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MUSCULOSKELETAL

Longitudinal change in quantitative meniscus measurements in knee osteoarthritis—data from the Osteoarthritis Initiative

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Abstract

Objective We aimed to apply 3D MRI-based measurement technology to studying 2-year change in quantitative measurements of meniscus size and position.

Methods Forty-seven knees from the Osteoarthritis Initiative with medial radiographic joint space narrowing had baseline and 2-year follow-up MRIs. Quantitative measures were obtained from manual segmentation of the menisci and tibia using coronal DESSwe images. The standardized response mean (SRM=mean/SD change) was used as measure of sensitivity to longitudinal change.

Results Medial tibial plateau coverage decreased from 34.8 % to 29.9 % (SRM -0.82; $p<0.001$). Change in medial meniscus extrusion in a central image (SRM 0.18) and in the central five slices (SRM 0.22) did not reach significance, but change in extrusion across the entire meniscus (SRM 0.32; $p=0.03$) and in the relative area of meniscus extrusion (SRM 0.56; $p<0.001$) did. There was a reduction in medial meniscus volume (10 %; $p<0.001$), width (7 %; $p<0.001$), and height (2 %; $p=0.08$); meniscus substance loss was strongest in the posterior (SRM -0.51; $p=0.001$) and weakest in the anterior horn (SRM -0.15; $p=0.31$).

Conclusion This pilot study reports, for the first time, longitudinal change in quantitative 3D meniscus measurements in knee osteoarthritis. It provides evidence of improved sensitivity to change of 3D measurements compared with single slice analysis.

Key Points

- *First longitudinal MRI-based measurements of change of meniscus position and size.*
- *Quantitative longitudinal evaluation of meniscus change in knee osteoarthritis.*
- *Improved sensitivity to change of 3D measurements compared with single slice analysis.*

Keywords Longitudinal meniscus change · Quantitative MR imaging · Knee osteoarthritis · MRI Osteoarthritis Knee Score (MOAKS) · Quantitative meniscus position

Abbreviations

WORMS	Whole Organ Magnetic Resonance Imaging Score
BLOKS	Boston Leeds Osteoarthritis Knee Score
MOAKS	MRI Osteoarthritis Knee Score
OA	Osteoarthritis
JSW	Radiographic joint space width
JSN	Joint space narrowing
OAI	Osteoarthritis Initiative
OARSI	Osteoarthritis Research Society International
DESSwe	Double echo steady state sequence with water excitation

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IWTSE	Intermediate-weighted turbo spin echo
c	Central slice
c5	Central five slices
SRM	Mean change / Standard deviation change

Introduction

The function of the menisci is to reduce knee joint contact stress, to warrant a more spatially uniform transmission of forces across the femorotibial joint, and thereby keep the contact stress of the cartilage and subchondral bone within reasonable limits [1–4]. Meniscal lesions can be of traumatic or degenerative nature [5] and are often associated with meniscal extrusion [6–9], because the loss of matrix integrity reducing meniscal structural stiffness [10, 11] and meniscus lesions, particularly in the posterior horn, has been shown to alter tibiofemoral contact mechanics [12]. Meniscus lesions and extrusion are frequently found in the general population [13, 14], and are important in the pathophysiology of knee osteoarthritis [15, 16]. Radiological evaluation of meniscus lesions and extrusion are therefore of great interest, and semi-quantitative grading systems have been developed, such as the Whole Organ Magnetic Resonance Imaging Score (WORMS [17]), the Boston Leeds Osteoarthritis Knee Score (BLOKS [18]) and the magnetic resonance imaging Osteoarthritis Knee Score (MOAKS [19]). Whilst these scoring systems are ideally suited to score the nature and location of meniscus pathology [16], the sensitivity to change is limited, because only changes exceeding a full score can be captured, and only a few study participants generally display such relatively large changes over an observation period of 1–2 years [16]. Scoring within-grade changes is not part of published scoring systems, but has been shown to be clinically relevant, and these were shown to be associated with osteoarthritis (OA) risk factors and outcomes [20]. Fully quantitative measurements of meniscus position and size may thus be of interest in longitudinal studies of knee osteoarthritis. For instance, quantitative measurements of cartilage thickness changes were more sensitive at revealing relationships with risk factors of progression than semi-quantitative scores of cartilage lesions [21]. Recently, a quantitative magnetic resonance imaging (MRI)-based three-dimensional (3D) technique has been developed for measuring meniscus size and position relative to the tibia [22]. Further, their intra-observer [23, 24] and inter-observer reliabilities [25] have been documented, and normal data for healthy reference subjects have been provided [23, 26]. Quantitative measurements of extrusion were shown to correlate with semi-quantitative (MOAKS) scores and to display a stronger correlation with tibial coverage by the meniscus than the latter [27]. Further, meniscus extrusion and tibial coverage were contributors to radiographic joint space width (JSW) measurements [28, 29]. 3D meniscus measurements cross-sectionally discriminated between knees a) with and without radiographic knee osteoarthritis [30]; b) with and without radiographic joint space narrowing (JSN) [31]; and c) with and without knee pain [24].

