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Evaluation of a Photographic Chondropathy Score (PCS) for pathological samples in a study of inflammation in tibiofemoral osteoarthritis

D. A. Walsh F.R.C.P., Ph.D.†‡*, A. Yousef F.R.C.S., M.Sc.§, D. F. McWilliams Ph.D.†, R. Hill†, E. Hargin B.Sc.† and D. Wilson‡

† *Academic Rheumatology, University of Nottingham, Clinical Sciences Building, Nottingham City Hospital, Hucknall Road, Nottingham NG5 1PB, UK*

‡ *Back Pain Unit, Sherwood Forest Hospitals NHS Foundation Trust, Mansfield Road, Sutton in Ashfield NG17 4JL, UK*

§ *Orthopaedics and Trauma, Sherwood Forest Hospitals NHS Foundation Trust, Mansfield Road, Sutton in Ashfield NG17 4JL, UK*

Summary

Objective: Severity of structural change in knee osteoarthritis (OA) can be measured radiologically, macroscopically or microscopically. Existing methods have limitations for use in laboratory studies. We have developed a Photographic Chondropathy Score (PCS) for use with pathological samples. We have compared the ability of the different severity measures to distinguish between samples obtained at total knee replacement surgery or postmortem (PM), and to detect associations between structural severity and synovitis.

Method: Tibial plateaux and femoral condyles were collected from 84 patients undergoing surgery or PM. Each sample was photographed and scored. Limits of agreement and repeatability coefficients were calculated for PCS. Scores for radiological joint space narrowing (JSN) and osteophytes, histological cartilage changes (Mankin), and synovitis were assigned. Data were analysed using Mann–Whitney *U* tests, Spearman's correlation coefficient or logistic regression.

Results: A total of 116 knees were analysed from 84 patients. Both medial tibial plateaux and total joint PCS showed good repeatability, internal consistency and reliability between observers. PCS, radiographic and Mankin's scores were all modestly positively correlated (*r* values 0.28–0.55). PCS and Mankin scores were greater in surgical than PM samples. Synovial inflammation was associated with higher PCS and radiological JSN scores (*r* values 0.43–0.48), irrespective of diagnosis.

Conclusion: Macroscopic, microscopic and radiographical severity scores are complementary measures of structural severity in knee OA. Synovial inflammation was associated with increased OA structural severity, suggesting a possible role of chronic synovitis in cartilage damage.

Key words: Arthroscopy, Osteoarthritis, Cartilage, Inflammation, Grading.

Abbreviations: PM postmortem, OST osteophyte, JSN joint space narrowing, EDTA ethylenediaminetetraacetic acid, PCS photographic cartilage osteoarthritis severity score, SFA Système Française D'Arthroscopie, TKR total knee replacement.

Introduction

Osteoarthritis (OA) of the knee is a common cause of pain and disability and is of great socioeconomic importance. The current treatments of OA address symptoms of pain, disability and distress, with little impact on structural disease progression.

A variety of methods have been described for measuring structural change in OA. Changes in cartilage structure, chondrocyte phenotype, and loss of matrix components can be detected by histology. Fibrillation, fissuring and loss of articular cartilage may be macroscopically apparent at the joint surface. Loss of articular cartilage contributes to joint space narrowing (JSN) on weight-bearing radiographs, and new bone formation results in the formation of osteophytes (OSTs). Different methods are used to measure OA structural change in different types of studies, depending on the scientific question, local expertise and practicalities.

Histological grading is most commonly used in laboratory research. Methods based on that described by Mankin are sensitive to pathological change, but require invasive tissue sampling[1–4]. Histological methods permit associations to be explored between severity and other pathological processes in the same region, although it may not always be valid to generalise results to the joint as a whole.

Macroscopic methods for scoring the appearance of articular surfaces have been most extensively developed for arthroscopic studies[5]. The Système Française D'Arthroscopie (SFA) system is based on global assessment of OA changes in the articular surfaces of the knee, and has been validated across the range from mild chondropathy to severe OA[6–8]. The SFA system builds on a macroscopic severity score that was developed by Collins using

*Address correspondence and reprint requests to: Dr D. A. Walsh, Academic Rheumatology, University of Nottingham, Clinical Sciences Building, Nottingham City Hospital, Hucknall Road, Nottingham NG5 1PB, UK. Tel: 44-(0)-115-8231751; Fax: 44-(0)-115-8231757; E-mail: david.walsh@nottingham.ac.uk

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pathological samples[9,10], was based on factor analysis of data from arthroscopic examinations, and later simplified giving a scale from 0 to 100[7]. Macroscopic methods require access to intact tissues, but can be used to derive global scores for the joint or joint compartment as a whole.

Radiography permits serial weight-bearing measurements in living subjects. Radiographic methods may be less sensitive to OA cartilage change than are histological or macroscopic methods, especially in the lateral tibiofemoral compartment[8,11–14]. Other imaging methods such as MRI may display higher sensitivity in detecting OA cartilage change, but greater cost[15].

