Recent advances in research imaging of osteoarthritis with focus on MRI, ultrasound and hybrid imaging

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ABSTRACT

For imaging of osteoarthritis (OA), MRI plays a major role in the research setting, with compositional MRI techniques becoming increasingly more important thanks to their capacity to assess 'premorphologic' biochemical compositional changes of articular and periarticular tissues. Although radiography remains the primary imaging modality in OA clinical trials, known limitations for visualisation of OA features significantly limits the utility of radiography both clinically and in the research arena. Compositional MRI techniques can potentially supplement routine clinical MRI sequences to identify cartilage degeneration at an earlier stage when radiographs may be normal. Ultrasound can be a useful adjunct to radiography and MRI particularly for evaluation of hand OA and for the evaluation of synovitis. Emerging hybrid imaging techniques including PET/MRI and PET/CT allow evaluation of the joint with simultaneous assessment of morphological changes and metabolic activities, showing a potential for these hybrid systems to play an increasing role in OA research.

Introduction

In clinical practice and clinical trials, radiography remains the primary imaging modality for evaluation of osteoarthritis (OA). The European League Against Rheumatism (EULAR) task force and Osteoarthritis Research Society International (OARSI) have recently published recommendations regarding the use of radiography as the primary imaging modality for clinical assessment of OA (1, 2). Nonetheless, shortcomings of radiography are seen, including insensitivity to change, non-specificity, absence of reproducibility in longitudinal studies and challenges regarding positioning (Figs. 1-2) (3). Therefore, use of more advanced imaging modalities such as MRI and ultrasound has become important in OA research (3, 4). This is based on evidence that OA is a disease process involving multiple joint tissues including those not visible on radiography (5) and is a complex disease process with multiple phenotypes (6-8) that require evaluation by multimodality imaging assessment.

A recent systematic review and metaanalysis found that MRI-detected OA feature prevalence among asymptomatic uninjured knees were 4-14% in adults aged <40 years and 19-43% in those aged 40 years or greater (9), raising caution that these imaging findings may not be clinically meaningful should be interpreted only in the appropriate clinical context. In addition, research endeavors utilising modern hybrid nuclear medicine imaging techniques such as PET-CT, PET-MRI and SPECT-MRI are emerging. Other imaging modalities such as CT (10-12) and tomosynthesis (13, 14) have been applied only sparsely, and in a research context. The purpose of this review is to describe recent research developments in OA imaging, focusing on publications from 2016. Some older publications are cited where relevant for discussion of the subject matter. Literature on MRI and ultrasound will be the main focus, and the use of hybrid imaging techniques and their possible role in the future of OA imaging will also be covered. Summary overview of advantages and disadvantages of different imaging modalities are shown in Table I.

Magnetic resonance imaging

Recent findings from semiquantitative evaluation of osteoarthritis

To date multiple semiquantitative MRI scoring tools are available, as described in published review articles (15, 16). Research studies utilising semiquantitative MRI scoring systems continue to play an important role for OA researchers to further their understanding of



Fig. 1. Insufficient sensitivity to change by radiography. **A**. Baseline sagittal intermediate weighted fat suppressed image shows normal articular cartilage coverage in the medial femur and tibia. **B**. At 24 months follow-up there is circumscribed thinning of cartilage in the posterior medial femur (arrows). **C**. Baseline radiograph does not show any abnormalities in regard to joint space width. Note definite osteophytes at the medial tibia (arrow). **D**. At 24 months follow-up no change is observed in regard to joint space width or osteophyte presence (arrow).



Fig. 2. Positioning. Serial radiographs of the same knee acquired consecutively. A. Anterior posterior radiograph of the knee acquired with a positioning frame with 4 degrees flexion shows discrete lateral joint space narrowing (arrows). B. Radiograph of the same knee acquired with 6 degrees flexion shows slight decrease in joint space with (arrows). C. Radiograph obtained with 8 degrees flexion shows marked joint space narrowing compared to the image obtained with 4 degrees flexion (arrows). Knee flexion has marked influence on joint space width and may lead to false positive or negative findings particularly in longitudinal studies.

