Clinical and translational MRI assessment capabilities at osteoarthritis knee joint

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ANNOTATION. Magnetic resonance imaging (MRI) has become an increasingly important imaging modality in osteoarthritis (OA) research and is widely used in ongoing efforts to understand the pathogenesis of OA and develop structural and disease-modifying drugs for OA. MRI offers semiquantitative, quantitative, and compositional assessment of knee OA and can visualize tissues that are not visible on radiography, including but not limited to cartilage, menisci, bone marrow lesions, synovitis, and muscle. It is now recognized that contrast-enhanced MRI is more accurate in assessing synovitis than non-contrast MRI. Due to its ability to visualize multiple tissue pathologies associated with pain in three dimensions, MRI is the best imaging modality for OA.

Key words: osteoarthritis, magnetic resonance imaging, MRI, MRI evaluation, radiography, cartilage, bone marrow lesions, synovitis, meniscus, meniscus root, semi-quantitative, quantitative, knee joint

Introduction. Recent achievements in the field methods magnetic resonance tomography (MRI) helped researchers osteoarthritis (OA) understand process OA diseases and identify biomarkers progression diseases . Visualization osteoarthritis to a large extent degrees is based on radiography , and narrowing articular cracks revealed on radiograph , still is the only one structural ultimate point recognized Management By sanitary supervision behind quality food US and European Food and Drug Administration agency By medicinal means How proof efficiency drugs For treatment osteoarthritis modifying disease (DMOAD).) in phase III clinical tests However, the inherent limitations of radiography are well documented and, according to some researchers, are a possible reason why effective DMOAD has failed to be discovered to date [1].

MRI can visualize several important pathologic features of knee OA, including cartilage, meniscus, synovitis, and bone marrow lesions (BML), although these MRI findings may be present in a significant proportion of asymptomatic individuals, and lesions detected on MRI may not always be clinically significant [2]. However, the OA research community is increasingly using MRI for structural assessment of joints in epidemiological and clinical studies of OA [3]. OA imaging may be wide classified as “ morphological ” and “ compositional ”. The first include semi-quantitative [4] and quantitative [3] approaches, while the latter includes relatively new methods including dGEMRIC , T 2 mapping, T 1 rho , sodium imaging and diffusion imaging [5]. Target this unsystematic descriptive review is to introduce brief review selected original articles published mainly behind latest three years in which are described latest trends and developments in OA research using data obtained using MRI . In that review basic attention will focused on knee OA joint , joint , most wide studied in OA research .

Technical Considerations

To provide optimal assessment signs of OA detectable on MRI, researchers necessary choose relevant sequences impulses A detailed discussion of these technical issues has been published previously [4]. In brief, semiquantitative assessment of focal cartilage defects and BML is best achieved using a short tau inversion recovery sequence or one of the fluid-sensitive (i.e., T2-weighted, average-weighted, or proton density-weighted) fat-suppressed spin echo sequences [6 , 7]. For longitudinal studies using semi-quantitative assessment of OA features, within-grade changes should be recorded to ensure sufficient sensitivity to change [8•].]. More moreover , readers images must be fully trained to They could distinguish true anomaly signal arising because of pathological changes , and artifacts reminiscent pathological changes signal For example , an artifact sensitivity Maybe to look like So same as damage cartilage Although MRI can be powerful research tool , when wrong use she Maybe give misleading or unfaithful data .

