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Review

Osteoarthritis year 2013 in review: imaging

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SUMMARY

Purpose: To review recent original research publications related to imaging of osteoarthritis (OA) and identify emerging trends and significant advances.
Methods: Relevant articles were identified through a search of the PubMed database using the query terms "OA" in combination with "imaging", "radiography", "MRI", "ultrasound", "computed tomography", and "nuclear medicine"; either published or in press between March 2012 and March 2013. Abstracts were reviewed to exclude review articles, case reports, and studies not focused on imaging using routine clinical imaging measures.
Results: Initial query yielded 932 references, which were reduced to 328 citations following the initial review. MRI (118 references) and radiography (129 refs) remain the primary imaging modalities in OA studies, with fewer reports using computed tomography (CT) (35 refs) and ultrasound (23 refs). MRI parametric mapping techniques remain an active research area (33 refs) with growth in T2*- and T1-rho mapping publications compared to prior years. Although the knee is the major joint studied (210 refs) there is interest in the hip (106 refs) and hand (29 refs). Imaging continues to focus on evaluation of cartilage (173 refs) and bone (119 refs).
Conclusion: Imaging plays a major role in OA research with publications continuing along traditional lines of investigation. Translational and clinical research application of compositional MRI techniques is becoming more common driven in part by the availability of T2 mapping data from the Osteoarthritis Initiative (OAI). New imaging techniques continue to be developed with a goal of identifying methods with greater specificity and responsiveness to changes in the joint, and novel functional neuroimaging techniques to study central pain. Publications related to imaging of OA continue to be heavily focused on quantitative and semiquantitative MRI evaluation of the knee with increasing application of compositional MRI techniques in the hip.

Research in osteoarthritis (OA) relies heavily on data obtained from imaging, ranging from development of quantitative imaging techniques for non-invasive measurement of cartilage compositional changes, to biomechanical investigations, to large population studies such as the Osteoarthritis Initiative (OAI) that yield new insight into the pathogenesis of OA. In this review we will discuss articles published between March 2012 and March 2013; highlighting new avenues of research in imaging techniques and applications that are likely to be of interest to the diverse readership of *Osteoarthritis and Cartilage*. The review will begin with a discussion of quantitative techniques for evaluation of articular cartilage and meniscus, followed by review of cartilage morphometry and semiquantitative scoring systems for evaluation of OA, and will end with discussion of clinical publications where the focus was imaging methodology or novel application.

Quantitative imaging of OA

Quantitative compositional imaging techniques of cartilage and meniscus

In part stimulated by data on cartilage T2 mapping from the OAI, compositional magnetic resonance imaging (MRI) techniques are now frequently applied in clinical research as early markers of degeneration preceding visible damage to cartilage, or more recently meniscus. Basic research continues to produce incremental improvement of existing techniques as well as novel methods for evaluating connective tissues with greater responsiveness and specificity to mechanism of tissue degeneration. A brief synopsis of new developments in compositional imaging techniques is provided in Table I.

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Table I
Synopsis of new developments in compositional imaging techniques

Technique	Application	New development
Cartilage T2	Evaluation of cartilage collagen	Use of texture analysis to measure change in spatial distribution of T2 Demonstration of longitudinal responsiveness to change Adjunct to routine clinical MRI with improved sensitivity for detection of early cartilage damage Concerns over systematic bias in T2 values between different MRI vendors
Cartilage T2*	Evaluation of cartilage collagen	Good reproducibility Early demonstration of feasibility in evaluation of the hip
dGEMRIC	Evaluation of cartilage glycosaminoglycan	New acquisition techniques for faster measurement of T1 Concerns over specificity for [gag] changes Clinical studies using dGEMRIC to guide operative management in the hip
Contrast enhanced CT	Evaluation of cartilage glycosaminoglycan	Development of novel CT contrast agents Feasibility studies in small rodent models of OA
T1rho	Evaluation of cartilage glycosaminoglycan	Predictive of progressive cartilage loss Concerns over specificity of for [gag] changes
	Evaluation of the meniscus	Pilot data demonstrating T1rho elevation in degenerated meniscus Appears to be primarily sensitive to changes in meniscus water content
Sodium MRI	Evalulation of cartilage glycosaminoglycan	Development of new acquisition techniques to suppress signal from synovial fluid Concerns over reproducibility
gagCEST	Evaluation of cartilage glycosaminoglycan	Improved acquisition techniques Preliminary validation data in the intervertebral disc and cartilage repair tissue
Diffusion	Evaluation of cartilage water mobility	New techniques for calculating apparent diffusion coefficient and T2 Validation of diffusion tensor imaging as a marker of collagen anisotropy
Ultra-short TE	Evaluation of the osteochondral junction	New acquisition technique to isolate signal from the zone of calcified cartilage