OA disease mechanisms and ultimately to assist in efforts to develop diseasemodifying therapies for OA. In these scoring systems, the joint is typically divided into multiple 'subregions' and osteoarthritis structural features, such as cartilage damage, meniscal pathology, bone marrow lesions (BMLs), effusion and synovitis are evaluated in each subregion of the joint. Existing semiquantitative scoring systems include, but are not limited to, Whole Organ MRI Score (WORMS) (17), MRI OA Knee Score (MOAKS) (18), Hip OA MRI Score (HOAMS) (19), Outcome Measures in Rheumatology (OMERACT) hand OA MRI scoring system (HOAMRIS) (20), Anterior Cruciate Ligament Osteoarthritis Score (ACLOAS) (21), Scoring Hip Osteoarthritis with MRI (SHOMRI) (22). In addition, a dedicated contrast enhanced MRI based synovitis scoring system is available (23, 24). Over the last two years, additional scoring systems have been introduced. The Knee Inflammation MRI Scoring System (KIMRISS) focuses on potentially reversible MRI biomarkers of active knee OA. *i.e.* bone marrow lesions (BMLs, i.e. ill defined T2 hyperintensity within the subchondral marrow - a feature shown to be associated with pain in osteoarthritis). with the use of an online web-based interface. BMLs are scored using a template superimposed onto each sagittal slice of acquired MR images, and the reader clicks on the segments that contain BMLs (25).

The OMERACT MRI Task Force developed the thumb base OA MRI score (TOMS) for assessment of inflammatory and structural abnormalities in a specific hand OA subset (26, 27). In this scoring system, the first carpometacarpal and scaphotrapeziotrapezoid joints were specifically assessed for synovitis, subchondral bone defects, osteophytes, cartilage and bone marrow lesions on a 0-3 scale. The Hip Inflammation MRI Scoring System (HIMRISS) enables assessment of BMLs and synovitis in hip OA, and had capacity to define responders to hyaluronic acid injection in hip OA based on WOMAC50 response three months after the procedure (28). Using the MOAKS scoring method and data from the Foundation for the National Institute of Health (FNIH) biomarkers consortium project, studies showed that 24-month MOAKS changes in cartilage thickness and surface area, effusion-synovitis (fluid distension of synovial cavity that represents effusion and/or synovitis which cannot be accurately discerned on non-contrast enhanced MRI), Hoffa-synovitis (signal changes within infrapatellar fat pad which is used as a surrogate marker for synovitis on non-contrast enhanced MRI), and meniscal morphology were independently associated with OA disease progression, suggesting these factors may serve as biomarkers in clinical trials of disease-modifying interventions for knee OA (29, 30).

Cartilage damage is important in the OA disease process and progression (Fig. 3). Both partial-thickness and full-thick-

Modality	Use	Advantages	Disadvantages
Radiography	 Assess osteophytes and joint space narrowing Severity classification based on Kellgren and Lawrence grading or Osteoarthritis Research Society International Atlas First line imaging modality for routine clinical care of osteoarthritis 	• Widely available • Low cost	 Minimal radiation Unable to depict most of osteoarthritis features including cartilage defects, meniscal damage, bone marrow lesions, synovitis, ligamentous damage Problem with reproducibility when comparing multiple time points because joint space width can changes depending on the positioning of the knee joint Limited sensitivity to change
MRI	 Evaluation of all articular and periarticular structures including cartilage, meniscus, ligaments, bone marrow lesions, subchondral cysts, osteophytes, synovitis, effusion Contrast enhanced MRI can accurate evaluate synovitis Most important imaging modality for research Currently limited clinical role in routine patient care of osteoarthritis 	 Detailed morphologic analysis using using semiquantitative and quantitative techniques Pre-morphologic analysis (biochemical composition of articular tissues) using compositional techniques No radiation 	 Costly Advanced compositional techniques may be limited to academic institutions with specialised software and hardware May be contraindicated in some patients (<i>e.g.</i> cardiac pacemaker)
Ultrasound	 Evaluation of superficial articular structures such as synovium, cartilage, and bone for synovitis, effusion, chondrocalcinosis, and erosion Popular choice for rheumatologists for quick in-office evaluation of synovitis, effusion and erosion 	 Ability to depict active synovitis using Colour Doppler imaging Readily available in rheumatology outpatient clinic setting No radiation No need for intravenous contrast to assess synovitis 	 Unable to assess deep articular structure Unable to assess bone marrow Limited anatomical details compared to MRI
Hybrid imaging	 Depiction of active metabolism in combination with detail anatomical information Not used for routine clinical management of osteoarthritis currently 	• Ability to assess early metabolic and morphologic markers of osteoarthritis across multiple tissues	 Higher radiation dose than radiography, especially PET/CT Relatively limited availability

Table I. Summary of advantages and disadvantages of various modalities for osteoarthritis imaging.