MRI of cartilage

Semi-quantitative assessment of cartilage

Several semi-quantitative scoring systems have been published, including the two most widely used systems: the Whole Organ MRI Score (WORMS) and the Boston-Leeds OA Knee Score (BLOKS), as well as the newer MRI OA Knee Score (MOAKS) [4 , 9]. Laberge Longitudinal Study et al . found that obesity increased the prevalence and severity of cartilage damage over 36 months [10]. Crema et al . revealed that predominant damage cartilage (i.e. assessment By WORMS scale two or more) and loss cartilage over time time are associated with the occurrence of BML in the same or tibiofemoral compartments . Their results support the hypothesis that close coupling of the osteochondral unit is important for the progression of knee OA [eleven].]. Recent research indicate that focal defects cartilage increase risk development of knee OA joint Roemer et al. found that the presence of predominant cartilage damage and noncartilage pathology at baseline increased the risk of subsequent cartilage loss in the same subregion [12]. A recent population-based study found that focal cartilage defects in older adults are common, that most defects remain stable over 2.9 years, and that the initial degree of cartilage defect predicts the risk of knee arthroplasty over five years [13].]. Using data from the Osteoarthritis Initiative, Virayavanich et al . found that frequent knee flexion was associated with a higher prevalence of knee cartilage damage (especially in the patellofemoral region) and with an increased risk of progression of cartilage damage in asymptomatic middle-aged subjects who had risk factors for knee OA [14].

Quantitative morphometry of cartilage

Quantitative cartilage morphometry has been used in several recent OA studies [15-18] . Quantitative measures of articular cartilage structure, such as loss of cartilage thickness and exposed areas of subchondral bone, have been reported to be predictors of knee arthroplasty [18]. However, researchers wishing to use a quantitative morphometry approach in a multicenter study should note that data obtained from different segmentation groups should only be pooled when equivalence of the cartilage metrics of interest has been demonstrated: Schneider et al . revealed that differences in segmentation groups were the main cause of measurement variability in most cartilage regions for all image series [19].]. Eckstein et al. reported weak to moderate correlation and consistency between individual short- and long-term cartilage loss and between initial

and follow-up periods [20]. These results confirm the theory that more long-term periods observations preferable For receiving reliable results regarding losses cartilage in individual knees . McAlindon et al. conducted a two-year, randomized, placebo-controlled, double-blind clinical trial in 146 participants with symptomatic knee OA to determine whether vitamin D supplementation reduced symptoms and structural progression of knee OA [21]. By compared with placebo , reception vitamin D during two years at a dose sufficient For promotion Plasma 25-hydroxyvitamin D levels above 36 ng / ml ., not reduced knee pain or loss volume cartilage in patients with symptomatic knee OA joint

Cao et al. cross-sectional study found that spinal bone mineral density (BMD) of the total body, femur, and/or lateral tibia was significantly and positively associated with femoral, lateral tibial, and/or patellar cartilage thickness in subjects with ROA, after adjusting for potential confounders [22]. In longitudinal direction high total body BMD was associated with an increase thickness femoral cartilage , high BMD of the spine was associated with an increase thickness femoral and lateral tibial cartilage , and high medial tibial BMD department spine was associated with an increase medial thickness tibial cartilage in patients with radiographic research OA. So way like systemic and subchondral BMD is positive associated with an increase thickness cartilage in patients with ROA, which allows assume that the body's MIC Maybe have protective Effect against thinning cartilage for knee OA joint

Widmaier et al. reported that a high body mass index (BMI) was associated with increased daily load (i.e., change in thickness) of knee articular cartilage [23]. Them Not less , still to come define , explains whether This increase day loads in people with high BMI are increased risk of OA associated with obesity , or instead of this indicates on change mechanical properties cartilage in these of people .

Compositional MRI of cartilage

Compositional MRI allows visualize biochemical properties hyaline cartilage He Maybe be sensitive to early premorphological changes that Not visible on conventional MRI. Compositional visualization changes cartilaginous matrix Maybe be made using advanced MRI methods , including delayed MRI of cartilage strengthening gadolinium (dGEMRIC), T1 rho and T2 mapping . Two from them , dGEMRIC and T1 rho, use advantages concentrations strongly negative charged glycosaminoglycans (GAG) in healthy hyaline cartilage ; a loss of these GAGs in focal areas affected possible early disease , maybe be visualized Both dGEMRIC and T1 rho focus on density charge in cartilage . On the contrary , on T2 concentration is affected complex combination orientation collagen and hydration cartilage