Cartilage T2 mapping

Cartilage T2 mapping has become commercially available on clinical scanners and is becoming a standard technique in clinical research primarily evaluating knee articular cartilage. In clinical practice, the addition of a sagittal T2 mapping sequence improved sensitivity for detection of early cartilage injury while providing slightly lower specificity compared to surgical evaluation of cartilage[1]. Historically these techniques measure bulk or regional T2 values of cartilage. Although early degeneration will increase T2 there is recognition that this response is non-linear and that frequently more advanced degeneration produces a heterogenousspatial distribution of T2 without further change in the bulk T2 properties of cartilage. Using quantitative texture analysis Joseph *et al.* identified more heterogeneous T2 values in OAI subjects at risk for OA compared to healthy controls (Fig. 1)[2,3]. Measuring T2 heterogeneity rather than absolute T2 time makes the analysis less susceptible to systematic bias when comparing measurements obtained using different techniques or instrumentation. Although T2 reproducibility is good for multi-center studies such as the OAI using identical instrumentation and tight quality control[4], systematic bias of 5 ms–10 ms has been reported between vendors[5] which is larger than the change in T2 generally observed with OA.

More recently T2* mapping, which uses a 3D gradient echo acquisition, has been developed to provide higher spatial resolution and obtain signal from the short T2 signal present in cartilage near the osteochondral junction. In contrast to T2 which increases with early cartilage degeneration, T2* values decrease. Although T2* reproducibility of knee cartilage is good[6], it will likely have greater application in the hip where volume averaging and low spatial resolution limits T2 mapping. A recent validation study with femoral head cartilage specimens found a statistically significant decrease in T2* values with higher Mankin scores[7]. As with cartilage T2 values[8], cartilage T2* values are sensitive to joint loading[9] indicating factors impacting joint loading prior to the MRI exam must be considered when developing protocols.

Recent reports from the incident cohort of the OAI support the use of cartilage T2 as an early marker of cartilage degeneration, demonstrating responsiveness to cartilage change over time[10,11]

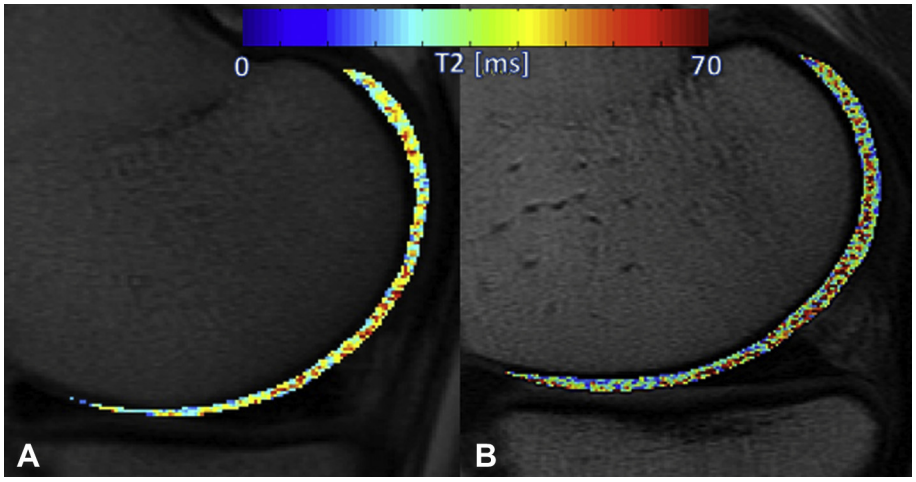

Fig. 1. Cartilage T2 Texture Map: (Image courtesy of Gabrielle Joseph, University of California, San Francisco) Representative cartilage T2 maps from the OAI overlaid on the image obtained from the first echo of the multi-slice multi-echo sequence. While both subjects have a K–L grade of 0, the mean and spatial distribution of the cartilage T2 values differs. Subject B (right) has elevated mean T2 values as well as greater T2 heterogeneity as indicated by elevated gray level co-occurrence matrix (GLCM) texture parameters. Both subjects have a WORMS score of 0 (normal) in the medial femur, however, subject B developed a focal cartilage defect (WORMS = 2) at 4-year follow-up.

and an association of T2 elevation with pain[12]. Elevated cartilage T2 has been reported for post-traumatic knee OA 7–11 years following anterior cruciate ligament (ACL) tears[13] as well as 6 months after ACL reconstruction when there is no difference in cartilage volume or thickness[14]. With the onset of OA there is no difference in cartilage T2 between subjects with or without ACL pathology[15].

