (TrF = femoral trochlea; MT = medial tibia; LT = lateral tibia; cMF = central (weight-bearing) part of the medial femoral condyle; pMF = posterior part of the medial femoral condyle).

- A. Most posterior aspect of the trochlea (TrF) marked in the intercondylar region by a line (= anterior line; small dashes) perpendicular to the femoral shaft. [The line with the large dashes is explained in B]

- B.** Most posterior aspect of the lateral femoral condyle marked by a line (=posterior line; large dashes) perpendicular to the TrF plane in A). The posterior lines in A-C (large dashes) define the plane in which the MF is separated into cMF and pMF.
- C.** The full line marks a plane at 75% of the distance between the TrF plane (small dashes) and a plane tangential to the posterior end of both femoral condyles (large dashes). This 75% plane is used to separate the medial femoral condyle (MF) into a central (weight-bearing) part (cMF) and into a posterior part (pMF).

Figure 2.

Bar graphs showing the standardized response mean (SRM) as a function of medial joint space narrowing (mJSN) grades 0 to 3) in the knees with less and more mJSN, respectively (grade 0 = no mJSN):

- Medial tibia (MT)
- Weight-bearing medial femoral condyle (cMF)
- Posterior medial femoral condyle (pMF)

Figure 3. Mean change in cartilage thickness (mm) in the medial tibia (MT), weight-bearing medial femoral condyle (cMF) and posterior medial femoral condyle (pMF) in knees with medial joint space narrowing grade 2 or 3 (n=33). The error bars show the one-fold standard deviation (SD) between subjects.

Table 1
Knees with less medial joint space narrowing (mJSN) (n=80)

Baseline cartilage thickness over the total area of subchondral bone (BL ThCtAB), mean change (MC) in ThCtAB over 12 months, standard deviation (SD in μm) of the change in ThCtAB, and standardized response mean (SRM) for various medial femoro-tibial regions of interest

	BL ThCtAB [mm]	MC [μm]	SD change [μm]	SRM
<i>Knees with less mJSN (n=80)</i>				
MFTC	3.54	-57	249	-0.23
MT	1.69	-21	73	-0.28
MF	1.85	-11	84	-0.13
cMF	1.85	-36	193	-0.19
pMF	1.85	-6.9	77	-0.09
<i>mJSN 0 knees (n=73)</i>				
MFTC	3.54	-35	141	-0.25
MT	1.69	-16	52	-0.32
MF	1.85	-3.7	68	-0.05
cMF	1.86	-19	117	-0.16
pMF	1.83	0.0	71	0.00
<i>mJSN 1 knees (n=7)</i>				
MFTC	3.47	-280	719	-0.39
MT	1.68	-66	189	-0.35
MF	1.93	-86	174	-0.49
cMF	1.79	-213	535	-0.40
pMF	2.01	-79	104	-0.76

MFTC = medial femoro-tibial compartment (=MT+cMF); MT = medial tibia; MF = medial femoral condyle; cMF = central (weight-bearing) medial femoral condyle; pMF = posterior medial femoral condyle.

Table 2
Knees with more medial joint space narrowing (mJSN) (n=80)

Baseline cartilage thickness over the total area of subchondral bone (BL ThCtAB), mean change (MC) in ThCtAB over 12 months, and standard deviation (SD in μm) of the change in ThCtAB and standardized response mean (SRM) for various medial femoro-tibial regions of interest

	BL ThCtAB [mm]	MC [μm]	SD change [μm]	SRM
<i>Knees with more mJSN (n=80)</i>				
MFTC	3.09	-80	174	-0.46
MT	1.54	-36	80	-0.45
MF	1.75	-18	74	-0.25
cMF	1.55	-44	119	-0.37
pMF	1.76	-31	93	-0.34
<i>mJSN 1 knees (n=47)</i>				
MFTC	3.41	-31	133	-0.24
MT	1.64	-26	70	-0.37
MF	1.80	-3.0	68	-0.04
cMF	1.76	-7.0	95	-0.07
pMF	1.79	-13	92	-0.14
<i>mJSN 2 knees (n=25)</i>				
MFTC	2.93	-146	214	-0.68
MT	1.52	-44	88	-0.50
MF	1.70	-45	73	-0.62
cMF	1.42	-101	144	-0.70
pMF	1.78	-57	81	-0.70
<i>mJSN 3 knees (n=8)</i>				
MFTC	1.72	-160	175	-0.92
MT	1.01	-73	109	-0.66
MF	1.60	-25	91	-0.28
cMF	0.72	-85	78	-1.09
pMF	1.52	-59	124	-0.47

MFTC = medial femoro-tibial compartment (=MT+cMF); MT = medial tibia; MF = medial femoral condyle; cMF = central (weight-bearing) medial femoral condyle; pMF = posterior medial femoral condyle.

Table 3

Significance level of differences in the mean change of cartilage thickness over the total area of subchondral bone (ThCtAB) between baseline and 1-year follow-up in knees with more medial joint space narrowing (mJSN) and less mJSN; paired analysis with the Wilcoxon signed rank test for various medial femoro-tibial regions of interest.

	More mJSN vs. less mJSN (n=80)	mJSN (1 to 3) vs. no mJSN (n=73)	mJSN 1 vs. no mJSN (n=47)	mJSN 2 or 3 vs. less mJSN (n=33)
MFTC	0.13	0.15	0.96	0.03 *
MT	0.23	0.29	0.98	0.08
MF	0.11	0.12	0.58	0.005 **
cMF	0.13	0.14	0.95	0.04 *
pMF	0.16	0.24	0.28	0.001 **

MFTC = medial femoro-tibial compartment (=MT+cMF); MT = medial tibia; MF = medial femoral condyle; cMF = central (weight-bearing) medial femoral condyle; pMF = posterior medial femoral condyle.

*
p < 0.05;

**
p < 0.01; Wilcoxon signed rank test for paired analysis of non-normally distributed data