A

Fig. 3. Evolution of cartilage damage over 2 years. A. Baseline fat-suppressed intermediate-weighted MRI shows an intact articular cartilage surface in the anterior lateral femur. There is diffuse full thickness cartilage damage at the patella. B. 12 months later extensive full thickness cartilage damage in the anterior lateral femur is observed that will be graded as a MOAKS 2.2 lesion (10-75% of subregion with any cartilage loss, 10-75% of subregion with full thickness cartilage loss) and a grade 5 lesion using the WORMS instrument (arrows). C. Another 12 months later there is definite increase in area extent of lesion (arrows).

ness focal cartilage defects appear to contribute equally to incident cartilage damage in knee OA (Fig. 4) (31). Patellofemoral cartilage integrity is affected by knee biomechanics during the gait (32) and extensor/flexor muscle balance (33). A population-based study indicated that asymptomatic subjects with abnormally high BMI (25 or greater) had a 3-fold increased odds of at least moderate MRI-depicted cartilage damage at the time of observation compared to those with normal BMI, supporting the importance of obesity in the pathogenesis of cartilage damage in knee OA at asymptomatic stage of disease (34). Meniscal pathology is thought to play an important role in disease onset and



Fig. 4. Focal cartilage defects are a hallmark of early, pre-radiographic OA. A. Sagittal intermediateweighted fat saturated image shows superficial focal defect at the lateral femur adjacent to the posterior horn of the lateral meniscus (arrow). B. Sagittal dual echo at steady state (DESS) image depicts slight signal alterations but an intact articular surface in this articular region and is not able to directly visualise the defect, despite higher spatial resolution of the DESS sequence. High resolution 3D gradient echo sequences are inferior to standard clinical 2D fast spin echo sequences.



Fig. 5. Contribution of meniscal pathology to joint space narrowing. A. AP radiograph of the knee shows medial osteoarthritis Kellgren-Lawrence grade 3 with definite osteophytes (arrowheads) and joint space narrowing (arrow). B. Coronal proton density-weighted fat suppressed MRI shows a more complete picture of the underlying pathology. There is marked full thickness cartilage loss at the medial femur (short arrow) and a large subchondral bone marrow lesion at the medial tibia (long arrow). Medial marginal osteophytes are also seen on the MRI (arrowheads). In addition there is marked meniscal extrusion contributing to radiographic joint space narrowing. C. Another knee shows discrete medial marginal osteophytes but no cartilage damage or meniscal pathology. 24 months later there is marked femoral and tibial cartilage loss (arrows) and severe medial meniscal extrusion. Both features contribute to radiographic joint space narrowing.

progression (Fig. 5). The presence of meniscal extrusion (defined as MOAKS grade 2 or 3) in middle-aged obese women is associated with incident radiographic knee OA (odds ratio 2.61, 95% confidence interval 1.11-6.13) and medial joint space narrowing (odds ratio 3.19, 95% confidence interval 1.59-6.41) after 30 months (35). History of partial meniscectomy is another known risk factor associated with incident knee OA (36).

Synovitis in OA can be assessed using MRI without intravenous contrast. As described earlier, Hoffa synovitis and effusion-synovitis are two indirect markers of synovitis in knee OA (18, 37). Although Hoffa synovitis was shown to be strongly associated with knee pain (38), some authors argue effusion-synovitis may be preferred over Hoffa-synovitis as a surrogate marker when contrastenhanced MRI (CEMRI) is not available. This is because effusion-synovitis showed superior correlations with pain using CEMRI-assessed synovial thickness as the reference (39). On the contrary, data from the MeTeOR trial assessing outcomes after partial meniscectomy showed only modest sensitivity and specificity of patient-reported knee swelling using effusion-synovitis on nonCEMRI as the reference, urging caution against using patient-reported swelling as a proxy of inflammation manifesting as effusion-synovitis (40). Thus, contradicting evidence exists regarding the utility of Hoffa synovitis and effusion synovitis as a marker of acute inflammation in OA.

This brings the important point that synovitis is optimally assessed using gadolinium-based contrast enhanced (CE) MRI which enables direct visualisation of inflamed synovium and differentiation of synovium from adjacent effusion, which is not possible without the use of gadolinium (Fig. 6) (41). Studies have shown CEMRI-detected synovitis is strongly associated with severity of radiographic knee OA and MRI-detected widespread cartilage damage (42). Based on CEMRI, higher degrees of synovitis were strongly associated with increase in WOMAC pain score (43) and increase in synovitis was also associated with cartilage deterioration (44).