Methods compositional MRI is usually Not used in modern clinical practice and remain research tools available only in some academic institutions Them Not less they used in clinical trials and observational research . In a placebo-controlled double blind pilot research hydrolyzate collagen at lung OA knee joint McAlindon et al. [24] showed that the dGEMRIC score increased (i.e., higher GAG content and better cartilage condition) for tibial cartilage sites of interest in patients receiving collagen hydrolyzate and decreased in the placebo group. Reliable difference observed at 24-week follow-up . Future research can determine related whether macroscopic changes cartilage with these

early results dGEMRIC . Souza et al. reported that acute loading of the knee joint resulted in a significant reduction in T1 rho and T2 relaxation times of the medial tibiofemoral compartment , especially in areas of cartilage with small focal defects [25]. These data indicate that change values rho T1 at mechanical load Maybe be associated with biomechanical and structural properties cartilage Hovis et al. reported that light exercise was associated with low cartilage T2 values , but moderate and strenuous exercise was associated with high T2 values for women, suggesting that activity level may influence cartilage composition [26]. Using a longitudinal study design, Lin et al . found that high and very low levels of physical activity were associated with greater progression of cartilage T2 measurements in asymptomatic middle-aged individuals, suggesting accelerated biochemical degeneration of the cartilage matrix over time [27]. In an interventional study evaluating the effects of weight loss on articular cartilage, Anandacoomarasamy et al . reported that improvement in articular cartilage quality was indicated by an increase in the dGEMRIC index over one year for the medial compartment, but not for the lateral compartment [28]. These results can reflect importance losses weight For possible clinical and structural improvements .

Also were researched various new compositional techniques . Raya et al. found that visualizing the diffusion tensor in vivo , based on the 7 T system MR was better than T2 mapping for distinguishing OA knees from non- OA knees [29]. Other work on 7 T systems has reported the reproducibility of the in vivo [thirty]. Other compositional methods that may be useful for further study are T 2* mapping [31] and sodium imaging [30].] cartilage. These methods seem promising , but their necessary do practical and compatible with standard MRI systems , before how their Can will use in research or For productions clinical diagnoses Recent study Newbould et al. showed that clinically feasible MRI sodium with tension fields 3 Tesla , average time visualization and attenuation liquid using T1 weighing successful differentiated healthy of people control groups and patients with OA.

MRI of the meniscus

Meniscal pathology is thought to be associated with knee joint disease OA because structural changes (eg, meniscal tears, maceration, or extrusion) can result in loss of normal function in buffering mechanical load on the tibiofemoral joint [32]. Englund et al. examined multiple risk factors for medial meniscus pathology in 791 knees from the MOST study with a normal medial meniscus at baseline and found that knee trauma and generalized OA, expressed as multiple knuckle bone overgrowths, varus alignment, and obesity, were risk factors for medial meniscal pathology. meniscus [33].