Exogenous contrast based techniques for evaluation of cartilage

The delayed Gadolinium enhanced MRI of Cartilage (dGEMRIC) technique is frequently used for evaluating cartilage glycosaminoglycan content [gag]; particularly in evaluation of the hip, with exploratory studies on inflammatory arthritis in the hand[16,17] and glenohumeral joint[18]. More recently techniques have been developed with computed tomography (CT) using novel iodinated contrast agents and micro CT to study [gag] changes of articular cartilage in small rodent models of OA and human hip cartilage[19–21].

Several studies evaluated technical factors related to the use of dGEMRIC in clinical research. A novel reconstruction algorithm has been proposed to improve reliability and reduce the amount of data needed to measure T1[22]. Co-registering images prior to calculating T1 has also been shown to reduce error[23]. The 3D variable flip angle sequence for quantitative T1 mapping provides rapid 3D coverage; which is advantageous in that all data points are acquired during a single acquisition, reducing error from patient motion and requiring shorter imaging times. A drawback of this technique is that it is very sensitive to variation in the transmitted B1 field particularly at 3 T where B1 variation is higher[24]. Since native cartilage T1 is not uniform some investigators have recommended acquiring baseline T1 values prior to injecting contrast to calculate difference in T1 relaxation ($\Delta R1$) for estimating [gag]. Recent studies in the hip[25], osteochondral allografts[26], and metacarpophalangeal (MCP) joints of patients with rheumatoid arthritis[17] suggest the calculation of $\Delta R1$ does not increase the diagnostic value of dGEMRIC.

Recent studies questioned the specificity of dGEMRIC as a marker of [gag] in early OA. It has been shown that Gd-DTPA$^{(-2)}$ equilibration into cartilage is slower than originally assumed and is dependent on factors other than [gag] such as collagen content and diffusion anisotropy of the matrix[27]. While this may lead to an overestimation of [gag], particularly in the deeper layers of cartilage, results from this study still indicate dGEMRIC is a sensitive marker for superficial cartilage degradation even at the relatively short equilibration times used in clinical studies. A separate ex vivo study found that changes in dGEMRIC T1 relaxation correlated with [gag]; however, no difference in either parameter was detectable between OA and reference cartilage[28]. These authors suggest that other factors such as alteration in diffusion or increased supply of contrast agent in the diseased joint may be important factors contributing to the dGEMRIC measurement *in vivo*.

The use of dGEMRIC for selecting patients for operative treatment of developmental dysplasia of the hip (DDH) or femoral acetabular impingement (FAI) is an active area of investigation[29,30]. In patients undergoing surgical treatment of DDH a low dGEMRIC index, indicative of low [gag] was a better predictor of premature failure than radiographic measures[31]. In DDH the dGEMRIC indices tend to be more diffusely low. This is in contrast to FAI where cartilage adjacent to sites of focal cartilage damage tend to be normal[29,32], suggesting a more diffuse pattern of cartilage injury. In the knee dGEMRIC has been used to monitor changes following high tibial osteotomy[33], patellar cartilage in patients treated with total knee arthroplasty without patellar resurfacing[34], and in a longitudinal study on the effect of weight loss[35].

T1 relaxation in the rotating frame (T1rho)

Recent validation studies obtained with OA and RA tissue samples[36,37] confirm previous results that T1rho is inversely correlated with cartilage [gag]; however specificity of T1rho for [gag] has been questioned. In a study of patients with acute ACL injuries there was a high spatial correlation of T1rho and T2 suggesting they are measuring related processes[38]. Cartilage T1rho values increase with age[39], early OA[8], in cartilage of compartments with focal cartilage lesions[40], and has been shown to be predictive of progressive cartilage loss at 2-year follow-up[41]. In patients with prior ACL reconstruction elevated T1rho is observed in subjects with residual anterior tibial translation compared to those with normal kinematics[42]. It is unclear if T1rho or T2 is superior in diagnosing early cartilage damage with studies demonstrating equivalent results[43] and others demonstrating superiority of T1rho[44].