Structural disease progression in OA is multifactorial. Inflammation is increasingly recognised as a potential contributor to structural change. Rapidly progressing OA is associated with higher baseline circulating levels of the acute phase reactant, C-reactive protein[16,17]. Cytokines that are expressed by the inflamed osteoarthritic synovium increase chondrocyte catabolic activity[18] and enhance angiogenesis[19], and proteases produced by inflammatory cells may directly compromise cartilage structure[20]. Synovitis therefore may contribute to cartilage damage in OA. Indeed, clinical and arthroscopic synovitis have been associated with radiological progression in human OA[21,22].

We aimed to develop and validate a measure of OA disease severity for use in pathological samples of tibiofemoral joints from both clinical and cadaveric cases. We have developed and tested three Photographic Chondropathy Scores (PCSs), based on the Collins and SFA systems. We have compared the PCS systems with other histological, macroscopic and radiographic measures of structural severity, and have used these methods to explore possible associations between histological synovitis and the severity of OA structural changes.

Materials and methods

Informed consent was gained from each donor (surgical cases) or next of kin (postmortem [PM] cases) according to protocols approved by the North Nottinghamshire Research Ethics Committee and Nottingham Research Ethics Committee 1 (Projects NNHA/420, NNHA/544, NNHA/673 and 05/Q2403/24)[23]. Tibial plateaux, femoral condyles and synovium were collected from 56 patients undergoing total knee replacement (TKR), all of whom fulfilled the American College of Rheumatology revised criteria for OA[24].

Additional samples were obtained from both knees of 28 recently deceased patients (PM). It was anticipated that OA would be prevalent in PM cases, but at milder severity than in patients undergoing TKR. Clinical data for PM cases were obtained by case notes review, by interview with the patient's bereaved relatives and by clinical examination PM. Relatives reported that they were unaware of any attendance with a doctor for knee pain in the last 12 months by PM cases. Four PM cases were believed to have had OA by their relatives. No Heberden's nodes, rheumatoid nodules or OSTs were apparent at the point of sample collection.

Patients with rheumatoid arthritis and other arthritides were excluded from the study. Four patients (all TKR) displayed clinical evidence of nodal OA in the hands.

PHOTOGRAPHIC CHONDROPATHY SCORES (PCSs)

Tibial and femoral plateaux were photographed from a fixed distance of 23 cm using a Kaiser RS 2 XA camera stand, under standard illumination with a Sony DSC-S85 CyberShot digital camera fitted with a Carl Zeiss lens at 4× zoom (Carl Zeiss Ltd., Welwyn Garden City, UK). Uncompressed images were stored using Tagged Image File Format (TIFF) at a resolution of 2272×1704.

The severity and extent of loss of surface integrity of articular cartilage were recorded on a Clinical Report Form for each of four articular surfaces from each knee; medial and lateral tibial plateaux and femoral condyles, using a method adapted from Dougados *et al.*[6] (Fig. 1). Patellae and trochlear regions were excluded from the photographic scoring system due to their typical absence from pathological samples obtained at TKR surgery.

Loss of surface integrity was graded according to appearance on the photographic image. Grade 0; normal – smooth, unbroken surface, homogeneous white to off-white colour. Grade 1; swelling and softening – a light brown homogeneous colouration. Grade 2; superficial fibrillation – lightly broken surface, white to off-white/light brown in colour. Grade 3; deep fibrillation – coarsely broken cartilage surface, dark brown, grey or red in colour. Grade 4; subchondral bone exposure – stippled white and dark brown/red in colour. The extent of each grade of surface change was delineated freehand on standardised diagrams of each articular surface. The percentage of each articular surface area attributed to each grade was estimated by the assessor.

Scores were based on data from the Clinical Report Form. Three scoring methods were applied to each of the four articular surfaces, and total scores derived by summation of each of the four component scores. Data are presented for the total scores, and scores for the medial tibial plateaux alone. The medial tibial plateau was selected as this is the commonest site of tibiofemoral OA, and was sampled for histological analysis.

The grading method of Collins[9] was interpreted as a classification tree for articular surface change (Fig. 2). The phrases 'more extensive' and 'large areas', which define Grade I:II and III:IV boundaries according to Collins, were arbitrarily interpreted as >50% of the articular surface. The medial tibial plateau Collins grade gave values that could range from 0 to 4, and the total Collins grade had a possible range from 0 to 16.

'Original SFA' scores were derived using the two original formulae described by Dougados *et al.*[6], depending on whether a compartment was medial or lateral, and on the percentage of articular surface that is allocated to each severity grade[6]:

$$\text{Medial score} = -2.2 + (\text{Grade } 1 \times 1.3) + (\text{Grade } 2 \times 2.2) + (\text{Grade } 3 \times 3.4) + (\text{Grade } 4 \times 7.2)$$

$$\text{Lateral score} = -2.4 + (\text{Grade } 1 \times 0.8) + (\text{Grade } 2 \times 2.3) + (\text{Grade } 3 \times 5.0) + (\text{Grade } 4 \times 6.1)$$

The medial tibial plateau PCS gave values that could range from −2.2 to +717.8. Total PCS was calculated as the sum of the scores for the four regions (both tibial plateaux and femoral condyles), giving a possible range from −9.2 to +2650.8.

