3D patellar shape is associated with radiological and clinical signs of patellofemoral osteoarthritis

Eijkenboom, J. F.A.; Tümer, N.; Schiphof, D.; Oei, E. H.; Zadpoor, A. A.; Bierma-Zeinstra, S. M.A.; van Middelkoop, M.

DOI
10.1016/j.joca.2022.12.008

Publication date
2023

Document Version
Final published version

Published in
Osteoarthritis and Cartilage

Osteoarthritis and Cartilage 31 (2023) 534–542

Osteoarthritis and Cartilage

3D patellar shape is associated with radiological and clinical signs of patellofemoral osteoarthritis

J.F.A. Eijkenboom †, N. Tümer ‡, D. Schiphof †, E.H. Oei §, A.A. Zadpoor ‡, S.M.A. Bierma-Zeinstra † ||, M. van Middelkoop † *

† *Department of General Practice, Erasmus MC University Medical Center Rotterdam, the Netherlands*
‡ *Department of Biomechanical Engineering, Delft University of Technology, the Netherlands*
§ *Department of Radiology & Nuclear Medicine, Erasmus MC University Medical Center Rotterdam, the Netherlands*
|| *Department of Orthopedics and Sports Medicine, Erasmus MC University Medical Center Rotterdam, the Netherlands*

ARTICLE INFO

Article history:
Received 6 June 2022
Accepted 20 December 2022

Keywords:
Osteoarthritis
Patella
Patellofemoral
Shape

SUMMARY

Objective: To examine the association between 3D patellar shape and 1) isolated magnetic resonance imaging (MRI)-based patellofemoral osteoarthritis (PFOA), 2) the morphological features of PFOA, and 3) the clinical symptoms of PFOA.

Design: MRI data from 66 women with isolated MRI-based PFOA and 66 age- and BMI-matched healthy women were selected from a cohort study. The patellae were manually segmented from MRI scans and used to create a 3D statistical shape model (SSM) of the patella. Structural abnormalities were semi-standardized scored on MRI using MRI osteoarthritis knee score (MOAKS). Regression analyses were applied to determine the associations between the shape parameters retrieved from the SSM, group status, clinical symptoms, and structural abnormalities.

Results: Four shape variants showed a statistically significant (<0.05) association with the group status. The mode responsible for most of the shape variations showed participants with PFOA possess a relatively thicker dorsal bump on the articular part of the patella, compared to patellae of control participants. Three of these variants showed an association with the presence of osteophytes and cartilage loss on the patella. Multiple associations were found between patellar shape and the clinical symptoms of PFOA.

Conclusions: Patellar shape is associated with the prevalence of MRI-based PFOA in women. Some shape variants were also associated with clinical symptoms. Interestingly, one particular shape variant associated with the presence of MRI-based PFOA was earlier shown to be associated with structural abnormalities associated with OA in a population aged under 40. This may suggest that patellar shape may be an early detectable risk factor for PFOA.

Introduction

Osteoarthritis (OA) is one of the most common causes for disability in elderly. Furthermore, the number of individuals affected by OA is suspected to increase further due to the overall increase of age and obesity in developed countries[1]. Knee OA is the most prevalent form of OA, with recent estimates as high as 22.9% in individuals aged 40 and over[2]. Absolute numbers are estimated at 654 million individuals worldwide[2]. Knee OA can be subdivided into patellofemoral OA (PFOA) and tibiofemoral OA (TFOA) and both can be present at the same time (complete knee OA). Although understudied, PFOA is a significant source of pain, joint stiffness, and functional limitation[3,4]. The prevalence of PFOA is high, with approximates of 50% of participants with Magnetic resonance imaging (MRI)-based knee OA having the signs of PFOA to some degree[5]. Additionally, a recent study suggested knee OA most commonly starts in the patellofemoral joint (PFJ)[6], adding to the importance of more research into this subtype of OA.

* Address correspondence and reprint requests to: M. van Middelkoop, Department of General Practice, Erasmus University Medical Centre, Wytemaweg 80, 3015 CN Rotterdam, the Netherlands.
E-mail addresses: j.eijkenboom@erasmusmc.nl (J.F.A. Eijkenboom), n.tumer-1@tudelft.nl (N. Tümer), d.schiphof@erasmusmc.nl (D. Schiphof), e.oei@erasmusmc.nl (E.H. Oei), a.a.zadpoor@tudelft.nl (A.A. Zadpoor), s.bierma-zeinstra@erasmusmc.nl (S.M.A. Bierma-Zeinstra), m.vanmiddelkoop@erasmusmc.nl (M. van Middelkoop).

https://doi.org/10.1016/j.joca.2022.12.008

While the exact aetiology of OA is not fully understood, joint biomechanics and the stresses generated in cartilage seem to play important roles in this regard[3]. Key factors in joint biomechanics, including joint loading[7,8], gait[9], and knee alignment[10] have been broadly studied and associated with the presence of OA. However, an important aspect of the PFJ, namely 3D bone shape, has only recently been studied. 3D bone shape has the potential to extract more detailed shape features as to compared with 2D alignment measures. Moreover, clinical tools employing 3D shape assessment may offer diagnostic value by detecting individuals who are at an increased risk of disease commencement and progression. Multiple studies have connected bone shape in the tibiofemoral joint to OA progression[11], to total knee replacement[12], or to the MRI-based features associated with OA (BMLs[13] and Kellgren–Lawrence scores[14]). However, very little research has focused on bone shape in the PFJ. Liao *et al.* were the first assessing the correlation between 3D patellar shape features with longitudinal changes of PFOA[15]. They showed that subjects demonstrating worsening of PFJ lesions exhibited a patella with equally distributed facets and a lateral bump. Though the evidence is still minimal and a better understanding of patellar shape may add to the early detection of high risk populations. Therefore, the purpose of this study is to examine the association between 3D patellar shape and isolated MRI-based PFOA in a larger population. Since not everyone with MRI-based OA has clinical symptoms, we additionally studied the clinical manifestations of PFOA and their associations with the shape variations in the patella.