A pilot study suggests T1rho is sensitive to early cartilage damage in the hip associated with FAI[45]. In the lumbar intervertebral disc a significant drop in T1rho is observed between Pfirmann grade II and III degeneration[46]. Although most studies use T1rho in analysis of knee articular cartilage, preliminary investigations report elevation of the T1rho of the meniscus in OA patients[47] and patients undergoing treatment for cartilage repair[48] suggesting it may serve as an early marker of meniscal degeneration. Interpretation of T1rho as a measure of compositional change in meniscal tissue remains uncertain. In a validation study of specimens obtained from knee arthroplasty patients both T1rho and T2 correlated strongly with water content, moderately with mechanical properties of the osteoarthritic meniscus, but weakly with regional differences in [gag] or collagen content[49] suggesting it may have limited utility as a compositional biomarker in the meniscus.

Other compositional techniques

Although sodium MRI of cartilage has been studied for over a decade it has not been widely applied due to the need for multinuclear capable high-field instrumentation, and the very short T2 times of sodium, which require advanced signal acquisition techniques, making quantitative analysis challenging[50]. In addition, the relatively low *in vivo* sodium concentration and weak MRI signal requires long acquisition times to generate an image; however, this can be reduced by a factor of 2 using compressed sensing techniques[51]. The dissemination of 3.0 T and more recently 7.0 T MRI units with continued improvement of multichannel dual tuned proton/sodium coil technology[52] has made it possible to reliably use this technology for human studies. Although good reproducibility has been reported at 3.0 T[53], it is substantially lower when measured on different days at 3.0 T and 7.0 T[54]. High sodium concentration in synovial fluid can make it difficult to detect changes in cartilage near the articular surface; however, as illustrated in Fig. 2 newer inversion recovery techniques can effectively suppress signal from synovial fluid[55] allowing characterization of OA cartilage with high accuracy[56].

Chemical Exchange Saturation Transfer MRI of glycosaminoglycans (gagCEST) is a relatively new proton based technique with potential to provide a more specific assessment of [gag]. Recent modifications improve efficiency of gagCEST and correct for inhomogeneity in the magnetic field, which can be a source of error[57]. Evaluation of [gag] in the nucleus pulposus of the lumbar disc has been studied using gagCEST[58,59] and in cartilage repair tissue following autologous osteochondral transplantation[60].

Several proof of concept studies were published on cartilage diffusion techniques. Recently a modification of the Dual Echo Steady State (DESS) sequence has been described that provides simultaneous 3D acquisition of T2 and apparent diffusion coefficient (ADC) maps[61]. The ability to simultaneously obtain multiparametric data from cartilage has potential to improve diagnosis of cartilage damage by combining features with high