'Revised SFA' scores were derived using modifications of the original SFA formulae described by Ayral *et al.*[7]. Revised SFA scores have possible ranges of 0–100 for each articular surface, or 0–400 for the total score. For each articular surface

$$\text{Score} = (\text{Grade } 1 \times 0.14) + (\text{Grade } 2 \times 0.34) + (\text{Grade } 3 \times 0.65) + \text{Grade } 4$$

Inter-observer reliability was determined by two observers (RH and EH) who independently derived scores from the photographic images of 98 knees (56 PM), each blinded to the scores allocated by the other observer.

In order to evaluate the validity of using photographs for scoring articular surface changes, 'macroscopic pathological scores' were derived for a subset of 77 knees (56 PM) using the methods described above, with direct visualisation and probing of fresh pathological samples, comparable with assessment at arthroscopy.

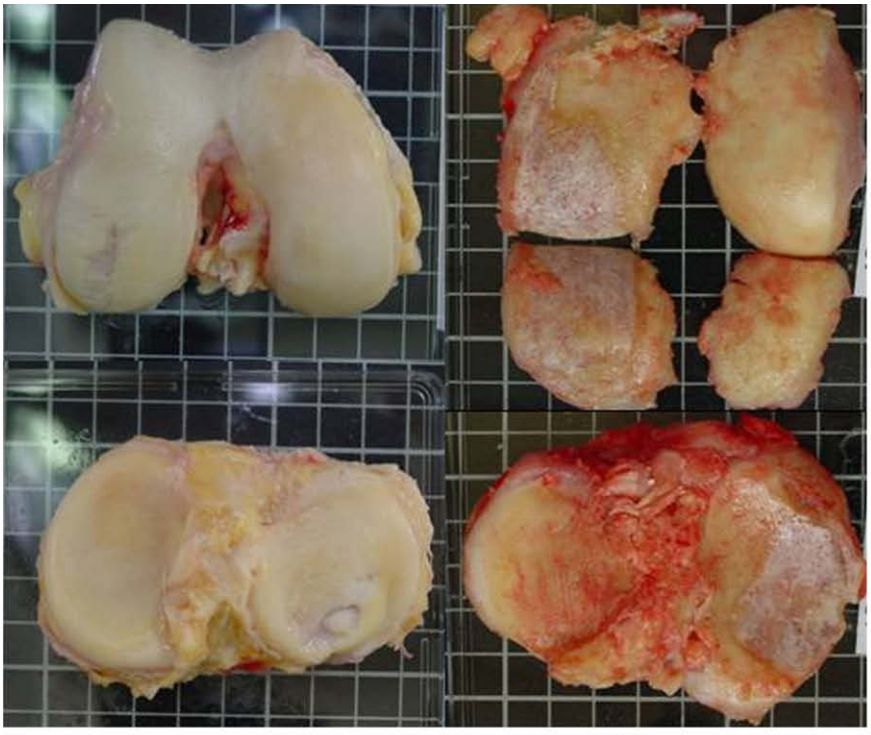
Additional validation was undertaken during the development of the photographic scoring system using a subset of 24 knees (16 PM). In order to evaluate the overall repeatability of the photographic scoring system, photographs of the 24 knees were re-graded and the extent of graded changes redrawn and re-scored by a single observer (RH) at least 2 weeks after and blinded to his initial grading. In order to evaluate the repeatability of estimating the extent of graded changes, one of us (RH) repeated his estimation of the extent of graded changes, using his original set of 24 diagrams, at least 2 weeks after and blinded to his previous estimations.