These observed associations imply that CEMRI is ideally suited for longitudinal evaluation of synovitis in OA, particularly for clinical trials for disease modifying drugs or other interventions.

In addition to non-osseous articular structures described above, osteophytes and BMLs also appear important in the OA disease process. Osteophytes are associated with knee pain both crosssectionally and longitudinally (45). BMLs are strong predictors of subsequent structural progression in knee OA including cartilage loss (46) (Fig. 7). Serum inflammatory markers (IL-6) were associated with BMLs in men and women with knee OA and IL-17F and IL-23 predicted BML worsening in women, suggesting an involvement of inflammation in BML pathogenesis in knee OA (47). Effusion detected by physical examination was shown to be associated with BMLs, implying that physical examination may potentially be used as a proxy for BML presence without costly MRI in the routine clinical care as well as screening for recruitment into clinical trials (48), at least at this time. In hand OA, BMLs are associated with pain, radiographic hand OA progression and incident joint tenderness (46,49,50). BMLs thus may be an important structural target for OA clinical trials.

Recent findings from quantitative evaluation of osteoarthritis features

Quantitative analyses based on MRI include measurement of size/thickness/ shape/volume of cartilage, osteophytes and BMLs, meniscus, effusion, and synovitis (Fig. 8). Such quantitative analyses are commonly performed based on 3D MR images, but they can also be performed on 2D MR images with modest loss of responsiveness compared to 3D scans (51). The use of locationindependent analysis has been proposed for quantitative evaluation of cartilage measures, given the spatial heterogeneity of cartilage loss in knee OA (52). A Local-Area Cartilage Segmentation (LACS) software method which utilises automated image analysis tools is available for fast and responsive cartilage volume measurement on MRI (53). Baseline lateral femoral cartilage volume loss has been documented to be



Fig. 6. Visualisation of synovitis using non-enhanced and contrast-enhanced MRI. A. Axial protondensity weighted fat saturated image shows marked hyperintensity within the joint cavity suggesting severe joint effusion (arrowheads). B. Axial T1 weighted fat saturated image after contrast administration clearly visualises severe synovial thickening depicted as contrast enhancement (arrows). Asterisk depicts true amount of effusion, which is only discrete and visualised as linear hypointensity within the joint cavity.



Fig. 7. Longitudinal assessment of bone marrow lesions (BML) in the lateral tibio-femoral compartment. **A.** Baseline sagittal intermediate-weighted fat-suppressed MRI shows a grade 2 MOAKS / grade 3 WORMS BML in the anterior lateral femur comprised of an ill-defined portion (large arrows) and a cystic component. In addition, there are small cystic BMLs in the subchondral lateral tibia. **C.** Follow-up 1 year later shows increase in overall lesion size in the lateral femur (arrows - now defined as grade 3 by both, MOAKS and WORMS). There is also slight increase in cystic portion of femoral BMLs in comparison to the previous visit.

associated directly with medial JSN progression at 48 months follow-up (54), and superolateral Hoffa's fat pad oedema is associated with patellar cartilage volume loss (55). Bone curvature changes predicted statistically significant efficacy of OA treatment based on a reduction in cartilage volume loss in a 2-year clinical trial of chondroitin sulfate with total to 120 subjects (56). Articular structures other than cartilage are increasingly being assessed using quantitative MRI approaches, *e.g.* effusion, synovitis and infrapatellar fat pad changes. In women, low serum levels

of endogenous estradiol, progesterone and testosterone were shown to be associated with increased knee effusionsynovitis volume (57). This association was not observed in men and thus this finding might explain some of the observed sex differences in OA structural changes. The role of the Hoffa's fat pad in the knee OA disease process remains controversial. One study suggested that infrapatellar fat pad (IPFP) signal increase and signal heterogeneity might be associated with radiographic/symptomatic progression of OA58), but another study showed the size and morphology of the infrapatellar fat pad was not related to knee pain (59).

Quantitative analysis can also be applied to the menisci. For example, quantitative measures of meniscal extrusion predicted incident radiographic knee OA (60). Recent developments include automated segmentation of articular tissue structures (61) and pulse sequence development focusing on accelerated image acquisition (62).