However, to our knowledge, changes of quantitative, 3D meniscus parameters have not been studied longitudinally. The aim of this pilot study was therefore to determine longitudinal (2-year) rates and sensitivity to change of quantitative measurements of meniscus size and position, and to examine to what extent these depend on age, sex, body mass index (BMI), baseline radiographic JSN grades, and /or baseline MOAKS meniscus lesion or extrusion scores.

Methods

Study participants

Measurements were performed in knees with baseline radiographic JSN. These have been demonstrated to display structural progression, i.e.. loss of femorotibial cartilage [32] and loss in radiographic JSW [33]. The subsample studied was drawn from the first half (2,678 cases) of the OA Initiative (OAI) cohort, a population based longitudinal cohort multicenter study aiming at identifying novel imaging biomarkers of knee osteoarthritis [34, 35]. Participants were between 45 and 79 years at baseline [34]; MRIs were obtained at annual intervals over 4 years [34–36]. Exclusion criteria were inflammatory arthritis, bilateral end stage knee OA, inability to walk without aids, or MRI contraindications. Informed consent was obtained from all participants and the study was approved by the local ethics committees.

The sample of 60 participants fulfilling the following inclusion criteria has been previously described in detail [31]: the subjects had a BMI of>25 kg/m^2, bilateral knee pain (i.e., pain on most days for at least 1 month in the past 12 months), unilateral medial joint space narrowing (JSN) OARSI grades 1–3 [37], and no lateral JSN in either knee (baseline clinical data OAI release No 0.2.1; http://www.oai.ucsf.edu/datarelease/). Twenty-two participants were men and 38 were women (Table 1). The distributions of medial JSN, baseline MOAKS lesions and extrusion scores in the medial meniscus in this sample have been reported previously [31]. Of the 47 participants, 37 had a MOAKS lesion≥1 in the posterior horn, 35 had one in the central part, and only five had one in the anterior horn. The total lesions load (sum of scores) was 135 in the posterior horn, 129 in the central part and 15 in the anterior horn, whereas 59.4 % of the JSN 1 and 60 % of the JSN 2/3 knees had MOAKS lesion scores≥2 in the posterior horn and only 8.1 % of those knees had MOAKS lesion scores≥2 in the anterior horn.

Table 1 Demographics and baseline meniscus data for the medial (MM) and lateral meniscus (LM)

	Baseline		2-year follow-up	
Demographics				
Gender	22 men, 38 women		18 men, 29 women	
Age	61.3±9.2 years		61.1±8.9 years	
Height	1.66±0.96 m		1.66±0.94 m	
Weight	86.6±13.0 kg		88.3±12.7 kg	
BMI	31.3±3.9 kg/m^2		31.9±3.7 kg/m^2	
Meniscus position	MM	LM	MM	LM
Tibial plateau coverage (%)	34.7±9.1	58.6±6.3	29.9±9.9	54.4±4.59
Extrusion distance c (mm)	3.35±1.96	-0.55±1.16	3.45±1.46	-0.52±1.13
Extrusion distance c5 (mm)	3.38±1.86	-0.56±1.11	3.50±1.48	-0.54±1.09
Extrusion distance mean (mm)	3.78±1.49	-1.47±1.84	3.87±1.55	-1.33±1.96
Extrusion area (%)	29.3±13.3	3.74±3.84	33.9±16.3	4.20±4.36
Meniscus size	MM	LM	MM	LM
Meniscus volume (cm^3)	1.96±0.70	1.96±0.61	1.76±0.68	1.87±0.49
Meniscus width c (mm)	7.39±2.10	10.7±2.42	6.72±2.10	10.0±2.01
Meniscus width c5 (mm)	7.53±2.16	11.1±2.42	6.91±2.08	10.3±1.95
Meniscus width mean (mm)	8.16±1.41	9.06±1.47	7.51±1.47	8.56±1.13
Meniscus height mean (mm)	2.73±0.48	2.64±0.40	2.66±0.49	2.69±0.32
Meniscus height max* (mm)	6.76±1.42	6.56±1.01	6.45±1.52	6.36±0.77