Materials and methods

Study population

For the current study, the baseline and follow-up (5 years) data of a subpopulation (RS-III-1) of the Rotterdam Study[16,17] were used. The Rotterdam study is a population-based cohort study in which the incidence and risk factors for chronic disabling diseases are investigated. The first 1116 women of RS-III-1, aged 45–60 years, were invited to participate in a sub-study investigating early signs of knee OA. Of these, 891 were included for the baseline measurements[18]. For the present study, we selected participants with isolated MRI-based patellofemoral osteoarthritis (iPFOA) at either baseline or follow-up. Participants with iPFOA were defined as patients having MRI-based PFOA while not having MRI-based tibiofemoral osteoarthritis (TFOA). Per patient with iPFOA, one matched control participant without PFOA and TFOA was included. One knee per subject was analysed for the current study purpose. Matching was performed for known risk factors for knee OA, including age and BMI and additionally for knee side and time moment (baseline or follow-up) using case-control matching in SPSS with Fuzzy matching of 1 for BMI and 2 for age and random case order when drawing matches. The Medical Ethics committee of the Erasmus Medical Centre approved the study (MEC 02.1015) and all the participants provided written consent.

Measurements

Identical measurements were performed at baseline and follow-up, including questionnaires, patient history, physical examination and an MRI of both knees. The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used from the questionnaires to report on patient reported outcomes, including the subscales pain, symptoms, function in daily living (ADL), sport and quality of life (QoL). Potential risk factors for PFOA, including history of patellar pain, crepitation and BMI were extracted from the patient history and physical examination. The presence of crepitus was investigated and was defined as a hearable grinding noise and/or palpable vibrations in the knee during active flexion or extension, detected by the hand of the investigator rested on the patella of the participant. One KOOS question (pain, going up or down stairs) was dichotomized and was used as a measure for pain during walking stairs, as this is a known important clinical feature of patellofemoral pain (PFP): 0) none and mild 1) moderate, severe, and extreme.

MRIs were made using a 1.5T MRI scanner (Signa Excite 2, General Electric Healthcare, Milwaukee, US). The participants were scanned using an eight-channel cardiac coil. This way both knees could be scanned at once without the need to reposition the participant. The MRI sequences included a sagittal spoiled gradient echo sequence with a fat suppression: TR/TE 20.9/2.3, a flip angle of 35, a slice thickness of 1.6 mm, and a field of view of 15 cm^2.

Definition of iPFOA

MRI-based knee OA was scored for PFOA and TFOA for each knee separately, using the MRI osteoarthritis knee score (MOAKS)[19]. The MOAKS scoring was performed by a trained human movement scientist. Randomly picked knees (30 subjects) from the RS-III-1 cohort sample were also scored by a highly experienced musculoskeletal radiologist to determine inter-rater reliability (prevalence adjusted bias adjusted kappa (PABAK) 0.47–0.93, moderate to nearly perfect)[18].

PFOA was defined as having a definite osteophyte and partial or full thickness cartilage loss in the patella or the trochlea (anterior femur)[20]. TFOA was described as the presence of a definite osteophyte and full thickness cartilage loss, or one of these features and two of the following features[19]: (1) subchondral bone marrow lesions (BML) or cyst not associated with meniscal or ligamentous attachments, (2) meniscal subluxation, maceration, or degeneration (including a horizontal tear) or (3) partial thickness cartilage loss. After this scoring, each knee was classified into one of four categories: (1) iPFOA, (2) iTFOA (isolated tibiofemoral osteoarthritis) (3) complete knee OA, and (4) no knee OA.

Statistical shape model of the patella

The same approach as described in a previous study[21] was followed to obtain 3D patellar bone surfaces based on MRIs. First, patellar bones were manually segmented from MRIs using MIPAV software (NIH, Bethesda, USA) while blinded for group status. The segmentations were performed by a researcher (J.E.) trained by a highly experienced musculoskeletal radiologist (E.O.). Second, 3D triangulated patellar surfaces (i.e., triangles with a maximum tangent edge size of 0.9 mm) were created using Geomagic (3D systems, North Carolina, USA).

A 3D statistical shape model (SSM) of the patella was built based on the triangulated bone samples. First, all the participants' patellae were registered using an unbiased registration algorithm, which minimized the differences in the position, orientation, and scaling among the patellae[22]. Following the registration, the corresponding points ($n = 15{,}924$) across the registered patellae were automatically established[22,23]. The registration parameters, including the scale parameter for the mixture of Gaussian, $\sigma = 0.6$, the number of points in the mean cloud, $n_m = 2000$, and the trade-off parameter, $\lambda = 10^{-3}$, were determined based on numerical experiments[22,23]. Finally, the main bone shape variations were extracted by performing a principal component analysis on the covariance matrix of the data vectors consisting of the 3D coordinates of the corresponding points for each bone samples. To discard shape modes describing noise and preserve the ones describing patellar shape variations, a parallel analysis was performed[24]. This analysis is

based on observed and simulated data[24], and the number of shape modes to be kept is found at their intersection.

Statistical analyses

Logistic regression analyses, with adjustment for age and BMI, were performed to test the association between the independent shape modes and group status (iPFOA vs matched controls). A *post-hoc* regression analysis was performed on shape modes associated with the presence of iPFOA to further investigate their relations with five possible structural abnormalities in the PFJ (i.e., patellar osteophytes, patellar BML, patellar cartilage loss, anterior femoral osteophytes, and anterior femoral BML).

As secondary analyses, logistic regression analyses were performed to study the association between the clinical features (crepitus, history of patellar pain and pain during walking stairs) and shape modes, adjusted for age and BMI. Additionally, linear regression analyses were performed to study the association between short term pain and function (KOOS subscales) and patellar shape modes. Sensitivity analyses were performed with adjustment for group status (iPFOA or control participants) for shape modes where significant associations were found.

Results are expressed in odds ratios (ORs) or Beta's with the accompanying 95% confidence intervals (CIs). The differences in the patient characteristics between the groups were tested using the Student's *t*-tests and Pearson's chi-square test. All the statistical analyses were performed using SPSS (version 16.0, SPSS Inc., USA) and a *P*-value <0.05 was considered statistically significant.

Results

Our study included 132 women, 66 participants with iPFOA and 66 control participants with no knee OA (Table I). As a result of participant matching, no differences between the groups were found in terms of age and BMI. Both groups were significantly different in terms of the presence of all MOAKS features, crepitation, and pain during walking stairs. Additionally, all iPFOA participants had lower KOOS scores as compared to their matched control participants.