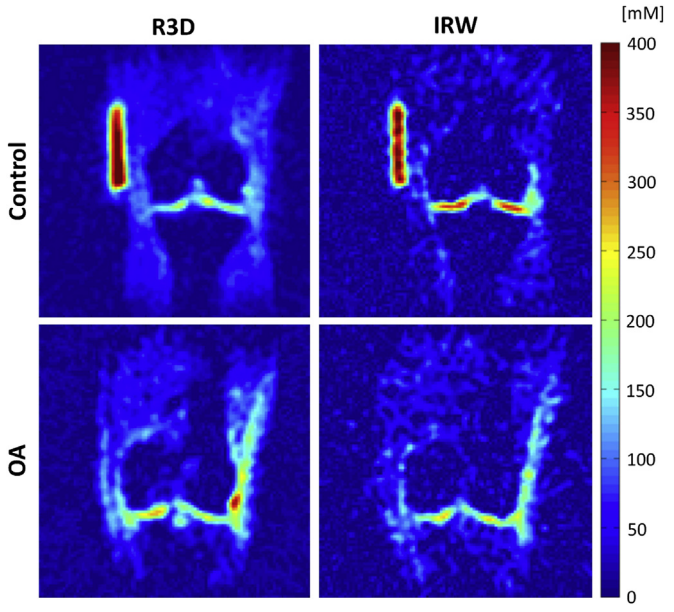

Fig. 2. Improved evaluation of articular cartilage signal with 23Na MRI (Image courtesy of Guillaume Madelin, Ravinder Regatte and Gregory Chang, New York University) Representative sodium maps from a control subject and patient with OA. Maps were reconstructed from data acquired with fluid suppression (inversion recovery [IR] wideband uniform rate and smooth truncation [WURST] [IRW] sequence) and without fluid suppression (radial 3D [R3D] sequence). Suppression of signal from synovial fluid with IR-WURST (IRW images) differentiates sodium signal in cartilage between OA subject and control not apparent without fluid suppression (R3D image). Reproduced from reference[56].

discrimination[62]. Diffusion tensor imaging (DTI) can measure fractional anisotropy of the cartilage collagen matrix with moderate reproducibility at 7.0 T[63]. A recent study in human cartilage specimens demonstrated higher transverse and longitudinal diffusivity in the superficial region of all samples with OARSI grades greater than 0 and significantly decreased fractional anisotropy in the deeper layers compatible with a loss of collagen anisotropy during early degeneration[64].

Ultra-short TE (UTE) MR imaging captures signal from protons with T2 decay too rapid to detect with normal acquisition techniques. Two recent papers demonstrated feasibility of UTE MRI to visualize the calcified cartilage layer, which is normally void of signal on conventional MRI[65,66]. Du *et al.* developed a dual inversion recovery (DIR) UTE technique with suppression of both water and fat which provides high contrast delineation of the zone of calcified cartilage (Fig. 3) and quantitative assessment of T2*, T1 and T1rho[65]. This has potential to provide novel information on early changes of OA at the osteochondral junction. Quantitative T2*-UTE has been recently applied for characterization of sub-clinical meniscal injury associated with acute ACL tear[67], and meniscal calcifications[68].

Quantitative cartilage morphometry

Using cartilage morphometry of OAI data, early cartilage thinning in the medial tibiofemoral compartment, particularly on the tibia was predictive of future knee replacement[69]. Although at the individual knee level 1 year changes in cartilage thickness are not a reliable proxy of long-term change, at the cohort and subcohort level tibiofemoral cartilage loss increased linearly over a 4-year period[70]. Rapid cartilage thinning has been reported to be more common in knees with KL grade >2 and frequent pain, most commonly in the central and external subregions of the medial weight-bearing femur[71]. Interestingly in knees with early radiographic OA, thicker cartilage is frequently observed in the external femoral subregions of compartments with marginal osteophytes and no joint space narrowing[72].

Semiquantitative imaging assessment of OA

MRI-based scoring methodology

Standardized semiquantitative MRI scoring methods are commonly used to assess disease burden and monitor disease progression[73] for study of the natural history of OA, to correlate clinical symptoms to pathological features of OA, and to identify risk factors for structural changes. Compared to quantitative measurements a limitation of semiquantitative scoring such as the Whole Organ MRI Score (WORMS) system is lower sensitivity to change over time[74], but this can be overcome with a modified scoring technique termed “within-grade” scoring of longitudinal changes. In this scoring method, which can be applied to any semiquantitative scoring systems (e.g., WORMS, MOAKS) available in the literature, readers record changes that do not fulfill the criteria for the original integer grading scale[75]. For example, if a