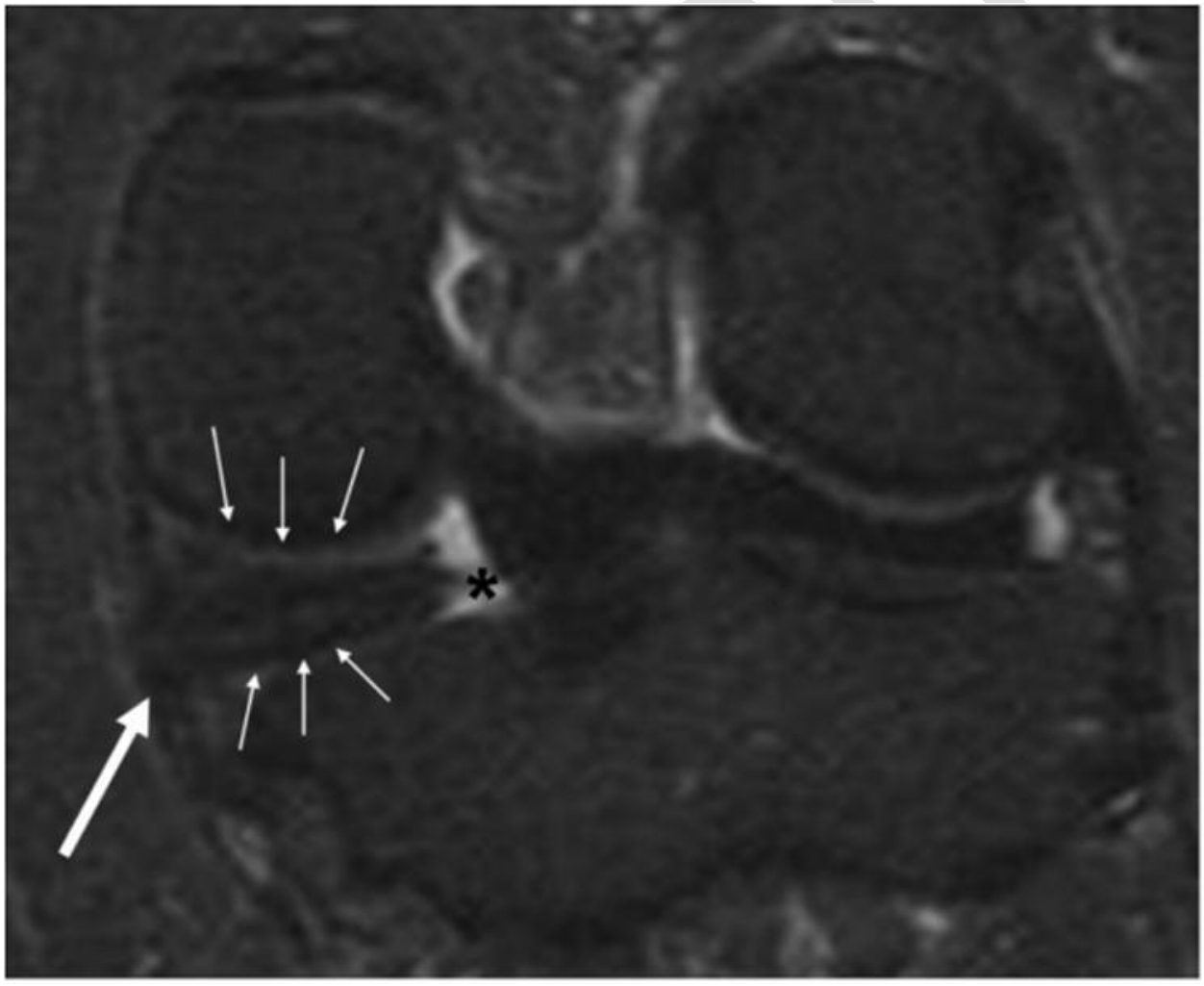
In his population-based study in South Korea, Kim et al . reported that the incidence of meniscal injury in their subjects (mean age 72 years) was 49.7% for men and 71.2% for women [34]. Heaviness knee pain much correlated with degree damage medial meniscus In the Stehling study et al ., when the knee was subjected to axial mechanical loading, subjects with degenerative knee abnormalities had significantly increased meniscus extrusion compared with healthy subjects [35]. In longitudinal controlled subsequent research subjects who have undergone arthroscopic partial medial meniscectomy (APMM), Wang et al . described an increased risk of subsequent cartilage damage at the tibial and patellofemoral joints in patients with APMM [36]. Using BML

and data from a multicenter osteoarthritis study, Crema et al . found that medial meniscus extrusion was associated with medial meniscal tears, medial cartilage damage, and varus deformity, whereas lateral meniscus extrusion was associated with lateral meniscal tears, lateral cartilage damage, and valgus deformity [37]. In a two-year clinical study of 161 patients with knee OA, Raynauld et al . showed that severe medial meniscus tear and medial meniscal extrusion detected by MRI at baseline were strong long-term predictors of total knee replacement [38]. Using data from the Osteoarthritis Initiative, Badlani et al . found that knees with meniscal tears with greater involvement and extrusion of the radius had a greater risk of subsequent development of radiographic OA [39].