The first 25 patellar shape modes were retained (Fig. 1) and analysed using logistic regression. The patellar shape variations described by modes 6 (OR 1.72, 95% CI 1.16–2.55), 13 (OR 1.65, 95% CI 1.12–2.44), 21 (OR 1.70, 95% CI 1.15–2.53), and 23 (OR 0.62, 95% CI 0.43–0.90) showed statistically significant associations with the presence of PFOA (Table II). These modes described 4.5%, 2.1%, 0.9%, and 0.8% of the total shape variation in the patellar bone, respectively (3D files available in online Appendix 3).

Shape mode 6 revealed mostly differences at the posterior aspect of the patella (Fig. 2). The participants with PFOA seemed to possess a relatively more pronounced dorsal bump at the articular surface of the patella and a slightly shorter medial margin of the patella (Fig. 2, mode 6, quartiles; −0.91, −0.30, 0.32). The control participants showed a less pronounced dorsal bump and a slightly longer medial margin of the patella (Fig. 2, mode 6, quartiles; −0.40, 0.27, 0.91). The control subjects' patellae had, in general, a thicker apex (Fig. 2, mode 13, quartiles; −0.18, 0.35, 0.99) as compared to those of the participants with PFOA (quartiles; −0.69, 0.04, 0.86). The hook-like configuration at the lateral aspect (Fig. 2, mode 21, quartiles; −0.85, −0.28, 0.62) and the medio-superior aspect (Fig. 2, mode 23, quartiles; −0.12, 0.54, 1.21) of the patella were more common in the participants with PFOA (control patient mode 21 quartiles; −0.30, 0.39, 0.78, mode 23 quartiles; −0.63, 0,00, 0.58).

Post-hoc analyses revealed that modes 6 and 13 were specifically associated with the presence of osteophytes, BMLs, and cartilage loss on the patella while mode 13 was additionally associated with BMLs on the femur (Table III). Mode 21 was associated with both osteophytes on the anterior femur and cartilage loss on the patella. Mode 23 was only associated with osteophytes on the patella.

Shape variations described by modes 1, 6, 14, and 20 were linked to crepitus (Table IV). While modes 15 and 21 were associated with

	PF OA (n = 66)	Control (n = 66)	*P*-value
Age, years (mean (SD))	57.8 (3.85)	56.3 (3.88)	0.882*
BMI, kg/m^2 (mean (SD))	27.5 (4.35)	27.4 (4.41)	0.729*
Presence of MRI-based features (n (%))			
Osteophytes patella	42 (64%)	0 (0%)	<0.001†
Osteophytes anterior femur	40 (61%)	0 (0%)	<0.001†
BML patella	51 (78%)	26 (39%)	<0.001†
BML anterior femur	32 (49%)	13 (20%)	<0.001†
Cartilage loss patella	59 (89%)	14 (21%)	<0.001†
Presence of clinical features (n (%))			
Crepitation	36 (56%)	30 (45%)	0.218†
History of patellar pain	25 (40%)	8 (13%)	<0.001†
Pain during walking stairs	22 (34%)	4 (6%)	<0.001†
KOOS subscales 0–100 (mean (SD))			
Pain	85.8 (17.0)	96.8 (10.4)	<0.001*
Symptoms	83.7 (18.0)	95.4 (8.4)	<0.001*
ADL	89.4 (15.5)	97.3 (9.5)	<0.001*
Sport	71.7 (31.6)	93.3 (18.2)	<0.001*
Quality of life	74.7 (24.9)	94.2 (12.4)	<0.001*

* Student's *t*-test.
† Pearson chi-square.

Table I

The characteristics of the study population

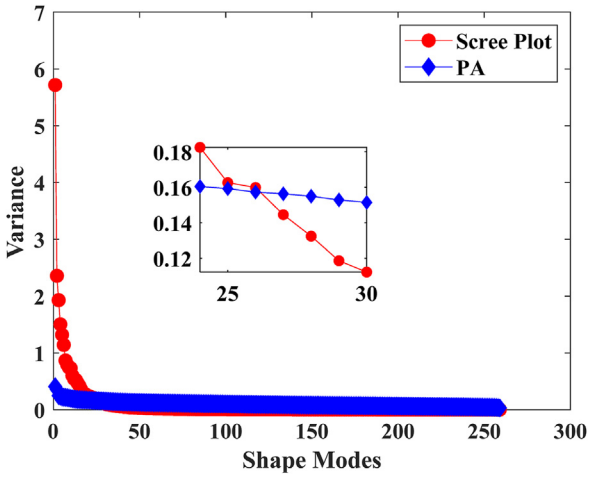

Fig. 1 Osteoarthritis and Cartilage

Parallel analysis. The observed data (red, scree plot) and the simulated data (blue, parallel analysis) insect at mode 25. Thus, all shape modes up to the intersection (25) were retained for statistical analysis.

Shape modes	Crude OR	Adjusted* OR
Mode 1	0.93 (0.63–1.36)	0.93 (0.62–1.38)
Mode 2	1.06 (0.73–1.52)	1.09 (0.75–1.58)
Mode 3	1.21 (0.84–1.74)	1.27 (0.87–1.83)
Mode 4	0.77 (0.53–1.13)	0.79 (0.53–1.17)
Mode 5	1.36 (0.95–1.95)	1.44 (0.99–2.10)
Mode 6	**0.58 (0.39–0.86)*P* = 0.006**	**0.58 (0.39–0.87)*P* = 0.008**
Mode 7	1.35 (0.96–1.91)	1.32 (0.93–1.88)
Mode 8	0.79 (0.54–1.15)	0.78 (0.53–1.15)
Mode 9	0.77 (0.55–1.08)	0.79 (0.55–1.13)
Mode 10	0.82 (0.58–1.14)	0.84 (0.60–1.19)
Mode 11	1.31 (0.92–1.87)	1.32 (0.92–1.90)
Mode 12	1.14 (0.81–1.61)	1.17 (0.82–1.68)
Mode 13	0.70 (0.48–1.00)*P* = 0.051	**0.61 (0.41–0.90)*P* = 0.012**
Mode 14	0.88 (0.60–1.29)	0.90 (0.61–1.32)
Mode 15	1.40 (0.96–2.04)	1.40 (0.95–2.07)
Mode 16	1.03 (0.72–1.47)	1.05 (0.73–1.50)
Mode 17	0.78 (0.56–1.10)	0.75 (0.53–1.07)
Mode 18	0.81 (0.56–1.87)	0.82 (0.56–1.21)
Mode 19	1.08 (0.76–1.53)	1.03 (0.72–1.49)
Mode 20	0.92 (0.66–1.28)	0.80 (0.68–1.34)
Mode 21	**0.57 (0.39–0.85)*P* = 0.005**	**0.59 (0.40–0.87)*P* = 0.008**
Mode 22	0.94 (0.69–1.29)	0.90 (0.65–1.24)
Mode 23	**1.61 (1.13–2.30)*P* = 0.09**	**1.61 (1.12–2.32)*P* = 0.011**
Mode 24	0.92 (0.65–1.28)	0.88 (0.63–1.25)
Mode 25	1.14 (0.81–1.61)	1.12 (0.79–1.59)

* Adjusted for age and BMI. Significant associations ($P < 0.05$) are typed using a bold font.