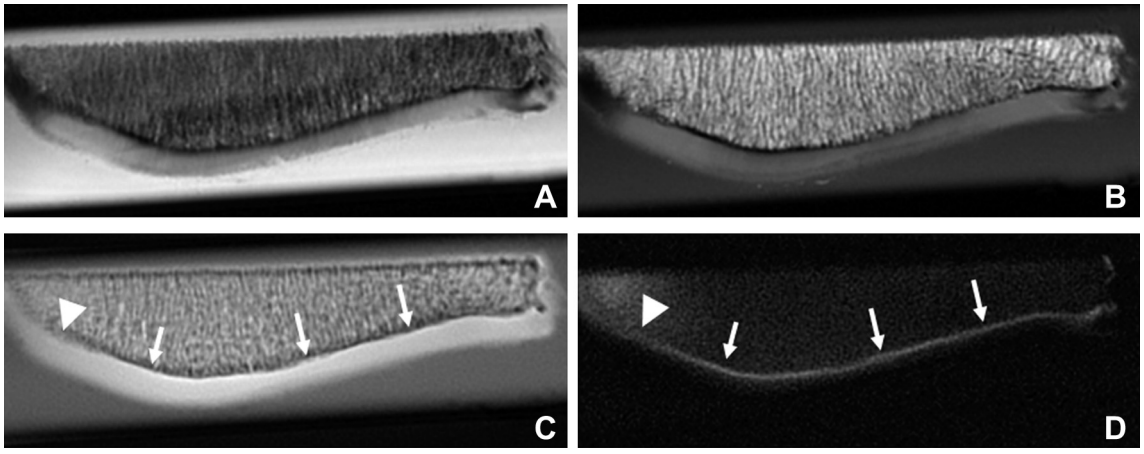

Fig. 3. Imaging the zone of calcified cartilage (ZCC) (Image Courtesy of Jiang Du and Christine Chung, University of California, San Diego). Images of an osteochondral patella specimen were obtained using (A) proton density-fast spin echo (PD-FSE), (B) T1-FSE, (C) Conventional UTE, and (D) Dual Inversion Recovery (DIR)-UTE sequences. Suppression of signal from marrow fat and the long T2 component of cartilage water provides high contrast of the short TE signal from the ZCC region of cartilage on the DIR-UTE image (arrow). An area of morphologic cartilage degradation in the lateral patellar facet (arrowhead) demonstrates reduced signal and an increase in thickness of signal from the ZCC layer. Reproduced from reference[65].

grade 1 BML has clearly increased in size at follow-up imaging but is still classified as grade 1 by a scoring system (e.g., WORMS), then the reader assigns a grade of 1.5 to this lesion to indicates the fact that the lesion has increased in size.

Choice of MR pulse sequences

Semiquantitative assessment of knee OA can be reliably performed using 3D turbo spin-echo (TSE) MRI with substantial to almost perfect agreement and high accuracy when compared to conventional 2D TSE MRI[76]. The 3D acquisition provides a single image data set that can be reconstructed into any plane and may be a useful option in future large-scale OA studies. However due to lower in-plane resolution and image blurring due to modulation of the point spread function by differences in tissue T2, 3D TSE reconstruction images have lower image quality compared to 2D images.

MRI of synovitis

Non-contrast-enhanced MRI (NCEMRI) can monitor synovitis using T2 hyperintensity within the infrapatellar fat pad as a surrogate marker. Using NCEMRI and Boston-Leeds Knee OA Score (BLOKS), Knoop and colleagues showed quadriceps weakness was associated with the presence of synovitis in knee OA patients[77]. More recent studies indicate contrast-enhanced MRI (CEMRI) is more specific for synovitis compared to NCEMRI and is better correlated with pain[78]. Using semiquantitative scoring of CEMRI as the reference for synovitis, NCEMRI has a sensitivity of 0.71–0.88 but has relatively low specificity (0.30–0.55)[78]. Location of synovitis appears to be an important part of the assessment. Meniscal damage of the posterior horns is associated with adjacent perimeniscal synovitis (adjusted odds ratio 2.5, 95% CI 1.3–4.8) but not with synovitis of the posterior cruciate recess, suggesting synovitis at these two locations has different pathomechanisms[79]. Baker and colleagues demonstrated a positive association between plasma mediators of inflammation and CEMRI-assessed synovitis[80].

MRI of cartilage

Using the WORMS score Laberge and colleagues showed obesity increases the prevalence and worsening severity of cartilage damage over 36 months[81]. Crema and colleagues showed prevalent cartilage damage (i.e., WORMS score $\geq$2) and cartilage loss over time are associated with incident bone marrow lesions in the same tibiofemoral compartments, supporting the significance of the close interrelation of the osteochondral unit in the progression of knee OA[82]. Several recent studies provide evidence that focal cartilage lesions increase risk of OA. Roemer and colleagues demonstrated the presence of non-cartilaginous pathology, as well as prevalent cartilage damage at baseline, increase the risk of subsequent cartilage loss in the same subregion[69]. A recent population-based study indicates cartilage defects in older adults are common and the majority of defects remained stable over 2.9 years; however, baseline cartilage defect grade predicted risk of knee replacement surgery over 5 years[70].