MeTeOR) study was recently published [40]. Study MeTeOR is yourself multicenter randomized controlled research involving symptomatic patients aged 45 years and older with a rupture meniscus discovered on MRI, and signs of mild OA or average degrees gravity that determined availability defects cartilage identified on MRI. Researchers random way allocated 351 patients on surgery and postoperative physiotherapy or on standard mode physiotherapy (with the possibility go to operation By discretion patient and surgeon). Patients were examined through six and 12 months . Primary result was difference between groups regarding changes index physical functions University Western Ontario and University McMaster (WOMAC) (range from 0 to 100, where more high points indicate on more heavy symptoms) through six months after randomization . In analysis intentions treat Not was discovered significant differences in functional improvement between researched groups through six months after randomization . However , 30% of patients assigned to the group physiotherapy , moved on operation within first six months

Should note that gap roots meniscus is absolutely other phenomenon than gap themselves meniscus Guermazi Research et al . found that an isolated tear of the medial posterior root of the meniscus (i.e., without tearing the body or anterior and/or posterior horns of the medial meniscus) is associated with episodic and progressive loss of medial tibiofemoral cartilage [41•]. Meniscal root tears can lead to meniscal extrusion as the meniscus loses the ligament that attaches it to the tibial plateau. Fig. 2). So Thus , in OA studies there is no should ignore ruptures root meniscus In addition to morphological visualization meniscus using ordinary MRI sequences described above , in publications reported about use various MRI methods . Wenger et al. used a within-person comparative approach and found that painful knees had less tibial plateau meniscal coverage and greater meniscal body extrusion compared with pain-free knees from the Osteoarthritis Initiative subgroup [42]. Authors used 3D meniscus segmentation method , which provides quantitative measurements size meniscus , position and others variables Using data from the Osteoarthritis Initiative, a more recent study by the same group of researchers found altered meniscus position and shape (i.e., greater protrusion) in both knees with medial osteoarthritis compared with control knees without OA [43], implying that these findings may be related to the pathogenesis of OA and/or disease sequelae. Using the dGEMRIC method to assess meniscal substance in the knees of OA patients and normal control knees of young adults, Li et al . revealed significant differences between groups when using both ionic and nonionic contrast agents [44]. Authors came to the conclusion that difference in meniscal T1Gd between patients with

OA and normal subjects Not determined distribution charge , or maybe be associated with changes in kinetics washing out and washing out . Wang et al. revealed that T 1 rho values are higher in certain subregions of the meniscus and tibiofemoral cartilage, suggesting that regional damage to both femorotibial hyaline cartilage and menisci may be associated with osteoarthritis [45]. Williams et al. used a T2 * mapping technique with ultrashort time-enhanced echo (UTE) to detect human meniscal degeneration in vitro and in vivo in subjects at risk of developing OA [46]. In that research on corpses and people observed significant promotion UTE-T2* values in menisci subjects with damage front cruciform ligaments , but without clinical signs anomalies subsurface meniscus This opening indicates that UTE-T2* mapping is sensitive to subclinical degeneration meniscus , but Bye unknown , maybe whether changed intrameniscal biochemical indicators predict progression degeneration and rupture meniscus or development of OA.