* average of the top 1 % height/thickness values; BMI=body mass index; c=central slice; c5=central five slices

Forty-seven of the 60 participants had follow-up MRIs at 2-year follow-up (18 men, 29 women), whereas 13 dropped out from the study or missed the 2-year follow-up exam. The subsample of 47 participants with follow-up had a slightly greater BMI (31.7±3.8 kg/m^2) than the original sample of 60 participants (31.3±3.9 kg/m^2) [31]. Of the 47 knees, 37 were medial radiographic JSN grade 1, and ten were medial JSN grade 2/3. Thirty-two percent of the JSN knees had a medial meniscus lesion MOAKS score of 0–1, 32 % had a score of 2–5, and 36 %>6; 9 % had an extrusion score of 0, 23 % of 1, 47 % of 2, and 21 % had a score of 3.

MR image acquisitions

MR images were acquired for each knee with a 3 Tesla Magnetom Trio magnet (Siemens Erlangen, Germany) and quadrature transmit-receive knee coils (USA Instruments, Aurora, OH) [36, 38]. For the quantitative meniscus analysis, coronal multi-planar reconstruction of the sagittal double echo steady state sequence with water excitation was used (DESSwe: reconstructed slice thickness=1.5 mm, in-plane resolution 0.37 mm×0.7 mm, interpolated to 0.37 mm×0.37 mm) [39, 40]. Meniscus segmentation and morphometry from the DESS have been shown to yield acceptable inter-observer reliability and good agreement with measurements made from a coronal intermediate-weighted turbo spin echo (IW-TSE) sequence (repetition time=3700 ms, echo time=29 ms, slice thickness=3 mm, in-plane resolution 0.36 mm×0.36 mm;) [25] and high intra-observer reproducibility [23, 24]. The advantage of the DESS is that it provides greater spatial resolution and better delineation of the tibial cartilage surface, and also has been validated for accurately depicting the tibial cartilage with a precision error (root mean square coefficient of variation in % for paired analysis) for cartilage volume and a thickness of 1.8–2.2 % for a coronal multiplanar reconstruction of the DESSwe [41].

Quantitative analysis of the meniscus

Images were initially checked for adequate quality. Manual segmentation of the medial and lateral tibial plateau surface area (including the area of cartilage surface and denuded areas of subchondral bone=ACdAB [22, 26]) and the surfaces of both menisci was performed by a single operator (K.B.) (Fig. 1). Quantitative analysis was performed using dedicated image analysis software (Chondrometrics GmbH, Ainring, Germany) [22, 26]. Manual segmentation started anteriorly and ended posteriorly in the image in which both the tibial cartilage and the menisci could be reliably identified. Internally, the borders of the menisci were defined by the internal margin of the cartilage surfaces of the medial and lateral tibia, because these are continuous with the transverse and menisco-femoral ligaments, and because no intrinsic anatomical demarcation could be used to separate these structures. We then calculated the size of the tibial plateau, the proportion of the plateau covered by the meniscus (i.e., tibial coverage), and the mean meniscus extrusion distance (i.e., the