Compositional evaluation of osteoarthritis features

Compositional MRI allows evaluation of the biochemical properties of articular and periarticular tissues, enabling assessment of early pre-morphologic changes that cannot be detected on conventional MRI. Compositional MRI has been commonly applied for ultrastructural assessment of cartilage, but the technique can also be applied to other tissues such as meniscus (62) and ligaments (63). Such compositional MRI techniques include T2/T2*/T1rho mapping, delayed gadolinium enhanced MRI of cartilage (dGEMRIC), sodium imaging, gagCEST imaging, and diffusion MRI (64, 65). A recently published systematic review and meta-analysis showed cartilage compositional MRI techniques are reliable, and in the case of T1rho and T2 relaxometry, can discriminate between subjects with OA and controls (66).

T2 mapping is routinely available on most MR systems and is a well validated technique. For example, T2 map signal variation can potentially predict symptomatic knee OA progression in asymptomatic individuals to potentially serve as an early OA imaging marker (67). Also short-term longitudinal evaluation of T2 map and texture changes may serve as an early indicator of cartilage at risk for progressive degeneration after ACL injury and reconstruction surgery (68). T2* mapping can be performed using shorter acquisition times than T2 mapping thanks to the 3D acquisition of data (69). The Extended Phase Graph (EPG) modelling enables a simple linear approximation of the relationship between the two DESS signals, allowing accurate T2 estimation from one DESS scan (70).



Fig. 8. 3D cartilage quantification. Coronal reformated 3D DESS image depcits the medial and lateral tibiofemoral wieght-bearing cartilage as a hyperintense structure between the hypointense subchondral bone and the articular cavity. After segmentration cartilage is depicted in turquoise. Manual, semi-automated and automated techniques for tissue segmentation from MR images are available with manual segmentation being the current gold standard.



Fig. 9. 2-¹⁸F-fluoro-2-deoxy–D-glucose (FDG) positron emission tomography (PET). **A.** Reconstructed low-resolution coronal computed tomography image depicts joint space narrowing of the medial tibio-femoral joint (arrow) and definite osteophytes at the medial and lateral joint margins (arrowheads). **B.** Coronal fusion image of PET and CT marked pathologic glucose accumulation in the perimeniscal region (arrow) representing active synovitis. Note high sensitivity of PET for hypermetabolism but low specificity and poor spatial localisation without correlation with additional cross-sectional imaging (as CT or MRI).

T1rho mapping is sensitive to early cartilage degeneration and may complement T2/T2* mapping, but it requires special pulse sequences that are available at select few academic institutions and acquisition can be time consuming and can be costly (71). A study which measured meniscal T1rho and T2 values showed a significant decrease in T1rho/T2 signal in the posterior horn of lateral meniscus 2 years after ACL tear and reconstruction surgery, suggesting potential tissue recovery after ACL injury (72). The same study also showed elevated T1rho/T2 signal in the posterior horn of medial meniscus of injured knees at 2 years, correlating with knee cartilage T1rho/T2 signal elevations, implying involvement of the posterior horn of medial meniscus in subacute cartilage degeneration after ACL injury and reconstruction (72).

Sodium imaging correlates directly with GAG tissue content, but is limited

by the requirement for specialised hardware, long scan times and low spatial resolution. A feasibility study based on 7T MRI data demonstrated sodium MRI can detect decrease of apparent sodium concentration in cartilage over time in patients with knee OA (73). dGEMRIC is limited by the need for intravenous injection of gadolinium contrast agent and long scan time secondary to the presence of time gap between injection and imaging, but can be used to quantitatively determine cartilage sulfated GAG content in knee OA patients (74) in routine clinical MRI systems at 1.5T and 3T (75, 76), as well as in a highfield system at 7T (76). gagCEST is a relatively new compositional MRI technique that is specific for GAG concentration but only available at 7T ultra high filed MRI and research efforts to optimise image acquisition technique continue (77, 78). In a recent phase I clinical trial of the knee, dGEMRIC was shown to be more sensitive and accurate imaging tool in evaluation of cartilage GAG contents in vivo compared to gagCEST (79). Diffusion tensor imaging of articular cartilage may be a promising technique for detection of OA at an early disease stage, although its role in both clinical patient care and research setting remains to be determined and research efforts are continuing (80).

Ultrasound

Ultrasound has become an important tool in the clinical evaluation of articular structures. In the setting of OA research, ultrasound has been most commonly deployed in the evaluation of hand OA, compared to imaging of larger joints such as the knee and hip. Ultrasound enables evaluation of synovial hypertrophy, hyperaemia, and effusion in OA-affected joints. Thanks to its wide availability and relatively lower cost compared to MRI, in addition to its capacity to detect tissue-specific morphologic changes that cannot be visualised by radiography, ultrasound is thought to be a useful imaging technique as an adjunct to radiography (81, 82).