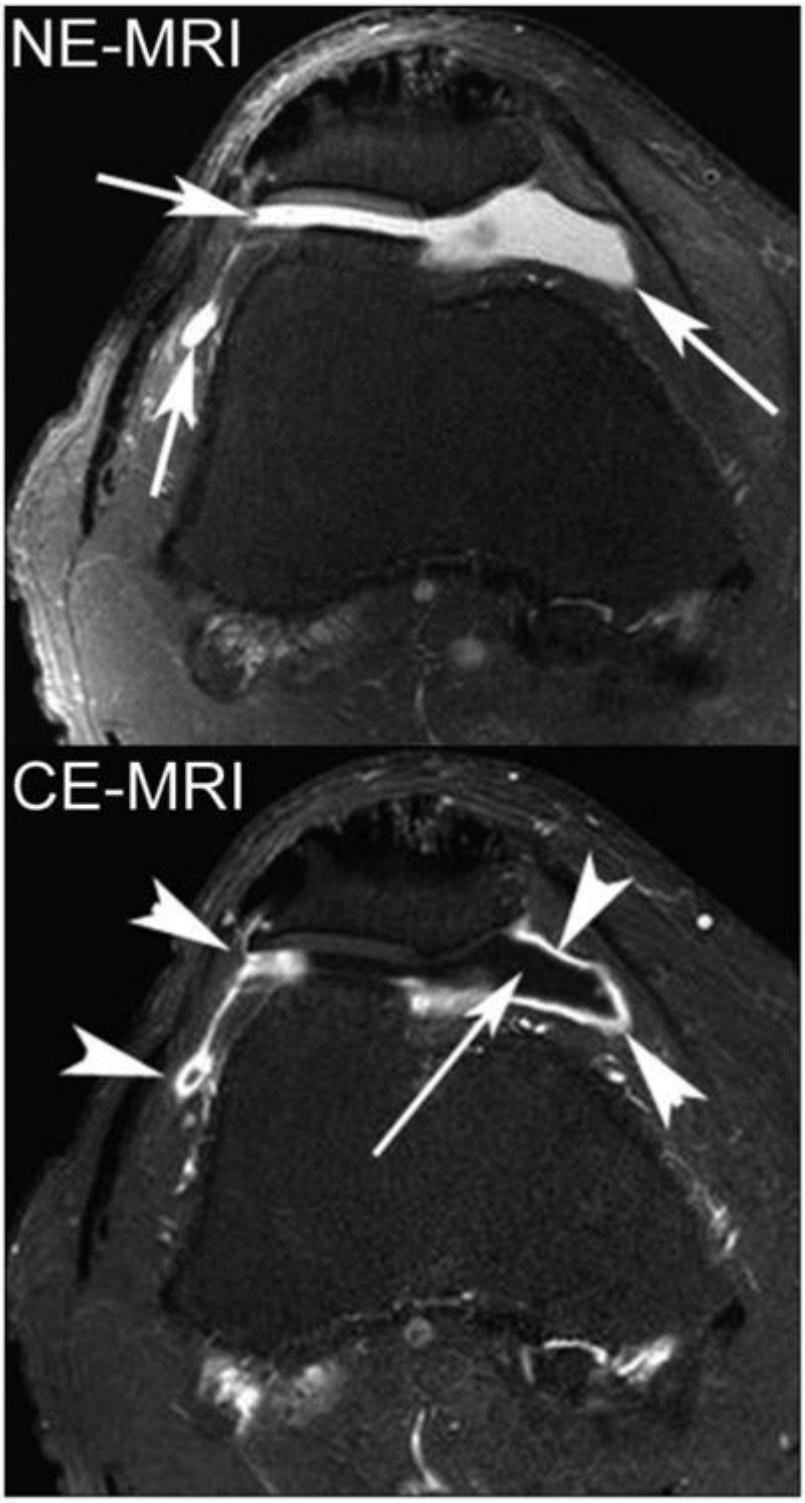
Rice. 2

Image weighted By density protons , suppressed fat in the crown showing gap medial root rear meniscus (asterisk) with simultaneous protrusion meniscus (large arrow). Please pay attention Also on neighboring damage femoral and tibial cartilage (small arrows) by compared to the side side .