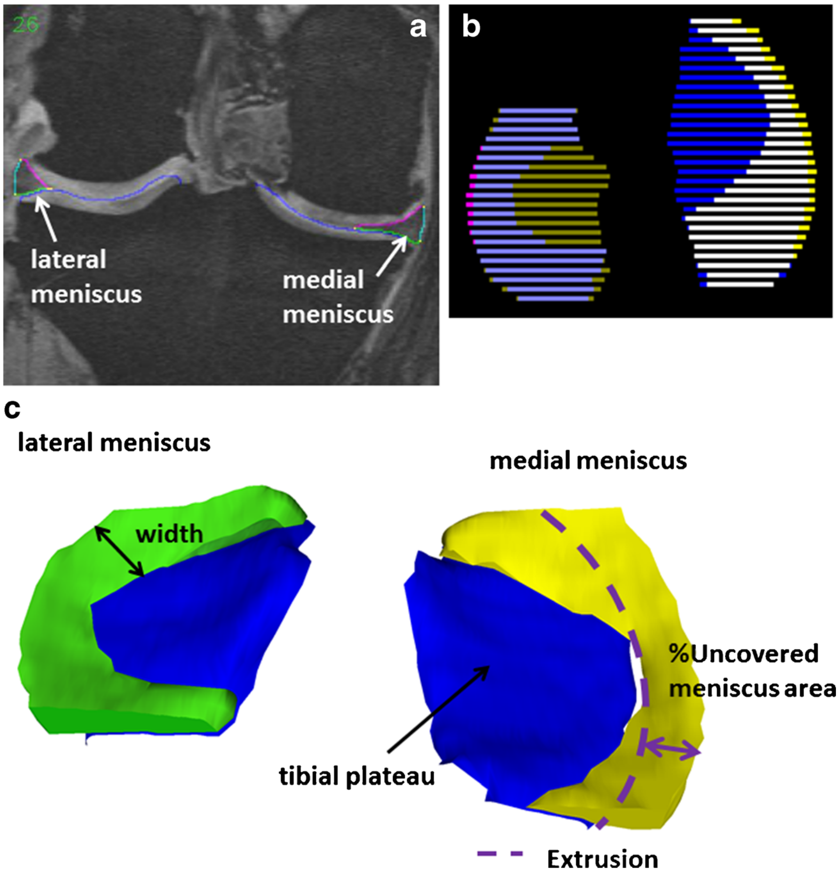

Fig. 1 *a, b*) Manual segmentation of the coronal reconstruction of the double echo steady state (DESS) sequence with water excitation, showing the segmentation of the tibial plateau cartilage and that of the medial (right) and lateral (left) meniscus (tibial area, femoral area, and external area), *b*) the medial meniscus (*white*) covering the medial tibial plateau (*blue*), with the extruding medial meniscus area (*yellow*) and the lateral meniscus (*violet*) covering the lateral tibial plateau (*green*) with the extruding lateral meniscus area (*pink*); *c*) 3D reconstruction of the medial and lateral meniscus covering the tibial plateau, measurements of meniscus width and uncovered extrusion area are drafted schematically

distance between the external margin of the meniscus vs. the tibial plateau) for a central slice, relative to the anterior and posterior margin of the tibial plateau (c), for the central five slices (c5), and for the entire meniscus (Fig. 1). We further computed the relative area of the meniscus surface not covering (i.e., extruding) the tibial plateau, the meniscus volume, and the meniscus width (c, c5, total) and height. Volumes were also computed for the central part, as well as for the anterior and posterior meniscus horns [22].

Semi-quantitative analysis

Baseline semi-quantitative MR imaging readings of meniscal integrity and position were performed by a musculoskeletal radiologist (A.G.) using the MOAKS scoring system [19]. These were performed based on fat-suppressed sagittal and non-fat-suppressed coronal IW-TSE images [36]. Meniscus morphology was evaluated for both menisci in the anterior and posterior horn and the meniscus body, and divided into seven different grades (0=normal; 1=signal change; 2=radial tear; 3=horizontal tear; 4=vertical tear; 5=complex tear; 6=partial maceration; 7=complete maceration). Meniscus extrusion was also classified, with grade 0 representing<2 mm; grade 1 representing 2–2.9 mm; grade 2 representing 3–4.9 mm, and grade 3 representing>5 mm extrusion [19].

Statistical analysis

Mean values and standard deviations (SDs) were determined for all quantitative meniscus measurements, at baseline and at 2-year follow-up. The longitudinal changes between baseline and follow-up are reported as absolute and percent values, as well as their 95 % confidence intervals; a paired t-test was used to evaluate whether these changes were significantly different from zero. As a measure of the sensitivity to change (or "responsiveness"), we used the standardized response mean (SRM=mean change / SD change) [42]. General linear models and one-factorial ANOVA were used to evaluate the impact of age, sex, BMI, JSN, MOAKS lesions and extrusion scores on longitudinal changes in key quantitative parameters.