For example, a recent study comparing erosive and non-erosive hand OA patients showed that Power Dopplerdetected synovial hyperaemia was found more frequently in erosive hand OA compared to non-erosive hand OA, and patients with erosive hand OA had more moderate-to-severe synovitis detected by gray scale ultrasound than those with non-erosive hand OA (83). A longitudinal observational study showed synovial hypertrophy and hyperaemia are significantly associated with radiographic progression of hand OA after 5 years (84). Also, ultrasounddetected osteophytes predicted incident radiographic and clinical hand OA in the same joints 5 years later (85). Using an ultrasound-based semiguantitative scoring system (86), an observational study showed that ultrasound can be used to assess femoral osteophytes and medial meniscal extrusion in subjects with and without symptomatic knee OA (81). Another observational study demonstrated monthly alcohol intake was associated with synovitis in hand OA, although underlying reason for such an association remains unknown (87). With regard to advance in our understanding of OA pathogenesis for research purpose, ultrasound based studies may be limited compared to MRI based studies due to the fact ultrasound allows evaluation of only a select few pathological features and compared to MRI which enables essentially all articular structures including those which cannot be evaluated by ultrasound. On the other hand, ultrasound is more useful in routine clinical care because of availability, lower cost, lack of need for intravenous contrast for assessment of active synovitis.

Hybrid nuclear medicine imaging

PET imaging with 18F-fluorodeoxyglucose (FDG) or 18F-fluoride (18F⁻) enable imaging of active metabolism and visualisation of bone metabolic changes seen in the OA disease process (Fig. 9). A pathologic feature of OA that is particularly relevant to PET imaging is synovitis, which shows increased metabolism. The well-known major limitation of PET imaging is limited anatomical resolution, which can be overcome by deployment of hybrid PET/CT and PET/MRI imaging, which can be utilised to assess early metabolic and morphologic markers of knee OA across multiple tissues (88).

All subchondral bone lesions (i.e. BML, osteophytes and sclerosis) show hypermetabolism compared to normal bone on MRI (88). 18F-NaF PET-MRI enables detection of increased subchondral bone metabolism in ACLreconstructed knees at 3T PET-MRI system, suggesting its potential use as a marker of early OA progression (89). 18F-NaF PET-CT could be used for imaging of temporomandibular joint for depiction of arthralgic joint in the form of raised maximum standardised uptake value (SUVmax), with which correlation with therapeutic response was also possible (90). 18F-FDG PET-CT was shown to be useful for detecting regions of hypermetabolism in the affected joints with localisation of pain (91). The same study also showed a potential role of SUV measurements as an index of inflammatory activities in the knee joint (91). Moreover, research efforts have been made to utilise SPECT/CT for OA imaging (92, 93). SUVmax of quantitative bone SPECT/ CT was highly correlated with radiographic and MRI parameters for medial compartment knee OA (92). Additionally, bone tracer uptake on SPECT/ CT showed positive correlation with the degree and size of cartilage lesions depicted on MRI (93). At present, the use of PET/MRI or SPECT/CT in OA imaging is not routinely performed in a clinical setting and published literature evidence is limited to studies showing feasibility of these techniques in OA imaging research. However, these hybrid techniques allow combined information of structural imaging and molecular (metabolic) imaging techniques and thus likely play an increasing role in OA research.

Conclusions

In the field of osteoarthritis imaging, MRI continues to play a major role in the research setting, with compositional MRI techniques becoming increasingly more important thanks to their ability to assess 'pre-morphologic' biochemical compositional changes of articular and periarticular tissues. Although radiography remains the primary imag-

ing modality for defining inclusion/ exclusion criteria as well as the primary structural endpoint in OA clinical trials, known limitations for visualisation of OA features significantly limits the utility of radiography both clinically and in the research arena. Compositional MRI techniques can potentially supplement routine clinical MRI sequences to identify cartilage degeneration at an earlier stage when radiographs are normal. Different compositional techniques are complementary and offer information on different biochemical components of cartilage and other joint tissues. The applicability and responsiveness of these techniques in clinical trials need to be established in the near future. Ultrasound can be a useful adjunct to radiography and MRI particularly for evaluation of hand OA. Emerging hybrid imaging techniques including PET/CT and PET/MRI allow evaluation of the joint with simultaneous assessment of morphological changes and metabolic activities, showing a potential for these hybrid systems to play an increasing role in OA research.

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