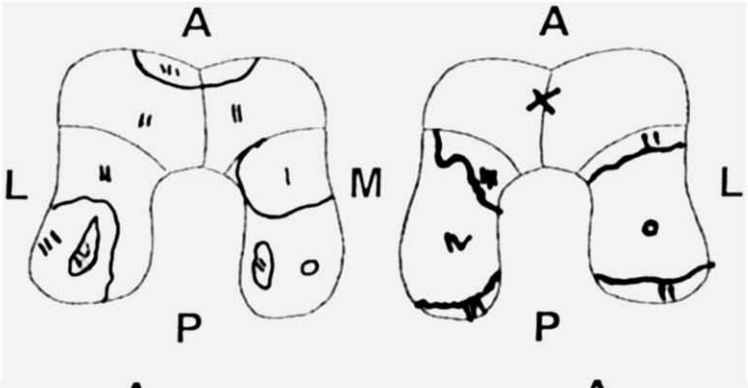
RADIOGRAPHIC SCORING

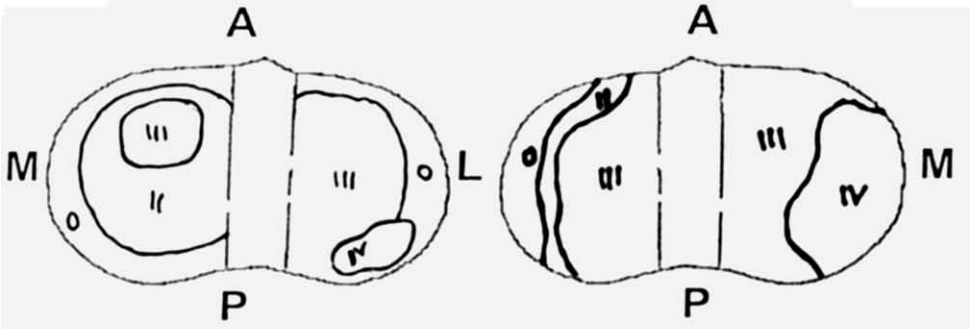
Pre-operative postero-anterior knee radiographs were obtained from all patients undergoing joint replacement surgery and were examined by an observer who was blinded to patient details and histological and macroscopic findings. Radiographs were not available for PM cases. JSN and OST scores were assigned to tibiofemoral joints for each case using a line drawing atlas[25]. A total Radiological OA Severity Score was calculated as the sum of the JSN and OST scores. Possible scores ranged from 0 to 6 and 0 to 12 for JSN and OST scores, respectively, and from 0 to 18 for total Radiological OA Severity Score, with higher scores indicating greater severity.

HISTOLOGICAL GRADING OF SEVERITY OF OA CHANGES IN ARTICULAR CARTILAGE

Samples of medial tibial plateaux and synovium were fixed in neutral-buffered formalin and then wax embedded. A mid-coronal slice across the entire







	Tibial plateaux		Femoral condyles	
Grade[a]	Lateral[b]	Medial	Medial	Lateral
0	15			80
I				
II	15			20
III	70	55	20	
IV		45	80	

	Tibial plateaux		Femoral condyles	
Grade[a]	Medial[b]	Lateral	Lateral	Medial
0	15	20		60
I				35
II	60		50	5
III	25	70	35	
IV		10	15	

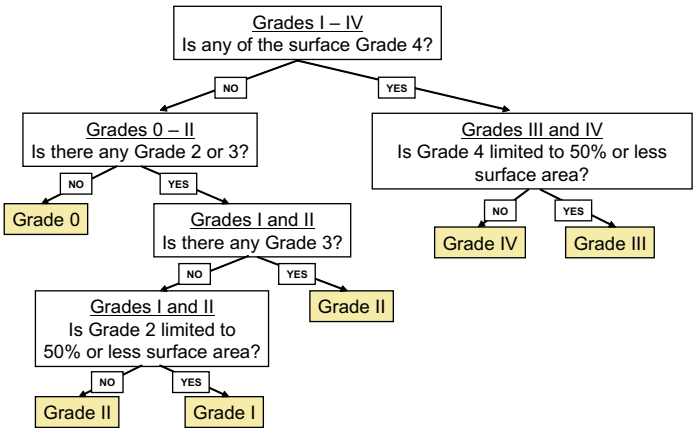


Fig. 2. Classification tree for Collins grading of OA changes at the articular surface. Collins grades (allocated Roman numerals) are based on the presence, extent and severity of OA changes at the articular surface. Severity of changes is allocated Arabic numerals as described for other photographic scoring systems in the text.

breadth of each medial tibial plateau was decalcified in 10% ethylenediaminetetraacetic acid (EDTA) and 10 mM Tris buffer (pH 6.95) at room temperature, then divided into three equal parts prior to wax embedding.

Scores were allocated according to the appearance of the axial (weight-bearing) one third of the mid-coronal slice of each medial tibial plateau. Samples from a total of 99 knees (56 PM) contained the region of interest, and were allocated Mankin's scores. Sections (5 μm) of medial tibial plateau were stained with safranin O[1]. Samples that displayed severe OA changes with no remaining articular cartilage (two knees in each group) were allocated maximum grades of 14.

HISTOLOGICAL GRADING OF SYNOVIAL INFLAMMATION

Samples from 71 knees (41 PM) displayed synovial lining cells and were assessed for Histological Inflammation Grade. Synovium sections (5 μm) were stained with haematoxylin and eosin and graded 0–3 (normal to severe inflammation)[26].

All image analysis was carried out using a Zeiss Axioskop-50 microscope using transmitted light and 10× objective lens (Carl Zeiss Ltd., Welwyn Garden City, UK).