Table II Osteoarthritis and Cartilage

The associations between the group status (participants with PFOA (***n*** = 66) and control participants (***n*** = 66)) and patellar shape modes (OR with 95% CI)

a history of patellar pain, modes 13 and 21 were associated with pain during walking stairs. *Post-hoc* analyses adjusted for the group status revealed that the associations between shape, crepitus, and the history of patellar pain remained largely unchanged, while the associations with pain during walking stairs was less pronounced and did not reach statistical significance (online Appendix 1).

Finally, multiple associations were present between the patellar shape and KOOS subscales (Table V). Mode 21 was associated with all KOOS subscales. Additionally, mode 1 was associated with the sport subscale, mode 2 was associated with the pain, ADL, and sport subscale, and mode 13 was associated with the pain and quality of life subscale. *Post-hoc* analyses adjusted for group status showed that these associations remained largely intact, as only one lost statistical significance (mode 13 and KOOS pain, online Appendix 2).

Discussion

We aimed to study whether patellar shape is associated with MRI-based OA in the PFJ. Four shape variants showed statistically significant differences between the participants with PFOA and control subjects. *Post-hoc* analyses showed that osteophytes and cartilage loss on the patella were the most prominent MOAKS features associated with these four shape variants. One shape variant, namely shape mode 21, showed clear associations with multiple clinical complaints associated with PFOA.

There has been extensive research on the association between knee alignment, trochlear morphology, and PFOA, which shows that there is strong evidence for an association between PFOA and patellar alignment[10]. Macri *et al.* showed that MRI-based PFOA is associated with anterior knee pain, suggesting that the MRI-based features of OA may contribute to localized symptoms[25]. More recent studies have additionally shown that patellofemoral frontal plane alignment is associated with patellar cartilage volume reduction[26] and osteophyte worsening in women[27]. Since 2D alignment and basic trochlear measures tell only a part of the story, more recent research has focused on 3D shape analysis in the knee[12,15]. These analyses have, for example, shown that the 3D femoral shape predicts total knee arthroplasty as a result of knee OA[12]. Furthermore, 3D patellar and trochlear bone shapes have been shown to be associated with the progression of MRI-based features of PFOA[15]. In this study, Liao *et al.* have shown that subjects with an increased level of the MRI-based degeneration of PFOA exhibit a patella with a lateral bump or hook, which seems to be in line with our findings as a longer lateral side of the patella was associated with PFOA (mode 21). However, while Liao *et al.* reported no associations between this lateral bump or hook and self-reported symptoms, we also found an association between this patellar shape and a history of patellar pain, pain during walking stairs, and all the subscales of the KOOS scoring system. This may indicate that a bump on the lateral, non-articular part of the patella influences joint biomechanics which may lead to the development of structural abnormalities and pain. Alternatively, lateral malalignment associated with OA might cause adaptation of the patella shape, with the lateral facet wrapping around the femoral condyle to form a hook. However, longitudinal data and validation in other datasets is required to investigate this association, and the direction of the association further, preferably including both the patellar and femoral parts of the PFJ.