Results

Quantitative measurements of the medial meniscus

Coverage of the tibial cartilage by the medial meniscus decreased from 34.7 % to 29.9 % after 2 years (Table 1). The changes were highly significant ($p<0.001$) and showed a high sensitivity to change (SRM -0.82; 95 % CI [-1.15/-0.48]; Table 2).

The mean extrusion distance for the medial meniscus was around 3–4 mm at baseline, depending on whether the measurement was taken in a single central slice, the central five slices, or across the entire joint (Table 1). Longitudinal change in medial meniscus extrusion distance in the central slice (+232±1260 μm; +7.2 %; $p=0.21$; SRM 0.18) or the central five slices ($p=0.14$; SRM 0.22; Table 2) did not reach statistical significance. However, the extrusion distance across the entire meniscus, including the anterior and posterior horns, showed a longitudinal change of +212±663 μm; +5.8 % and reached statistical significance ($p=0.03$; SRM of 0.32). The relative area of the meniscus extruding the tibia increased significantly from 29.3 % to 33.9 % medially ($p<0.001$; SRM 0.56; Tables 1 and 2).

Over 2 years, there was a significant longitudinal decrease in medial meniscus volume (-9.5 %; $p<0.001$; SRM -0.56; Table 2). The volume loss in the central part (-7.5 %; SRM -0.39) was similar, but was stronger in the posterior (-13.3 %; SRM -0.51) than in the anterior horn (-2.8 %; SRM -0.15). The mean width of the medial meniscus was approximately 8 mm at baseline, depending on whether the measurement was taken in a single central slice, the central five slices, or across the entire joint; the mean height was 2.73 mm, and the maximal height 6.76 mm (Table 1). The SRM was greater (more negative) for longitudinal width change of the entire meniscus (-0.72) than for the width determined in a central slice (-0.42) or in the central five slices (-0.48; Table 2). There was also a significant reduction in the maximum height of the medial meniscus (-3.7 %; $p<0.05$; SRM -0.32), but the change in the mean height did not reach statistical significance (-1.8 %; $p=0.08$; SRM -0.26; Table 2).

Relationship of medial meniscus changes with baseline variables

There was no significant association between 2-year changes in medial tibial coverage, meniscus extrusion area, and medial meniscus volume and age, sex or BMI ($p>0.29$). The longitudinal reduction in medial tibial coverage and meniscus volume, and the gain in extrusion tended to be greater in JSN 2/3 than in JSN 1 knees, but did not reach statistical significance ($p=0.08$ to 0.31).

There was a trend towards a greater longitudinal decrease in medial tibial plateau coverage (Fig. 2a), greater increase in medial meniscus extrusion area (Fig. 2b) and greater medial meniscus volume loss over 2 years (Fig. 2c) with greater baseline MOAKS lesions scores, but the relationships did not reach statistical significance ($p=0.06$ to 0.37). There was no evidence for a statistically significant relationship of longitudinal meniscus changes with baseline MOAKS extrusion ($p=0.24$ to 0.72).

Quantitative measurements of the lateral meniscus

Coverage of the tibial cartilage by the meniscus decreased from 58.6 % to 54.4 % laterally over the 2-year observation period (Table 1), with a significant change ($p<0.001$) showing a sensitivity to change that was similar to that in the medial compartment (SRM -0.96; Table 3). Lateral tibial plateau coverage did not show a significant association with age (r=-0.08, $p=0.60$) or BMI (r=-0.06, $p=0.71$), and did not differ significantly between men and women (-3.4±3.4 vs. -3.7±4.0, $p=0.82$). The mean extrusion distance for the lateral meniscus assumed negative values (Table 1) since the external border of the meniscus was "inside" the lateral tibial plateau cartilage. There was only a small longitudinal increase in

Table 2 Medial meniscus: Two-year change in quantitative measures of size and position