DATA ANALYSIS

The "Outcome Measures in Rheumatology" OMERACT filter was used as a framework for describing the validity of the PCS[27–29]. Statistical analyses used SPSS for Windows (SPSS Inc., Chicago, USA). Internal consistency was determined as Cronbach's alpha. Reliability between observers and between scores based on direct visualisation of pathological samples and on photographs is expressed as limits of agreement[30]. Ninety five percent of differences between two observers are expected to lie within these limits of agreement. Measurement error between repeat estimates of scores is expressed as repeatability coefficients[31]. Discriminatory power was estimated as the number of samples that would be required in order to have 90% power to detect as significant the difference in OA severity observed between TKR and PM groups[32]. Comparisons between groups were made using the Mann–Whitney test and associations were expressed as Spearman's rank correlation coefficients. Associations between the presence or absence of inflammation and structural severity measures (per tertile) were tested for independence on diagnostic group (TKR or PM) by logistic regression analysis, and expressed as odds ratios. Descriptive data are presented as medians with interquartile ranges (IQR). Results were considered of statistical significance at a threshold of $P = 0.05$.

MATERIALS

DePeX mounting medium, Superfrost Plus™ microscope slides, ethanol and xylene were from WVR International Ltd., Poole, UK. Mayer's haematoxylin and eosin were from Raymond A. Lamb Ltd., Eastbourne, UK. Hydrochloric acid and acetic acid were from Fisher Scientific, Loughborough, UK. Haematoxylin, safranin O, ferric chloride, and fast green FCF were from Sigma Aldrich, Poole, UK.

Results

PATIENTS

A total of 116 knees were analysed from 84 patients (29 female). Sex distribution was similar for TKR and PM samples, but patients donating TKR samples were slightly older (median age 69, IQR 60–76 years) than those donating PM samples (median age 64, IQR 60–69 years, $z = 2.0$, $P = 0.05$).

VALIDITY OF THE PCS SYSTEM

Truth

Content validity: comprehensiveness. The PCS and Mankin scores for the medial tibial plateaux in this study were distributed across the whole range of severity (Fig. 3). However, PCS based on the revised SFA system showed a U-shaped distribution [Fig. 3(A)].

Criterion validity: internal consistency and repeatability. Total PCS scores displayed good internal consistency between the four component regions (Cronbach's alpha = 0.89–0.91). Medial tibial plateau PCS scores increased with increasing total PCS scores (r values = 0.91–0.94, $P < 0.001$).

PCS scores displayed good repeatability between measurements by the same observer using the same

Fig. 1. Severity of chondropathy at the articular surface determined macroscopically on pathological samples of tibiofemoral joints. Femoral condyles and tibial plateaux from PM (images on left) and TKR (images on right) cases. From top to bottom showing digital photographs of femoral condyles and tibial plateaux, schematic diagrams showing the extent of each grade of surface appearance, and tables of the estimated percentage of joint surface attributed to each grade. Scoring sheet reproduced with permission from Dougados *et al.*[6], Copyright Elsevier and the Arthroscopy Association of North America.