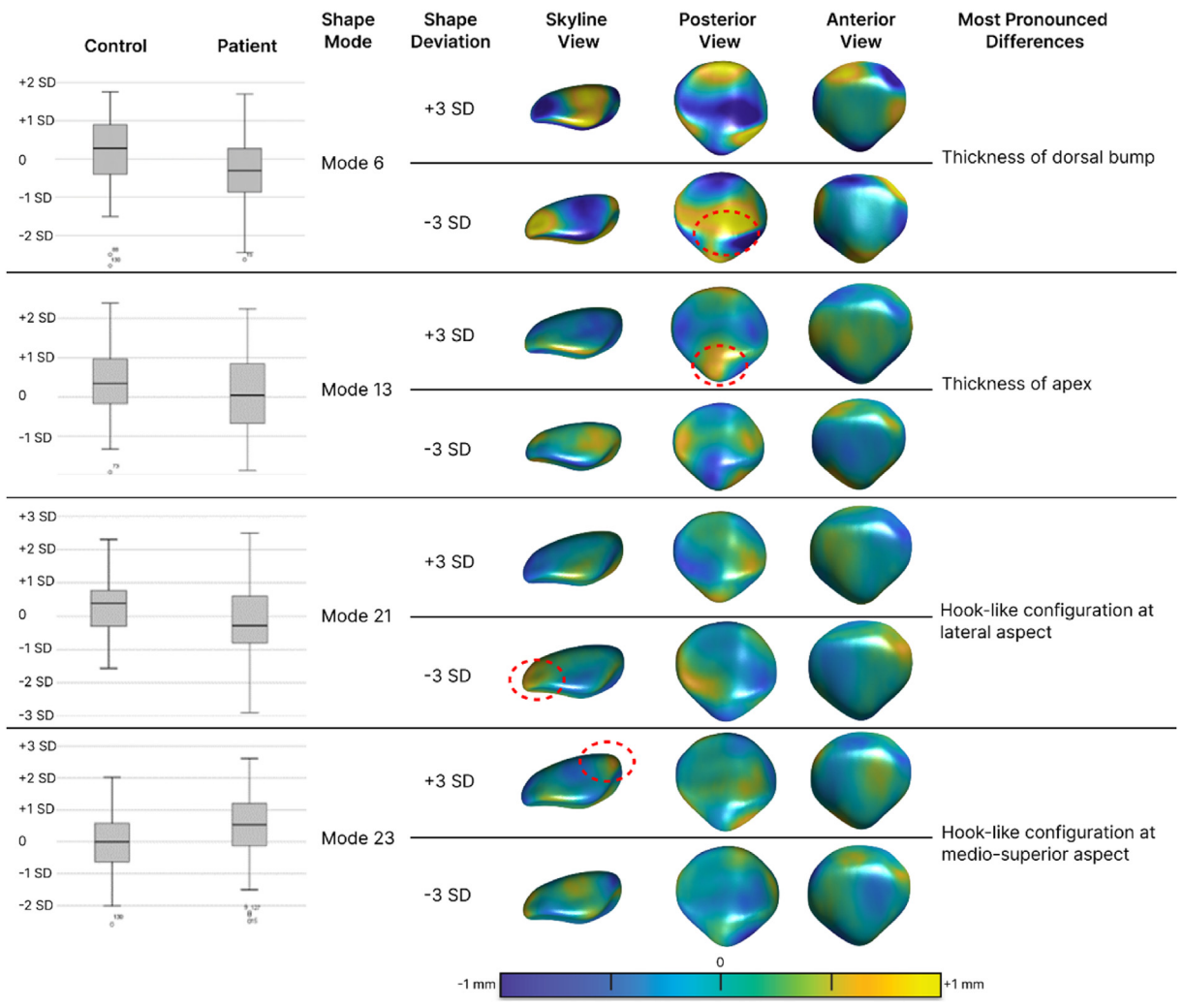

Fig. 2

Osteoarthritis and Cartilage

The distributions and distance maps for the associated modes. Distance maps in mm, yellow colour indicates a positive distance from the mean shape while a blue colour indicates a negative distance from the mean shape. Dotted line shows most pronounced differences in each shape mode. For example, mode 6: In the boxplot we see that the population with PFOA more closely resembles a negative standard deviation. The extreme shapes in the negative direction (−3SD) show a thicker more pronounced (yellow) dorsal bump on at the articular part of the surface of the patella compared to the mean shape.

While we found four shape variants associated with MRI-based PFOA, not all of these were associated with clinical symptoms and the explained variance was small. While shape mode 6 (responsible for 4.5% of the shape variations), was associated with structural PF OA features, it was only associated with crepitus in terms of clinical symptoms. On the other hand, the seemingly subtle shape variations in mode 21 (responsible for 0.9% shape variation) were found to be associated with almost all clinical symptoms. This may suggest that distinct patellar shapes are associated with specific MRI-based and clinical features in participants with MRI-based PFOA. It is unclear why this seemingly subtle difference in shape has multiple clinical effects and therefore further validation in other study populations is mandatory.

The shape model applied in the current study was previously applied in a young population (14–40 years) showing symptoms of PFP and was compared to an age- and sex-matched control group (unpublished data)[28]. This provides us with the unique opportunity to compare the shape variations in the PFOA population as described in the current study with these found in this younger PFP population. This is of particular interest as it has been frequently suggested that PFP may be a precursor of PFOA, as they share multiple risk factors, including malalignment[29]. It is, therefore, particularly interesting to see that in both populations (i.e., PFP and PFOA), shape mode 6 is associated with structural abnormalities[28], while showing no association with pain. The participants with PFOA who had a more pronounced dorsal bump suffered from a higher risk of bone marrow lesions, cartilage loss, and osteophytes on the patella compared to the control participants. Since the dorsal bump of the patella is one of the main articular surfaces in the PFJ, it can be hypothesized that this

Shape modes	Osteophytes patella ($n = 42$)	Osteophytes anterior femur ($n = 40$)	BMLs patella ($n = 77$)	BMLs anterior femur ($n = 45$)	Cartilage loss patella ($n = 73$)
Mode 6	**0.55 (0.37–0.84)*P* = 0.006**	0.68 (0.45–1.03)	**0.60 (0.40–0.90)*P* = 0.012**	0.83 (0.56–1.22)	**0.49 (0.32–0.75)*P* < 0.001**
Mode 13	**0.64 (0.43–0.97)*P* = 0.033**	0.74 (0.49–1.11)	**0.68 (0.46–0.99)*P* = 0.045**	**0.59 (0.39–0.90)*P* = 0.014**	**0.64 (0.44–0.95)*P* = 0.025**
Mode 21	0.71 (0.48–1.06)	**0.62 (0.41–0.94)*P* = 0.025**	0.86 (0.60–1.24)	0.76 (0.51–1.11)	**0.62 (0.42–0.91)*P* = 0.016**
Mode 23	**2.42 (1.53–3.84)*P* < 0.001**	1.38 (0.95–2.02)	1.07 (0.77–1.50)	1.13 (0.80–1.61)	1.32 (0.94–1.87)

Adjusted for age and BMI. Significant associations ($P < 0.05$) are typed using a bold font.

Table III

Osteoarthritis and Cartilage

The associations between the MOAKS features associated with presence of PFOA and the patellar shape modes (OR with 95% CI), ***n*** = 132

aberrant shape in this part of the patella may lead to an aberrant type of joint loading, which may consequently lead to bone and cartilage damage. Though, so far only suggestive since longitudinal evidence is lacking, this shape abnormality on the dorsal side of the patella could however potentially be an early risk factor for bone or cartilage damage on the patella. Future research should further investigate this potential association as this may add to the understanding of the possible continuum between PFP and PFOA, even if participants with this abnormality do not always experience pain.