MRI synovitis

an important pathological feature of knee OA as it is known to be associated with pain [47, 48 , 49 , 50]. Maybe become DMOAD target . Synovitis Can evaluate using MRI with injection contrasting substances gadolinium or without him . Without injections contrast impossible conduct difference between synovial liquid (that There is articular effusion) and synovial shell , because What both They have the same hyperintensity on liquid-sensitive sequences with suppression fat , including recovery short inversions tau protein (STIR) and suppression fat T2-weighted sequences fast spin echo (FSE). So way for estimates synovitis using MRI without gain (NEMRI) as surrogate marker used T2 hyperintensity within fatty fabrics Hoffa . Using NEMRI and a semi-quantitative approach, Knoop et al . found that quadriceps weakness was associated with synovitis in patients with knee OA [51]. Zhang et al. found that variation in synovitis was associated with variations in knee pain in patients with knee OA [49].

It is important to note that the Loeuille study et al . correlated MRI results with histology results based on synovial biopsy and showed that contrast-enhanced MRI (CEMRI) can detect biopsy-proven synovitis, whereas NEMRI cannot [52••]. Crema et al. showed that CEMRI is more specific than NEMRI for synovitis and correlates better with pain [53]. Using the semiquantitative CEMRI score as the reference for synovitis, NEMRI has high sensitivity (0.71–0.88) but relatively low specificity (0.30–0.55) [53]. Although one study found that semiquantitative NEMRI -based synovitis scores were associated with CEMRI- based synovitis measurements [54], increasing evidence in the literature suggests that CEMRI is the best option for MRI-based assessment of synovitis (Figure 1). Identification places in which arises synovitis , it seems important part estimates . Posterior horn meniscus injury is associated with adjacent perimeniscal synovitis (adjusted odds ratio 2.5, 95% CI 1.3–4.8) but not with posterior cruciate recess synovitis, indicating that synovitis at these two sites may have different pathomechanisms [55].]. Baker et al. found a positive association between plasma inflammatory mediators and synovitis assessed by CEMRI [56]. For future clinical and epidemiological studies focusing on synovitis, more than one CEMRI- based semi-quantitative scoring system is available [48 , 56]. Latest Published Guermazi Rating System et al . allows for a comprehensive assessment of synovitis of the entire knee joint, including assessment of 11 anatomical locations [48•], although this system needs to be confirmed by future studies. NEMRI- based scoring systems are also available [9 , 57–59] and are now much more widely used than CEMRI- based scoring systems . Where the use of CEMRI is not possible, NEMRI is still a valid alternative for assessing synovitis, provided investigators are aware of the limitations of NEMRI , as described above.



picture 1

Comparison unenhanced (NE-MRI) and MRI with contrast increased (CE-MRI) synovitis at osteoarthritis knee joint Axial NE-MRI shows signal equivalent fluids in the cavity joint that indicates articular peripatellar effusion recesses (arrows). Impossible distinguish effusion and inflammation synovial shell , because What both They are depicted How hyperintense . In contrast , axial FE-MRI shows noticeable synovial gain (arrows), which Can clearly distinguish from effusion depicted How hypointensity (arrow).

MRI of bone marrow lesions (BML)

BML detected on MRI may itself be a nonspecific finding and may indicate pathological processes other than OA [60], in the context of knee OA, they are an important feature and are widely studied in the OA research community. Recent studies using MRI suggest that BML may be a potential imaging biomarker for quantifying structural changes in knee joints affected by OA [61].