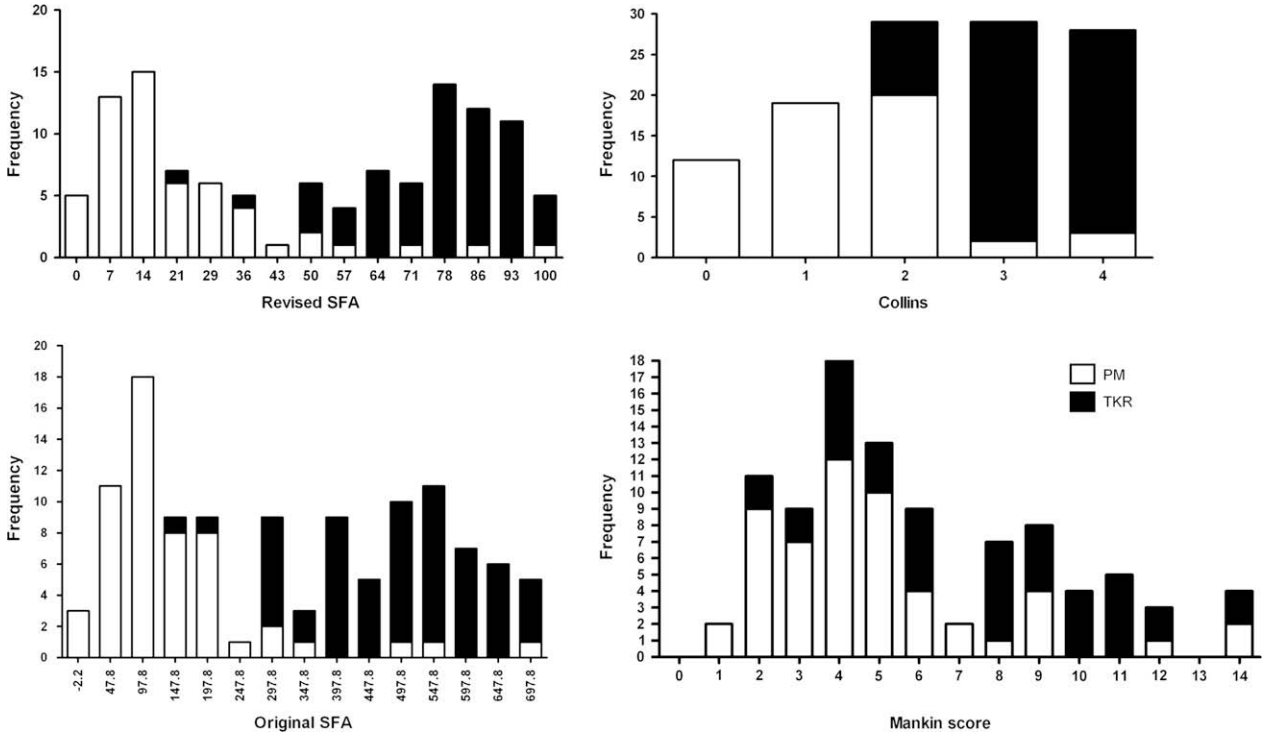


Fig. 3. PCS and Mankin score distributions are heterogeneous. Histograms showing distributions of PCS and Mankin scores for the medial tibial plateux. Radiography was not available for PM cases. Samples showed chondropathy scores throughout the whole range of the grades (B–D). The revised SFA system (A) revealed a U-shaped distribution, with fewer cases with intermediate grades of chondropathy, which was less apparent with other grading systems. Mankin scores indicated a skewed distribution, with apparently more cases displaying less severe chondropathy.

Table I
Characteristics of PCSs

	Medial tibial plateau			Total		
	Original SFA	Revised SFA	Collins	Original SFA	Revised SFA	Collins
Possible range	−2.2 to 717.8	0−100	0−4	9.2 to +2650.8	0−400	0−16
Cronbach's alpha	NA	NA	NA	0.91	0.91	0.89
Intra-observer repeatability						
Overall	210	41	1.5	958	149	5.2
Area estimate	45	6.2	0	112	18	1.1
Inter-observer agreement						
95% limits of agreement	−189 to +423	−27 to +65	−1.4 to +3.2	−387 to +1107	−57 to +159	−2.7 to +8.0
Difference	117*** (86−148)	19*** (14−23)	0.9*** (0.7−1.1)	358*** (282−434)	51*** (41−62)	2.6*** (2.1−3.2)
Agreement between direct and photographic scores						
95% limits of agreement	−113 to +134	−13 to +17	−0.9 to +1.1	−354 to +374	−45.6 to +48.0	−3.1 to +2.7
Difference	+11 (−4 to +25)	+1.7 (−0.02 to +3.4)	+0.1 (−0.1 to +0.2)	+10 (−32 to +52)	+1.2 (−4.1 to +6.6)	-0.2 (−0.5 to +0.2)
Associations with other OA structural severity scores						
Mankin	0.53***	0.54***	0.53***	0.54***	0.55***	0.54***
Total radiographic	0.43***	0.42***	0.48***	0.43***	0.42***	0.40***
OSTs	0.38**	0.37**	0.44***	0.41***	0.41***	0.37**
JSN	0.39**	0.37**	0.36**	0.29*	0.28**	0.32*

Differences between observers and between direct and photographic scores are given as means (95% confidence interval [CI]). Associations are expressed as Spearman's rank correlation coefficients. ***$P \leq 0.001$, **$P \leq 0.01$, *$P < 0.05$.

photographs (Table I). Scoring of articular surface diagrams by the same observer was highly repeatable (Table I). PCS scores displayed good agreement between the two observers (Table I). EH allocated higher grades than did RH (all $P < 0.001$).

Criterion validity: association with other measures of OA severity. Good agreement was found for scoring chondropathy, with no significant differences between direct assessment of the fresh pathological sample and assessment of standardised photographs by the same observer (Table I).

In the absence of a 'gold standard' measure of OA severity, the PCS methods were evaluated by comparison with established histological and Radiographic OA Severity Scores. High Mankin scores were associated with high total Radiographic OA Severity Scores in TKR cases ($r = 0.48$, $P = 0.002$). OST and JSN scores were associated with each other ($r = 0.43$, $P < 0.001$), and associations between total Radiographic OA Severity Scores and Mankin scores could be attributed to positive associations of Mankin scores with OST score ($r = 0.43$, $P = 0.005$) or JSN score ($r = 0.34$, $P = 0.03$).

PCS increased with increasing Mankin score, and (in TKR cases) with total Radiographic OA Severity Score (Table I). This association could be attributed to positive associations with JSN score or OST score.

Discrimination

TKR samples displayed more severe chondropathy than did PM samples. PCS scores and Mankin scores were each higher for TKR samples than for PM samples (Table II). In order to have 90% power to detect as significant the difference in chondropathy between TKR and PM groups, <6 samples would be required using the PCS systems, or 27 samples using the Mankin score. The PCS system performed similarly in TKR or PM groups alone (Table III).