Shape modes	Crepitus ($n = 66$)	History of patellar pain ($n = 33$)	Pain during walking stairs ($n = 26$)
Mode 1	**0.63 (0.41–0.98)*P* = 0.039**	0.69 (0.43–1.12)	0.86 (0.52–1.42)
Mode 2	1.08 (0.75–1.58)	1.28 (0.83–1.97)	1.34 (0.85–2.13)
Mode 3	1.12 (0.78–1.61)	1.04 (0.67–1.62)	0.95 (0.59–1.51)
Mode 4	1.11 (0.75–1.65)	0.87 (0.56–1.35)	0.84 (0.52–1.35)
Mode 5	1.14 (0.80–1.64)	1.26 (0.83–1.91)	1.12 (0.72–1.75)
Mode 6	**0.64 (0.43–0.95)*P* = 0.026**	0.84 (0.55–1.28)	0.69 (0.43–1.08)
Mode 7	1.22 (0.85–1.75)	1.09 (0.74–1.60)	1.11 (0.73–1.70)
Mode 8	1.32 (0.90–1.95)	1.09 (0.70–1.70)	0.93 (0.58–1.48)
Mode 9	1.11 (0.78–1.57)	0.73 (0.48–1.11)	0.95 (0.61–1.46)
Mode 10	1.13 (0.81–1.58)	1.19 (0.81–1.76)	1.16 (0.76–1.77)
Mode 11	0.98 (0.69–1.39)	1.24 (0.82–1.89)	1.08 (0.69–1.67)
Mode 12	0.82 (0.57–1.12)	1.06 (0.70–1.60)	1.21 (0.78–1.89)
Mode 13	0.96 (0.66–1.39)	0.70 (0.45–1.10)	**0.59 (0.36–0.97)*P* = 0.036**
Mode 14	**1.60 (1.06–2.42)*P* = 0.027**	0.93 (0.60–1.46)	0.72 (0.44–1.19)
Mode 15	1.00 (0.69–1.45)	**1.81 (1.12–2.93)*P* = 0.015**	1.58 (0.96–2.61)
Mode 16	0.87 (0.60–1.25)	0.84 (0.55–1.28)	1.21 (0.77–1.90)
Mode 17	0.85 (0.60–1.20)	1.05 (0.71–1.55)	0.71 (0.45–1.10)
Mode 18	1.11 (0.75–1.64)	0.97 (0.62–1.50)	1.10 (0.69–1.77)
Mode 19	0.86 (0.60–1.24)	1.24 (0.82–1.88)	1.20 (0.77–1.89)
Mode 20	**0.61 (0.42–0.88)*P* = 0.009**	1.09 (0.73–1.62)	1.04 (0.69–1.58)
Mode 21	0.87 (0.60–1.25)	**0.50 (0.32–0.80)*P* = 0.004**	**0.55 (0.34–0.89)*P* = 0.015**
Mode 22	0.80 (0.58–1.11)	0.88 (0.61–1.28)	1.22 (0.82–1.83)
Mode 23	0.98 (0.70–1.37)	1.21 (0.81–1.81)	1.44 (0.93–2.23)
Mode 24	1.09 (0.77–1.54)	0.81 (0.54–1.20)	0.99 (0.65–1.50)
Mode 25	0.87 (0.60–1.26)	1.11 (0.73–1.70)	0.88 (0.57–1.36)

Adjusted for age and BMI. Significant associations ($P < 0.05$) are typed using a bold font.

Table IV

Osteoarthritis and Cartilage

The associations between the clinical features associated with presence of PFOA and the patellar shape modes (OR with 95% CI), ***n*** = 132

Shape modes	KOOS pain	KOOS symptoms	KOOS ADL	KOOS sport	KOOS QoL
Mode 1	2.69 (−0.30; 5.69)	2.80 (−0.20; 5.80)	1.11 (−1.58; 3.81)	**6.76 (1.26; 12.26)*P* = 0.016**	3.33 (−0.97; 7.63)
Mode 2	**−3.34 (−6.14; −0.53)*P* = 0.020**	−1.74 (−4.60; 1.12)	**−2.61 (−5.12; −0.10)*P* = 0.042**	**−5.47 (−10.67; −0.26)*P* = 0.04**	−3.92 (−7.97; 0.12)
Mode 3	−1.23 (−4.07; 1.62)	−1.93 (−4.77; 0.91)	−0.92 (−3.46; 1.61)	−2.19 (−7.44; 3.07)	−0.96 (−5.03; 3.12)
Mode 4	0.77 (−2.18; 3.71)	1.11 (−1.84; 4.05)	0.42 (−2.21; 3.04)	2.720 (−2.70; 8.13)	−0.41 (−4.62; 3.80)
Mode 5	−0.77 (−3.47; 1.93)	−0.46 (−3.17; 2.25)	−1.10 (−3.50; 1.30)	−0.69 (−5.74; 4.37)	−1.52 (−5.38; 2.34)
Mode 6	1.01 (−1.77; 3.80)	1.71 (−1.06; 4.49)	1.01 (−1.46; 3.49)	2.21 (−2.92; 7.33)	3.04 (−0.90; 6.98)
Mode 7	1.04 (−1.56; 3.65)	−0.02 (−2.64; 2.60)	0.31 (−2.01; 2.64)	1.44 (−3.39; 6.26)	0.50 (−3.23; 4.23)
Mode 8	−0.53 (−3.41; 2.34)	−1.80 (−4.66; 1.07)	−0.44 (−3.00; 2.12)	0.33 (−5.04; 5.71)	−0.45 (−4.57; 3.66)
Mode 9	−0.79 (−3.45; 1.86)	−1.20 (−3.85; 1.45)	−0.88 (−3.24; 1.48)	−1.34 (−6.30; 3.63)	−0.50 (−4.29; 3.30)
Mode 10	−1.20 (−3.73; 1.33)	−0.59 (−3.13; 0.33)	−1.30 (−3.55; 0.95)	0.21 (−4.48; 4.90)	−1.89 (−5.50; 1.72)
Mode 11	−0.68 (−3.31; 1.94)	−1.88 (−4.49; 0.72)	−0.69 (−3.03; 1.64)	−4.02 (−8.81; 0.77)	−2.01 (−5.74; 1.72)
Mode 12	−0.79 (−3.47; 1.89)	−1.34 (−4.02; 1.34)	−1.48; (−3.85; 0.90)	−4.17 (−9.10; 0.76)	−1.98 (−5.80; 1.84)
Mode 13	**3.01 (0.27; 5.75)*P* = 0.032**	2.42 (−1.34; 5.18)	2.18 (−0.28; 4.63)	4.84 (−0.27; 9.94)	**4.47 (0.56; 8.38)*P* = 0.025**
Mode 14	1.74 (−1.18; 4.65)	0.24 (−2.69; 3.17)	1.82 (−0.76; 4.41)	2.70 (−2.68; 8.09)	1.51 (−2.66; 5.69)
Mode 15	−1.97 (−4.78; 0.84)	−1.30 (−4.13; 1.53)	−1.51 (−4.02; 0.99)	−0.33 (−5.59; 4.94)	−3.31 (−7.31; 0.69)
Mode 16	−1.07 (−3.80; 1.66)	−0.15 (−2.89; 2.59)	−1.03 (−3.46; 1.40)	−3.37 (−8.40; 1.67)	−0.67 (−4.57; 3.24)
Mode 17	2.17 (−0.40; 4.73)	1.47 (−1.11; 4.06)	2.14 (−0.13; 4.42)	2.89 (−1.87; 7.64)	2.00 (−1.69; 5.69)
Mode 18	−1.69 (−4.58; 1.19)	−2.05 (−4.94; 0.83)	−1.67 (−4.23; 0.90)	−4.29 (−9.68; 1.10)	−1.53 (−5.66; 2.61)
Mode 19	0.32 (−2.41; 3.06)	−0.44 (−3.18; 2.30)	−0.65 (−3.08; 1.79)	1.60 (−3.47; 6.68)	0.61 (−3.31; 4.52)
Mode 20	0.26 (−2.28; 2.80)	0.51 (−2.03; 3.05)	0.39 (−1.87; 2.65)	0.99 (−3.70; 5.67)	−0.04 (−3.66; 3.59)
Mode 21	**3.85 (1.21; 6.49)*P* = 0.005**	**4.88 (2.29; 7.47)*P* < 0.001**	**3.49 (1.14; 5.83)*P* = 0.004**	**9.07 (4.24; 13.89)*P* < 0.001**	**6.95 (3.25; 10.64)*P* < 0.001**
Mode 22	−1.18 (−3.60; 1.25)	−0.13 (−2.57; 2.31)	−1.25 (−3.41; 0.90)	−1.68 (−6.16; 2.81)	−0.86 (−4.33; 2.62)
Mode 23	−1.96 (−4.45; 0.53)	−1.82 (−4.31; 0.68)	−1.22 (−3.45; 1.00)	−2.28 (−6.94; 2.37)	−1.96 (−5.53; 1.61)
Mode 24	−0.77 (−3.36; 1.83)	0.65 (−1.95; 3.25)	−0.84 (−3.15; 1.47)	−1.93 (−6.74; 2.89)	−1.86 (−5.56; 1.84)
Mode 25	0.27 (−2.38; 2.90)	0.26 (−2.40; 2.91)	0.54 (−1.82; 2.90)	−0.66 (−5.62; 4.30)	0.65 (−3.13; 4.44)