MRI of meniscus

Studies have shown meniscal pathologies are linked to the knee OA disease process[83]. Using WORMS scoring, Crema and colleagues demonstrated an association of medial meniscal extrusion with medial meniscal tears, medial cartilage damage, and varus alignment, while lateral meniscal extrusion was associated with lateral meniscal tears, lateral cartilage damage and valgus alignment[84].

Radiography-based semiquantitative scoring of knee OA

Radiography-based semiquantitative scoring of knee OA features can be done using Osteoarthritis Research Society International (OARSI) atlas or the Kellgren and Lawrence (K–L) grading system. A potential advantage to using the OARSI atlas is the ability to independently grade features of OA that may be lost when different features are pooled into a single grade. Javaid and colleagues showed unilateral knee pain was associated with radiographic joint space narrowing (grade $\geq$1) in the elderly with or at high risk of knee OA, based on the data from the Health ABC Study[85]. Several studies demonstrated substantial joint damage in individuals with little radiographic evidence of OA. Using data from the Framingham OA study, Guermazi and colleagues demonstrated a high prevalence of MRI-detected features of OA, such as cartilage damage, bone marrow lesions, osteophytes and synovitis in subjects without radiographic OA[86]. In a recent study of obese subjects with knee OA there was moderate to high correlation of BLOKS MRI and K–L radiographic scoring particularly in the medial tibiofemoral compartment[87]; however, this study observed extensive tissue damage even in mild radiographic knee OA. Despite low sensitivity for tissue damage, K–L grade is still commonly used to stratify subjects in OA research studies, e.g., the Meniscal Tear and Osteoarthritis Research (MeTeOR) trial[88] and the Strontium ranelate Efficacy in Knee Osteoarthritis triAl (SEKOIA) study[89].

Semiquantitative scoring in the hand and upper extremity

Haugen and colleagues scored erosive hand OA using K–L grading and reported erosive hand OA was associated with MRI-assessed subchondral bone attrition[90]. A randomized controlled trial, the Hydroxychloroquine effectiveness in reducing symptoms of hand OA (HERO), used changes in the Kallman score as a secondary endpoint of the study (radiographic structural change at 12 months)[91].

In the hand, CT demonstrated higher inter-reader reliability and detection rate for both first carpometacarpal and scaphotrapeziotrapezoid joint OA compared with radiography[92]. In a recent systematic review of imaging of hand OA, ultrasound and MRI were both more sensitive for detecting osteophytes and erosions than radiographs and found significant differences between patients and healthy controls[93].

A recent study comparing radiographic scoring of shoulder OA found excellent reliability of four accepted classification schemes[94]; however, MRI has been shown to provide more reliable assessment of glenoid version than axillary radiographs[95].

Ultrasound-based semiquantitative scoring

Ultrasound is used for semiquantitative scoring of hand OA features and less commonly for knee OA. Within the last 12 months, reliability of ultrasound for dichotomous and semiquantitative assessment of hand and knee OA features was reported[96–99]. Klauser and colleagues used semiquantitative assessment of synovial hyperemia (0–3 scale) using power-Doppler ultrasound to assess the efficacy of intra-articular hyaluronic acid injection in hand OA patients[100]. The study demonstrated a correlation between a decrease in power-Doppler ultrasound score for hyperemia and reduction in pain during the 4-week follow-up period. The aforementioned HERO study uses both gray-scale and power-Doppler ultrasound to score synovitis using a 0–3 scale[91].

Imaging and joint kinematics

Several studies used imaging to evaluate altered joint biomechanics and relationship to bone marrow edema. Elevated mean

articular contact stress and peak contact stress at baseline were associated with worsening WORMS scores for bone marrow lesions in the same tibiofemoral compartment at 30-month follow-up[101]. Knee malalignment is associated with increased risk of incident and enlarging bone marrow lesions as well as cartilage loss in the more loaded compartment of the tibiofemoral joint[102]. For knees with normal cartilage morphology, varus alignment was associated with incident medial cartilage damage supporting the notion that varus increases the risk of initial development of knee OA[103]. Similarly valgus malalignment increases risk of radiographic progression and incident OA as well as risk of lateral cartilage damage possibly by increasing the risk of meniscal damage[104]. Somewhat surprisingly even for subjects with valgus alignment, the prevalence of medial patellofemoral cartilage damage exceeded that of the lateral facet[105]. The pattern of knee malalignment differs by sex and ethnic groups. In analysis of the MOST study, women and African Americans are more likely to have lateral joint space narrowing than men and whites, respectively. The prevalence of bicompartmental disease is much higher in African Americans than in whites, but no difference was observed between sexes[106]. Patterns of malalignment have also been shown to differ with age[107].