OA SEVERITY AND HISTOLOGICAL SYNOVITIS

Higher medial tibial plateau and total PCS scores were associated with histological synovial inflammation (Table II). Association between Mankin score and histological synovial inflammation did not reach statistical significance ($r = 0.19$, $P = 0.14$). In univariate analyses, synovial inflammation grade was greater in TKR (median 0, IQR 0−1) than in PM samples (median 0, IQR 0−0, $z = 2.8$, $P = 0.006$), and was not significantly associated with age or sex. Logistic regression analysis revealed that associations of PCS scores with the presence or absence of inflammation were independent of diagnostic group (Table II).

For TKR cases, Radiographic JSN Score was associated with inflammation grade ($r = 0.47$, $P = 0.01$). However, significant associations were not found between inflammation grade and total Radiographic OA Severity Score ($r = 0.04$, $P = 0.83$) or OST score ($r = -0.09$, $P = 0.65$).

Discussion

We have developed scoring systems for measuring the severity of OA change in the tibiofemoral joint based on photographs of pathological samples. PCS permits measurement of structural severity for each articular surface, or in the tibiofemoral joint as a whole, comparable with methods developed in arthroscopy, and is applicable to pathological samples. The PCS system may usefully complement arthroscopic studies by permitting comparable assessment of pathological samples. PCSs displayed good validity according to a range of criteria described in the OMERACT filter. It was more sensitive than the histological and radiographic scoring methods used in this study for detecting associations between OA structural change and histological synovitis, and more sensitive than the histological scoring method in distinguishing between samples from patients undergoing joint replacement surgery and PM cases.

Table II
Associations of severity scores with disease group and histological synovitis

	Medial tibial plateau PCS			Total PCS			Histologic	Radiographic		
	Original SFA	Revised SFA	Collins	Original SFA	Revised SFA	Collins	Mankin	Total	OST	JSN
TKR median (IQR)	490 (400–599)	79 (67–89)	3 (3–4)	1738 (1507–1937)	257 (228–283)	11 (10–12)	8 (5–10)	15 (13–16)	10 (8–11)	5 (5–6)
PM median (IQR)	108 (69–176)	17 (9–28)	1 (1–2)	280 (124–594)	44 (18–87)	4 (1–6)	4 (3–6)	NA	NA	NA
z for difference	8.4***	8.5***	8.0***	8.6***	8.7***	8.7***	4.1***	NA	NA	NA
Required sample	4	3	5	2	2	3	27	NA	NA	NA
Association with synovitis (r)	0.48***	0.47***	0.44***	0.45***	0.43***	0.44***	0.19	0.04	−0.09	0.47*
Odds ratio of synovitis per tertile increase in severity score (95% CI)†	3.4* (1.2–9.4)	3.7* (1.3–11)	3.6* (1.2–11)	3.2* (1.0–11)	2.7 (0.8–9.0)	4.7* (1.4–16)	1.4 (0.6–3.0)	0.9 (0.4–2.2)	0.8 (0.3–2.0)	4.9 (0.9–27)

Required sample: estimated sample per group required for 90% power to detect observed difference at $P < 0.05$. Associations are given as Spearman's rank correlation coefficients.
***$P \leq 0.001$, **$P \leq 0.01$, *$P < 0.05$.
†Logistic regression analyses for PCSs and Mankin scores included diagnostic group.

VALIDATION OF THE PCS

Truth

Face validity. The PCS systems display good face validity. Chondropathy is a central pathological process in OA, and loss of articular cartilage leads to exposure of sensory nerves within subchondral bone. More extensive chondropathy is likely to indicate greater severity than are focal changes. The PCS systems directly address both extent and severity of chondropathy, whereas the Mankin system focuses only on a small sample of tissue.

Content validity. PCS systems displayed good content validity. Pathological samples from PM and TKR sources represented a wide range of chondropathy and PCS systems were applicable to both mild and severe OA. However, PCS scores based on the revised SFA system revealed a relative paucity of cases with moderate OA severity that was not apparent when using other methods. Furthermore, Mankin scores displayed a skewed distribution, reflecting their focus on remaining articular cartilage, irrespective of the extent to which subchondral bone is exposed.

Criterion validity. As in studies of arthroscopic assessment of articular cartilage change, we found important variation between observers in PCS[8,33]. Indeed, inter-observer differences appeared to be a more important source of variation than were different scoring algorithms or formulae. The use of digital photographs permits all samples in a study to be scored by the same observer, thereby avoiding inter-observer variation. Using photographs did not adversely affect the performance of the scoring system compared with direct visualisation and probing of the pathological sample. Direct probing has similarly been found to add little to arthroscopic scoring methods of chondropathy compared with video assessment[34].