	Absolute	%	95 % CI	SRM	95 % CI	(p)
Meniscus position						
Tibial plateau coverage (%)	-4.9	-14.0	[-6.6/-3.13]	-0.82	[-1.15/-0.48]	< 0.001
Extrusion distance c (μm)	+232	+7.2	[-138/602]	0.18	[-0.11/0.47]	0.21
Extrusion distance c5 (μm)	+253	+7.8	[-83/589]	0.22	[-0.08/0.47]	0.14
Extrusion distance mean (μm)	+212	+5.8	[18/407]	0.32	[0.03/0.52]	0.03
Extrusion area (%)	+5.2	+18.2	[2.5/7.9]	0.56	[0.24/0.86]	< 0.001
Meniscus size						
Meniscus volume (cm^3)	-0.185	-9.5	[-283/87.2]	-0.56	[-0.86/-0.24]	< 0.001
Meniscus width c (μm)	-532	-7.3	[-908/-155]	-0.42	[-0.71/-0.11]	< 0.01
Meniscus width c5 (μm)	-496	-6.7	[-800/-193]	-0.48	[-0.70/0.19]	< 0.01
Meniscus width (μm)	-595	-7.3	[-837/-354]	-0.72	[-1.04/-0.39]	< 0.001
Meniscus height (μm)	-49	-1.8	[-104/5]	-0.26	[-0.45/0.03]	0.08
Meniscus height max * (μm)	-247	-3.7	[-474/-20]	-0.32	[-0.61/-0.02]	0.03

* average of the top 1 % height/thickness values; for abbreviations, see Table 1

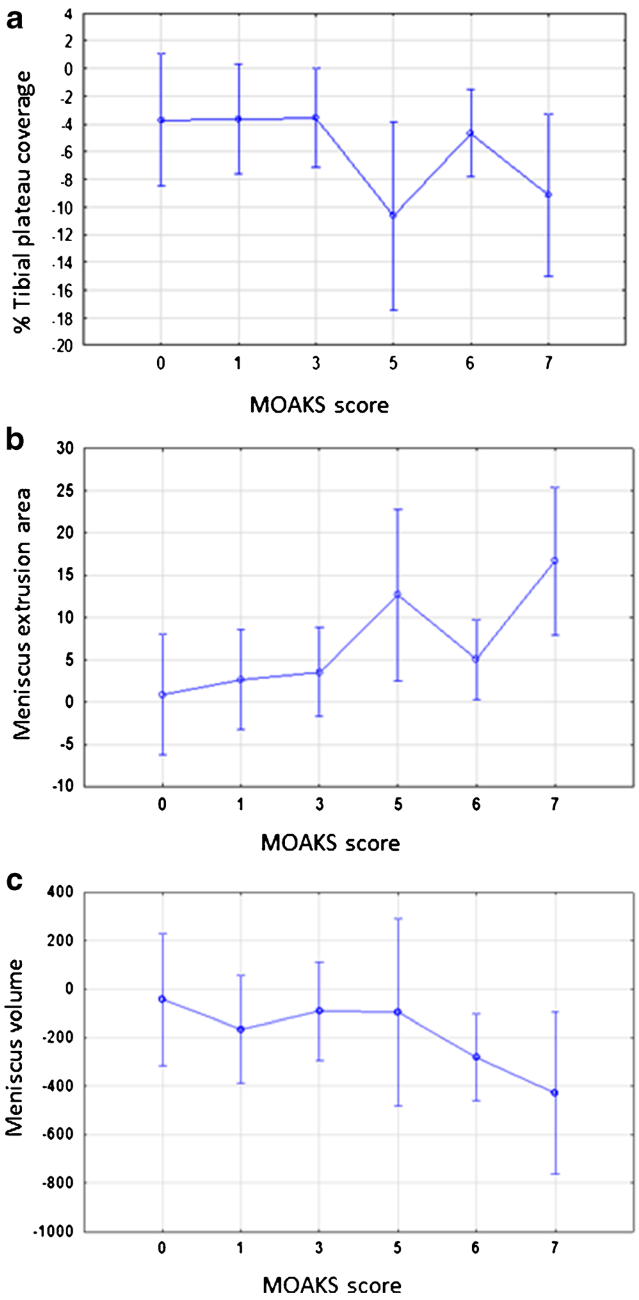

Fig. 2 Relationship between longitudinal changes in medial meniscus measurements and the baseline MOAKS medial meniscus lesion scores: *a*) tibial coverage by the meniscus (percent tibial plateau area covered); *b*) extrusion area (percent of the meniscus tibial area extruding the tibial plateau); *c*) volume

lateral meniscus extrusion distances and areas, without statistical significance (Tables 1 and 3).