Adjusted for age and BMI. Significant associations ($P < 0.05$) are typed using a bold font.

Table V

Osteoarthritis and Cartilage

The associations between the KOOS subscales and patellar shape modes (Beta's with 95% CI)

Strengths and limitations

Our study is unique as it investigated the potential associations between the shape and both MRI-based and clinical features of PFOA in a large population study. However, some limitations need to be addressed.

First, the use of manual segmentation introduces human bias. To combat this bias, the segmentation was done by one person only, blinded for group status. Secondly, we focused on the shape of the patella alone. While we were able to show differences between the groups in terms of the patellar shape, it is important to note that the shape combination of the trochlea and patella is probably very important as well for joint loading. Future shape models in the PFJ should, therefore, focus on the combined bone shapes, taking the entire PFJ into account. Finally, before the SSM were build, we planned to use parallel analysis to determine the number of modes included in our statistical analyses. This resulted in a large number of shape modes, of which the variance was relatively low. Consequently, given the large number of tests, a type 1 statistical error may have occurred. However, our results were consistent across multiple comparisons, adding confidence to our results.

Conclusions

Some features of the patellar shape seem to be associated with the presence of MRI-based PFOA in middle-aged women, of which some variants were also associated with clinical symptoms. Further validation in other study populations is mandatory, given the relatively low percentage of explained variance, but also to confirm the association of one particular shape mode. This shape mode, mostly pronounced on the dorsal side of the patella, was earlier shown to be associated with structural abnormalities associated with OA in a population aged under 40.

Author contributions

SB and MM conceived the study. DS and EO collected clinical data and applied MOAKS scorings. JE and NT post processed the data. JE and NT analysed the data. JE wrote the manuscript. NT, DS, EO, AZ, SB and MM edited the manuscript. EO and AZ supervised data post processing. SB and MM supervised data analysis and interpretation. All authors approved the final manuscript.

Conflict of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

Acknowledgements

This study was funded by the Dutch Arthritis Association.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joca.2022.12.008.