We found that higher PCS scores were associated with more severe radiological change. Similarly, greater chondropathy determined by arthroscopy has been associated with greater radiographic JSN, particularly in the medial tibiofemoral compartment[8,12]. However, articular surface appearance explained only a small part of the radiological severity scores. JSN on weight-bearing tibiofemoral radiographs may be an indication of meniscal rather than articular cartilage pathology[11,35,36]. Distraction of the lateral tibiofemoral compartment on weight bearing may also contribute to radiographic joint space width. A strong association has been demonstrated between arthroscopic scoring and changes detected by magnetic resonance imaging in the articular cartilage[15]. Weaker associations between scores based on direct visualisation and on plain radiographs indicate that some components of the radiographic scoring system are not directly dependent on articular cartilage change.

Our data further support the view that articular surface appearance partially reflects pathological change within the articular cartilage as determined histologically[3,4]. We also found associations between radiological severity scores and histological evidence of OA change in the articular cartilage. Previous studies have revealed inconsistent associations between radiological and histological OA severity, although these results may have been influenced by small sample sizes and different methods for radiological assessment[37,38]. Radiologically unaffected joint compartments may display histological evidence of OA, and this

Table III
Comparability between TKR and PM cases in the strength of associations between PCS and other severity scores or inflammation grade

	PCS					Histologic Mankin	Synovitis
	Medial tibial plateau		Total				
	Original SFA	Collins	Revised SFA	Original SFA	Collins		
TKR	0.99**	0.88**	0.70**	0.74**	0.68**	0.35*	0.35
PM	0.99**	0.86**	0.89**	0.88**	0.77**	0.31*	0.33*

Data are *r* values for associations with the medial tibial plateau revised SFA PCS system. Similarity of *r* values between PM and TKR subgroups indicates validity across a range of OA severity. $^{**}P < 0.01$ and $^{*}P < 0.05$.

may be particularly the case for the lateral tibiofemoral compartment[37,38].

Discrimination

PCS systems displayed good discriminant validity. PCS scores using the revised SFA formula displayed similar characteristics to those using the original formulae, but the Collins grading method displayed slightly lower power than SFA methods. Concomitantly, the PCS had a greater ability than other methods to detect associations between chondropathy and synovial inflammation.

Sensitivity to change was not addressed in this cross-sectional study, although data from arthroscopic application of the SFA systems indicate greater sensitivity to change than found in radiographic studies[12].

Feasibility

Photographic recording of articular surfaces permits use of the PCS system in a research setting, with standardised analysis by a single observer, and contemporaneous validation by a second observer, irrespective of the length of the period (often years) over which samples have been collected.

PCS and histological methods have some limitations due to the nature of pathological samples. Patellofemoral OA is a common source of pain and disability, although patellae are not routinely available for pathological examination after joint replacement surgery. Furthermore, the trochlea is commonly damaged or absent from surgical samples, precluding routine scoring of the patellofemoral joint. Radiological and arthroscopic studies may be preferable for determining associations between patellofemoral OA and histological synovitis.

PCS AND OA SEVERITY MEASURES AS RESEARCH TOOLS

The selection of PCS scoring method for a study may depend on factors other than its measurement characteristics; factors such as availability of tissue and need for comparability with arthroscopic studies. Radiographic, macroscopic and histological scoring systems reflect different, but related aspects of the OA process. Radiographic assessment of osteophytosis provides additional information on structural change. Direct visualisation of the articular surface provides a more precise assessment of the extent and severity of cartilage surface change. Histology can provide insights into chemical and cellular changes. The associations between each method, however, indicate that they all assess overlapping aspects of OA structural severity. In the absence of a gold standard for measuring OA structural severity, we recommend where possible using a variety of methods in any single study.

CLINICAL RELEVANCE OF OA STRUCTURAL SEVERITY

Severity of chondropathy determined at arthroscopy using the SFA system has been associated with the extent of disability in OA, and to a lesser extent with pain[8]. A contribution of structural change to pain is further supported by evidence that radiologically determined disease severity makes a significant, if limited, contribution to reported pain and disability[39–42].

Chondropathy as measured in this study is not sufficient to explain pain in OA. As in previous studies, we found that OA changes were prevalent in PM samples[3,4]. This may represent early or subclinical OA, as it is likely that the pathological process of OA precedes clinical symptoms. However, it remains unclear as to which features are specifically associated with disease rather than, for example, normal aging.

OA STRUCTURAL SEVERITY AND SYNOVITIS

Synovitis is a histological feature of OA. We have found that the severity of inflammation increases with increasing structural change at the articular surface, independent of patient group (TKR or PM). Histological synovitis appeared to be specifically associated with radiological JSN. This may indicate that the association between OA severity and synovitis is attributable to cartilage pathology.

Subclinical synovitis is found in early or mild disease[18,43], and clinical synovitis has been associated with radiological progression in human OA[21]. Furthermore, inflammation in adjacent synovium predicted progression of arthroscopically determined chondropathy in patients with OA[22]. These findings suggest that synovitis may be a cause, rather than merely a consequence of structural change. However, it is also possible that chondropathy facilitates synovial inflammation. Interventional studies will be required to determine the mechanism of the association between synovitis and the extent of chondropathy, by exploring the effects of inhibiting synovitis on structural disease progression.

Conflict of interest

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