To better understand the biological and mechanical pathways linking cartilage, bone, and bone marrow changes during OA progression, Kazakia et al . used microcomputed tomography (μCT), high-resolution peripheral quantitative computed tomography (HR - pQCT), and Fourier transform infrared spectroscopy (FTIR) to assess bone structure and BML composition associated with knee OA [62]. Trabecular the bone in BML was higher By volumetric share , with great quantity or more thick trabeculae , which were more lamellar By structure By compared with trabeculae in unaffected areas . Compound trabecular BML fabrics had more low content phosphates and carbonates . Present infiltration bone brain fibrous collagen network and signs increased remodeling bones . These structural and compositional changes were specifically localized in areas underlying degradation cartilage , confirming paradigm focal interactions between bone , bony brain and cartilage at progression of knee OA joint

In population research subjects with knee pain Ip et al . found that BML was present in 11% of patients without OA, in 38% of patients with pre-radiological OA (degree Kellgren-Lawrence <2 on radiography , but with noticeable damage cartilage on MRI) and in 71% of patients with radiographic OA. [63]. BML were much associated with pain at rise By stairs , but not with pain at walking or with common WOMAC score . In another population-based study, the Framingham Osteoarthritis Study , Guermazi et al . reported that 52% (371/710) of individuals without radiographic OA had BML , regardless of pain status [2]. Stein et al . studied 160 participants from subgroups progression initiatives By osteoarthritis and found that knees with a gap front cruciform ligaments (ACL) had much more BML in the lateral parts hips than knees without ACL rupture . Using data from the MOST study , Hayashi et al . reported that knee malalignment is associated with an increased risk of occurrence and increase in BML in the more loaded tibiofemoral joint regions [64]. These results highlight the influence of joint biomechanics on the structural integrity of the entire joint, including subchondral bone [65]. Also using data MOST study , Zhang et al. [49] showed that BML changes detected on MRI were associated with corresponding variations in knee pain. The decrease in BML was associated with the disappearance pain that allows suggest that subchondral bone Maybe be potential target For individual therapy

The report by Dore et al. described the possible association of systemic and nutritional risk factors with the subsequent development of BML , supporting the hypothesis that subchondral bone metabolism is not dependent solely on the biomechanical properties of localized loading [66]. Randomized clinical trial reported by Laslett et al . found that a single infusion of zoledronic acid reduced knee pain and local BML size and increased percentage improvement over six months [67]. Recently were proposed two new method For quantitative estimates BML volume . Pang et al . [68] used a semi-automatic segmentation technique, which was validated against the

BLOKS scale for BML , and Ratzlaff et al . also used a semi-automatic method, which was validated against the WORMS scale for assessing BML [69]. Although both method were verified on correspondence established systems semi-quantitative ratings , more to come determine will whether these new methods play important role in clinical future OA trials .

Muscle MRI

MRI allows Great outline muscles and so way , maybe be used For measurements area transverse sections or length muscles lower limbs . Sattler et al. found that knees with frequent pain had smaller anatomical cross-sectional areas and experienced less load from the quadriceps femoris (but not other thigh muscles) compared with contralateral knees without knee pain at the same radiographic stage [70].]. Frequent pain apparently not influenced on correlation between anatomical area transverse section and force knee joint with OA. These data indicate that strengthening exercises quadriceps muscle , can be useful For treatment symptomatic knee OA joint Based on this, Ruhdorfer et al . found no significant lateral differences in anatomical cross-sectional area of the quadriceps femoris (or other thigh muscle) between knees with radiographic medial joint space narrowing (JSN) and knees without JSN , or between specific medial knee layers of JSN and contralateral knees without JSN , for men or women [71]. Two year olds longitudinal changes anatomical areas transverse sections muscles hips were small and significantly Not were different between knees with medial JSN and knees without JSN. These longitudinal data showed that more late X-ray stage of knee OA joint Not Necessarily associated with longitudinal decrease muscular functions

Conclusions

MRI has become powerful research tool For research OA community , and in the literature published All more data obtained using MRI . MRI overcomes inherent radiography restrictions and allows evaluate various tissues and pathological features associated with pain . For morphological analysis available semi-quantitative and quantitative approaches , and new ones compositional MRI methods show promise visualization premorphological changes in tissues , including cartilage and menisci . By Compared to NEMRI, CEMRI provides more accurate assessment synovitis for knee OA joint though first still is effective alternative when CEMRI is not available.

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