The baseline volume of the lateral meniscus was similar to that of the medial one (Table 1), with no significant longitudinal change in lateral meniscus volume over time (Table 3). Although there was a significant decrease in lateral meniscus width of around 5 % ($p<0.01$) over 2 years, there was a slight increase in mean height (+3 %), and a slight reduction in maximal height (-1.5 %; both these changes did not reach statistical significance; Table 3). Again, the SRM was greater (more negative) for change in width across the entire lateral meniscus (-0.69) than for the width determined in a central slice (-0.44) or in the central five slices (-0.60; Table 3). There was no significant correlation between the longitudinal increase in mean height in the lateral meniscus and the longitudinal increase in medial meniscus extrusion area ($r=0.12$, $p=0.44$), or lateral extrusion area ($r=0.10$, $p=0.49$).

Discussion

This is the first study to report the longitudinal rate of change in quantitative measurements of the medial and lateral meniscus size and position in radiographic knee osteoarthritis using a 3D MRI measurement technique. Our study confirms that 2-year changes of meniscus size and position can be captured, and that the sensitivity to change is greater when the total meniscus is evaluated rather than a single image in a central tibial location, or in a series of five central images. We found a statistically significant decrease in tibial plateau coverage by the medial and lateral meniscus in knees with medial baseline radiographic JSN. Medially, the longitudinal reduction in coverage was due to an increase in meniscus extrusion and reduction in width, whereas laterally, there was a reduction in meniscus width, but no change in extrusion. There was a significant longitudinal reduction of substance in the medial, but not the lateral meniscus; which was greater in the medial posterior horn than in central part or anterior horn. Although the sample size of this study was relatively small, longitudinal changes were statistically significant and the SRMs were high, particularly compared with longitudinal measurement of cartilage loss in knee OA [43]. Therefore the study provides “proof of concept” that the in vivo 3D meniscus measurement technology used here is feasible. The results motivate further application in larger cohorts for exploring the specific determinants of longitudinal change in meniscus morphometry.

Two-dimensional (2D) measurements of meniscus, as evaluated in a single central MRI slice, were shown to account for a substantial proportion of longitudinal changes in radiographic JSN scores [44], and to predict cartilage loss in symptomatic knee osteoarthritis [45]. The same measurement technology was used to evaluate longitudinal changes of meniscus parameters over 4 years in the Osteoarthritis Initiative healthy reference cohort [46], and a slight longitudinal increase in extrusion of the central part of the medial meniscus was reported, whereas the other measurements were relatively stable within each subject over time [46].

Our study shows that by applying a quantitative 3D measurement technique, the sensitivity to change (SRM) in meniscus extrusion and width is greater in comparison to the evaluation of a single central slice, or a series of five central

Table 3 Lateral meniscus: Two-year change in quantitative measures of size and position

	Absolute	%	95 % CI	SRM	95 % CI	(p)
Meniscus position						
Tibial plateau coverage (%)	-3.6	-6.2	[-4.7/-2.5]	-0.96	[-1.29/-0.59]	<0.001
Extrusion distance c (µm)	-24	+5.0	[-205/156]	-0.04	[-0.41/0.17]	0.79
Extrusion distance c5 (µm)	-19	+3.8	[-186/148]	-0.03	[-0.42/0.17]	0.82
Extrusion distance mean (µm)	+50	-3.6	[-221/322]	0.05	[-0.20/0.37]	0.71
Extrusion area (%)	+0.3	+8.2	[-0.4/1.1]	0.13	[-0.24/0.33]	0.39
Meniscus size						
Meniscus volume (cm^3)	-0.033	-1.7 %	[-95.8/29.5]	-0.16	[-0.36/0.20]	0.29
Meniscus width c (µm)	-561	-5.3	[-932/-190]	-0.44	[-0.71/-0.11]	<0.01
Meniscus width c5 (µm)	-609	-5.6	[-905/-313]	-0.60	[-0.89/-0.26]	<0.001
Meniscus width (µm)	-397	-4.4 %	[-566/-227]	-0.69	[-0.98/-0.34]	<0.001
Meniscus height (µm)	81	3.1 %	[34/129]	0.50	[0.16/0.77]	0.001
Meniscus height max* (µm)	-99	-1.5 %	[-223/25]	-0.23	[-0.46/0.11]	0.12