Patient symptoms and imaging

The correlation of specific imaging findings with patient symptoms remains elusive and controversial. Although knee pain was significantly associated with the presence of radiographic joint space narrowing and cartilage defect on MRI, synovitis and joint effusion on MRI were no more informative than radiographic KL grade of ≥ 2[85]. Data from the OAI found that the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Knee injury and Osteoarthritis Outcome Score (KOOS) knee pain and quality of life scores were poor indicators of tibiofemoral cartilage loss, assessed by decreasing mean medial and lateral joint space width on plain radiographs[108]. Guermazi and colleagues reported the prevalence of MRI findings associated with OA was similar for subjects with and without knee pain[86]. Although intra-articular MRI findings appear to be weakly associated with pain, greater baseline vastus medialis cross-sectional area (CSA) on MR was associated with lower knee pain at baseline (WOMAC) and reduced medial tibial cartilage loss over 2 years[109]. Additionally, an increase in vastus medialis CSA over 2 years was associated with reduced knee pain and less medial tibial cartilage loss. Wu and colleagues used gray-scale ultrasound to grade marginal osteophytes, synovitis, effusion, and meniscal extrusion using a 0–3 scale[99]. They showed suprapatellar effusion and medial compartment synovitis were positively linearly associated with knee pain. In a novel study, injury and degeneration of the knee meniscus was recently reported to be associated with reduced knee joint proprioceptive accuracy[110].

Several studies assessed pain and imaging after therapy. In a study evaluating cartilage repair of full thickness defects with mesenchymal stem cells, those subjects with improvement in WORMS scores demonstrated improved WOMAC pain scores[111]. Railhac *et al.* demonstrated an increase of total cartilage volume after 12 months treatment with chondroitin sulfate and a decrease in cartilage volume in the control group. An improvement of pain was observed in both the treatment and control groups, but was more significant in the treatment group[112]. A study evaluating 2 years of vitamin D treatment vs placebo in patients with knee pain and OA found no statistically significant difference in post-treatment WOMAC scores or MR changes in cartilage thickness, bone marrow lesion size, or radiographic joint space width (JSW)[113].

Functional neuroimaging is being used in the evaluation of central pain related to OA[114]. A recent study using the rodent medial meniscal tear model of OA and pharmacological MRI demonstrated increased supraspinal functional connectivity between brain regions in pre-clinical OA which could be modulated with matrix-metalloproteinase and cyclooxygenase-II (COX-2) inhibition[115]. Differences in regional cerebral blood flow were observed in subjects with painful OA of the carpometacarpal joint using pulsed continuous arterial spin labeling MRI suggesting dysregulated CNS appraisal and modulation of pain[116]. In the future it is likely that information gained from functional neuroimaging studies will become important tools for identifying and understanding the functioning of the central nociceptive system in OA.

Conclusions

Imaging plays a major role in OA research with continued publication along traditional lines of investigation. Translational and clinical research application of compositional MRI techniques is becoming more common driven in part by the availability of T2 mapping data from the OAI. New imaging techniques continue to be developed with a goal of identifying methods with greater specificity and responsiveness to changes in the joint, and novel functional neuroimaging techniques to study central pain. Imaging publications related to OA continue to be heavily focused on quantitative and semiquantitative MRI evaluation of the knee with increasing application of quantitative compositional imaging techniques in the hip.

Author contributions

All authors made substantial contributions to the following:

(1) The conception and design of the study, or acquisition of data, or analysis and interpretation of data.

(2) Drafting the article or revising it critically for important intellectual content.

(3) Final approval of the submitted manuscript.

Competing interests

Dr. Mosher is an Associate Editor for the journals *Osteoarthritis and Cartilage*, and *Radiology*. He has received consultancies, speaking fees, and/or honoraria from Medical Metrics, DePuy Orthopaedics, eImage, and Piramal Healthcare.

Dr. Walker is a consultant for Medical Metrics.

Dr. Petscavage-Thomas is a consultant for Medical Metrics.

Dr. Guermazi is the President of the Boston Imaging Core Lab, LLC, and has received consultancies from Merck Serono, Sanofi-Aventis and TissueGene.

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