References

1. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet 2019;393(10182):1745–59, https://doi.org/10.1016/S0140-6736(19)30417-9.
2. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. EClinicalMedicine 2020;29–30, 100587, https://doi.org/10.1016/j.eclinm.2020.100587.
3. van Middelkoop M, Bennell KL, Callaghan MJ, Collins NJ, Conaghan PG, Crossley KM, *et al*. International patellofemoral osteoarthritis consortium: consensus statement on the diagnosis, burden, outcome measures, prognosis, risk factors and treatment. Semin Arthritis Rheum 2018:1–10, https://doi.org/10.1016/j.semarthrit.2017.09.009.
4. Duncan R, Peat G, Thomas E, Wood L, Hay E, Croft P. Does isolated patellofemoral osteoarthritis matter? Osteoarthr Cartil 2009;17(9):1151–5, https://doi.org/10.1016/j.joca.2009.03.016.
5. Kobayashi S, Pappas E, Fransen M, Refshauge K, Simic M. The prevalence of patellofemoral osteoarthritis: a systematic review. Osteoarthr Cartil 2016;23(May):A189, https://doi.org/10.1016/j.joca.2015.02.968.
6. Lankhorst NE, Damen J, Oei EH, Verhaar JAN, Kloppenburg M, Bierma-Zeinstra SMA, *et al*. Incidence, prevalence, natural course and prognosis of patellofemoral osteoarthritis: the Cohort Hip and Cohort Knee study. Osteoarthr Cartil 2017;25(5):647–53, https://doi.org/10.1016/j.joca.2016.12.006.
7. Fok LA, Schache AG, Crossley KM, Lin Y-C, Pandy MG. Patellofemoral joint loading during stair ambulation in people with patellofemoral osteoarthritis. Arthritis Rheum 2013;65(8):2059–69, https://doi.org/10.1002/art.38025.
8. Hart HF, Ackland DC, Pandy MG, Crossley KM. Quadriceps volumes are reduced in people with patellofemoral joint osteoarthritis. Osteoarthr Cartil 2012;20(8):863–8, https://doi.org/10.1016/j.joca.2012.04.009.
9. Teng HL, MacLeod TD, Link TM, Majumdar S, Souza RB. Higher knee flexion moment during the second half of the stance phase of gait is associated with the progression of osteoarthritis of the patellofemoral joint on magnetic resonance imaging. J Orthop Sports Phys Ther 2015;45(9):656–64, https://doi.org/10.2519/jospt.2015.5859.
10. Macri EM, Stefanik JJ, Khan KK, Crossley KM. Is tibiofemoral or patellofemoral alignment or trochlear morphology associated with patellofemoral osteoarthritis? A systematic review. Arthritis Care Res 2016;68(10):1453–70, https://doi.org/10.1002/acr.22842.
11. Hunter D, Nevitt M, Lynch J, Kraus VB, Katz JN, Collins JE, *et al*. Longitudinal validation of periarticular bone area and 3D shape as biomarkers for knee OA progression? Data from the FNIH OA Biomarkers Consortium. Ann Rheum Dis 2016, https://doi.org/10.1136/annrheumdis-2015-207602.
12. Barr AJ, Dube B, Hensor EMA, Kingsbury SR, Peat G, Bowes MA, *et al*. The relationship between three-dimensional knee MRI bone shape and total knee replacement – a case control study: data from the osteoarthritis initiative. Rheumatology 1585–1593;55(9):2016, https://doi.org/10.1093/rheumatology/kew191.
13. Dube B, Bowes MA, Hensor EMA, Barr A, Kingsbury SR, Conaghan PG. The relationship between two different measures of osteoarthritis bone pathology, bone marrow lesions and 3D bone shape: data from the osteoarthritis initiative. Osteoarthr Cartil 2018;26(10):1333–7, https://doi.org/10.1016/j.joca.2018.06.011.
14. Bowes MA, Kacena K, Alabas OA, Brett AD, Dube B, Bodick N, Machine-learning, *et al*. MRI bone shape and important clinical outcomes in osteoarthritis: data from the Osteoarthritis Initiative. Ann Rheum Dis 2021;80(4):502–8, https://doi.org/10.1136/annrheumdis-2020-217160.
15. Liao TC, Jergas H, Tibrewala R, Bahroos E, Link TM, Majumdar S, *et al*. Longitudinal analysis of the contribution of 3D patella and trochlear bone shape on patellofemoral joint osteoarthritic features. J Orthop Res 2021;39(3):506–15, https://doi.org/10.1002/jor.24836.
16. Hofman A, Van Duijn CM, Franco OH, Ikram MA, Janssen HL, Klaver CC, *et al*. The Rotterdam Study: 2012 objectives and design update. Eur J Epidemiol 2011;26(8):657–86, https://doi.org/10.1007/s10654-011-9610-5.
17. Ikram MA, Brusselle G, Ghanbari M, Goedegebure A, Ikram MK, Kavousi M, *et al*. Objectives, *Design and Main Findings until 2020 from the Rotterdam Study*. Netherlands: Springer; 2020, https://doi.org/10.1007/s10654-020-00640-5.
18. Schiphof D, Oei EHG, Hofman A, Waarsing JH, Weinans H, Bierma-Zeinstra SMA. Sensitivity and associations with pain and body weight of an MRI definition of knee osteoarthritis compared with radiographic Kellgren and Lawrence criteria: a population-based study in middle-aged females. Osteoarthr Cartil 2014;22(3):440–6, https://doi.org/10.1016/j.joca.2013.12.017.
19. Hunter DJ, Guermazi A, Lo GH, Grainger AJ, Conaghan PG, Boudreau RM, *et al*. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI osteoarthritis knee score). Osteoarthr Cartil 2011;19(8):990–1002, https://doi.org/10.1016/j.joca.2011.05.004.
20. Schiphof D, Van Middelkoop M, De Klerk BM, Oei EHG, Hofman A, Koes BW, *et al*. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). *Osteoarthr Cartil* 2014;22(5):631–8, https://doi.org/10.1016/j.joca.2014.02.008.
21. R. Cheng J.N. Jackson, E.S. McCreedy, W. Gandler, J.F.A. Eijeknboom, M. van Middelkoop, et al., Patellar segmentation from 3D magnetic resonance images using guided recursive ray-tracing for edge pattern detection, In: *Medical Imaging 2016: Biomedical Applications in Molecular, Structural, and Functional Imaging*, **vol. 9788**, 2016,97880C, https://doi.org/10.1117/12.2217232.
22. van de Giessen M, Vos FM, Grimbergen CA, van Vliet LJ, Streekstra GJ. An efficient and robust algorithm for parallel groupwise registration of bone surfaces. In: Med Image Comput Comput Assist Interv 2012;15:164–71, https://doi.org/10.1007/978-3-642-33454-2_21. PMID: 23286127.
23. Tümer N, Blankevoort L, van de Giessen M, Terra MP, de Jong PA, Weinans H, *et al*. Bone shape difference between control and osteochondral defect groups of the ankle joint. Osteoarthr Cartil 2016;24(12):2108–15, https://doi.org/10.1016/j.joca.2016.07.015.
24. Tümer N, Arbabi V, Gielis WP, de Jong PA, Weinans H, Tuijthof GJM, *et al*. Three-dimensional analysis of shape variations and symmetry of the fibula, tibia, calcaneus and talus. J Anat 2019;234(1):132–44, https://doi.org/10.1111/joa.12900.
25. Macri EM, Neogi T, Tolstykh I, Widjajahakim R, Lewis CE, Torner JC, *et al*. Relation of patellofemoral joint alignment, morphology, and radiographic osteoarthritis to frequent anterior knee pain: data from the multicenter osteoarthritis study. *Arthritis Care Res* 2020;72(8):1066–73, https://doi.org/10.1002/acr.24004.
26. Teichtahl AJ, Wluka AE, Cicuttini FM. Frontal plane knee alignment is associated with a longitudinal reduction in patella cartilage volume in people with knee osteoarthritis. Osteoarthr Cartil 2008;16(7):851–4, https://doi.org/10.1016/j.joca.2007.12.002.

27. Macri EM, Felson DT, Ziegler M, Cooke T, Guermazi A, Roemer F. The association of frontal plane alignment to MRI-defined worsening of patellofemoral osteoarthritis: the MOST study EM. Osteoarthr Cartil 2019;27(3):459–67, https://doi.org/10.1016/j.joca.2018.11.004.
28. Eijkenboom JJ, Tumer N, Waarsing EH, et al. Patellofemoral pain patients show differences in 3D patellar shape compared to healthy control subjects. In: Osteoarthritis and Cartilage. Vol 29. Elsevier; 2021:S336-S337. https://doi.org/10.1016/J.JOCA.2021.02.438.
29. Crossley KM. Is patellofemoral osteoarthritis a common sequela of patellofemoral pain? Br J Sports Med 2014;48(6):409–10, https://doi.org/10.1136/bjsports-2014-093445.