* average of the top 1 % height/ thickness values; Abbreviations see Table 1

slices. Further, it compares very favourably with that reported in a meta-analysis on semi-quantitative scores of the meniscus in knee osteoarthritis [42]. Therefore, our current quantitative 3D approach should make it possible to explore determinants of longitudinal meniscus change with greater sensitivity in samples smaller than those for 2D technology. Longitudinal changes of 3D quantitative meniscus measurements, as described here, may be useful for predicting incident knee osteoarthritis, progression of knee osteoarthritis, incidence or worsening of knee pain and function, or knee arthroplasty as a clinical outcome [44], with future work having to explore these relationships [47]. Of particular interest may be to follow patients with acute meniscus lesions in previously healthy knees, and to track to what extent substance loss and extrusion progress over time, before the advent of symptom and radiographic change. Another potential areas of application is the comparison of knees before and after meniscus allograft transplantation, to evaluate meniscus functionality after surgery.

The proposed quantitative measurements are NOT suggested to replace semi-quantitative scores of meniscus lesions, as these quantitative measurements represent only indirect measurements of meniscus pathology. However, they do appear to provide robust and responsive measurements of meniscus extrusion and tibial coverage, with the latter not being directly assessed by the currently available scoring systems [17–19]. Further, meniscus maceration is associated with a reduction in meniscus substance loss, and longitudinal measurements of meniscus volume, width and height may enhance the ability to track substance loss longitudinally in patients with knee osteoarthritis.

A limitation of the current pilot study is the relatively small sample size, and that the observations were restricted to knees with medial radiographic JSN. Further studies are therefore needed to explore longitudinal change in quantitative 3D meniscus parameters in knees with early radiographic osteoarthritis (e.g., osteophytes, but no JSN), and to study the lateral meniscus longitudinally in subjects with lateral JSN. In this context, it is of note that our study showed that the change in tibial coverage was almost as strong laterally as medially. The observed decrease of lateral tibial plateau coverage appeared to result from a longitudinal reduction in meniscus width, but not from an increase in extrusion measurements; in the medial meniscus, in contrast, a longitudinal reduction in width and an increase in extrusion appeared to co-occur. Further, the longitudinal reduction in lateral meniscus width appeared to be at least partly compensated by an increase in mean height of the lateral meniscus, so that no significant change in volume was observed. However, there was a slight decrease in the maximum height of the lateral meniscus over time, suggesting that a change in lateral meniscus shape rather than in volume occurred. The medial meniscus, in contrast, displayed substantial substance loss (almost -10 %) over 2 years, with the reduction in height (-2 %) being less than that in width (-7 %), but with the change being in the same direction. The longitudinal changes observed in the medial meniscus appeared to be stronger in participants with greater baseline medial JSN grades, and in those with greater baseline maximum MOAKS lesions scores; however, this pilot study was underpowered to conclusively demonstrate statistically significant relationships with these potential determinants of longitudinal meniscus change.

The longitudinal volume change (substance loss) in the medial meniscus was strongest in the posterior horn, and was least in the anterior horn. At a subregional level, the greater volume loss appears to be related to the more advanced meniscus pathology in this sample, as expressed by the greater MOAKS lesion scores in the posterior than in the anterior horn [48]. Interestingly, there was also a statistically significant reduction in meniscus width of approximately 5 % in the lateral meniscus, despite a much smaller number of lesions

[27, 31]; in this sample, there were only seven lesions noted in the posterior horn, ten in the central part, and five anteriorly (MOAKS lesion≥1).

In conclusion, this is the first study reporting longitudinal change in quantitative 3D MRI measurements of the menisci in knee osteoarthritis, providing evidence that these measurements are sensitive to change. The 2-year standardized response mean (SRM) was greater when measuring the total meniscus in comparison to evaluating single images in central locations. No significant correlation was observed between the longitudinal increase in medial meniscus extrusion with age, sex or BMI, and the relationship with baseline JSN and MOAKS lesion or extrusion scores also failed to reach statistical significance. In knees with medial radiographic JSN, longitudinal observation differed for the medial and lateral meniscus, and the current findings recommend further exploration of quantitative meniscus measurement technology in knee osteoarthritis or other areas of application, such as meniscus transplantation.

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