

# The diagnosis of early osteoarthritis of the knee using magnetic resonance imaging

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**Abstract:** In consideration of the growing number patients with osteoarthritis (OA), orthopaedic surgeons and physicians have increasingly focused on the prevention of OA. If early OA can be diagnosed, it may be possible to intervene to prevent disease progression, in turn decreasing the treatment costs and increasing patient satisfaction. In the early diagnosis of OA, magnetic resonance imaging (MRI) is more sensitive and advantageous than plain radiograph, as the former offers several additional advantages, including the absence of radiation exposure. However, as the validated consensus criteria of early OA using MRI are lacking at present, its routine use in daily practice would not be recommended. In this chapter, we will highlight the recent studies on the evolving use of MRI to diagnose early OA.

Keywords: Early osteoarthritis (early OA); knee; magnetic resonance imaging (MRI)

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#### Introduction

Osteoarthritis (OA) of the knee is the most common joint disease, which is related to pain, disability (1). In 2012, the definition and classification of early knee OA was proposed by Luyten *et al.* (2); since then, the attention to early stage knee OA has increased, as identifying OA in its early stage would allow more optimal multimodal management to prevent or slow OA progression. More recently, international experts in OA have proposed classification criteria for early knee OA (3).

Magnetic resonance imaging (MRI) has advantage in the evaluation of structural changes during the progression of knee OA (4). MRI allows us to visualize all the tissues involved in OA pathology, such as cartilage, subchondral bone, meniscus, and soft tissue. Thus, MRI has great potential as a whole-organ imaging tool of the OA (5). In this chapter, we reviewed MRI assessments of early knee OA.

#### **MRI and definition of early knee OA**

In 2012, the definition and classification of "early" OA of the knee was proposed by Luyten *et al.* (2). According to this definition, early OA of the knee can be defined based on clinical and imaging findings, and should meet three criteria: (I) knee pain, (II) Kellgren-Lawrence (KL) (6) grade 0, I or II (osteophytes only) using plain radiographs, and (III) cartilage lesion confirmed by arthroscopy and/or OA-related MRI findings such as degenerations of cartilage and meniscus, and/or subchondral bone marrow lesions (BMLs).

MRI features of degenerative changes of the cartilage, BMLs, and/or meniscus are based on the Boston Leeds Osteoarthritis Knee Score (BLOKS), the Whole Organ Magnetic Resonance Imaging Score (WORMS) (7,8) and their comparisons (9,10). Specifically, at least two of the four following items need to be fulfilled (2):

- (I) Cartilage morphology scores: at least grade 3 (WORMS grade 3-6) (7);
- (II) Cartilage Score 1: at least grade 2 (BLOKS grade 2 and 3) (8);
- (III) Meniscal tears: at least grade 3 (BLOKS grade 3 and 4) (9);
- (IV) BML: at least WORMS grade 2 (7).

Related to this criteria of early knee OA, Hunter and his colleagues developed an MRI definition of structural knee OA (11) using the Delphi process (12,13). In this definition, definite osteophyte and/or full thickness cartilage lesion are essential for tibiofemoral OA definition on MRI. If the patient has only one out of these two features, two or more features out of four features (BMLs, meniscal lesions, partial thickness cartilage lesion, and/or bone attrition) should be fulfilled for the OA definition on MRI.

The definition of patellofemoral OA requires a definite osteophyte, and partial or full thickness cartilage lesion (11).

More recently, an expert group discussed potential classification criteria for early OA of the knee for use in a primary care setting, as consensus criteria for classifying early OA are lacking (3); however, MRI was not included in that draft proposal which consists of Knee Injury and Osteoarthritis Outcome score [Knee Osteoarthritis Scoring System (KOSS)], clinical examination, and plain radiograph (3). They provided consensus statements regarding MRI as follows, "*There was general agreement that MRI is a powerful technique that is needed in research on early OA. However, at present MRI is not recommended as an aid to identify or define early OA in routine clinical practice or primary care, in light of lack of validated consensus criteria, and the high population prevalence of structural joint changes detected by this method (3)."* 

# Semi-quantitative scoring system of knee OA using MRI

Semi-quantitative scoring of knee OA features using MRI has shown to be a valid method (4), and a couple of scoring systems have been reported. The WORMS was the first published scoring system, and it has been used extensively over a decade in the studies related to knee OA worldwide (7). Thereafter, three other knee scoring systems have been developed: the KOSS (14), the BLOKS (8), and the MRI Osteoarthritis Knee Score (MOAKS), which is a merger of the WORMS and BLOKS scoring tools (15-17). Plain MRI features are used in all these systems (18). The MOAKS was introduced by a panel of experienced OA researchers, and has shown very good to excellent reliability (15). The MOAKS refined the scoring of BMLs, articular cartilage, and the elements of meniscal morphology scoring, and consists of the scoring of seven sub-regions such as BMLs, cartilage, osteophytes, synovitis, meniscus, ligament/tendon and periarticular findings (15).

# Quantitative measurements of articular cartilage using MRI

Articular cartilage is the main tissue that is involved in the OA process (15). The cartilage compositional MRI techniques such as T1rho (T1 $\rho$ ) (19-23), T2 (22,24-26), and delayed gadolinium enhanced MRI of cartilage (dGEMRIC) (27-30) are sensitive to the alteration in cartilage extracellular matrix (ECM) composition, and allow us to detect these molecular changes before gross morphological changes become apparent (31,32).

T2 reflects the movement of free water proton molecules inside the cartilage matrix (22). The damage to collagenproteoglycan (PG) matrix and increased water content in degenerated cartilage may increase T2 relaxation times (22), and elevated T2 values were observed in patients with OA (22,24,33). T1rho was introduced as an alternative parameter to assess biochemical changes in cartilage (19-23,32,34,35). The changes to the ECM (i.e., loss of PG) would be reflected in T1rho measurements (22). It has been shown that T1rho values were elevated in OA patients (20-22,36). Even though both T1rho and T2 investigate slow motion of water protons, these measure different MR relaxation mechanisms; thus, these parameters can provide complementary information about macromolecular changes in articular cartilage (22). A recent systematic review and meta-analysis showed that these cartilage compositional MRI techniques are reliable, and can distinguish between subjects with OA and healthy cartilage in the case of T1rho and T2 MRI (31).

#### Association between MRI findings and incident OA

It has been shown that MRI-detected structural changes (i.e., osteophytes, meniscal damage, BMLs, and/or synovitis) may represent early OA in people without radiographic OA, and are associated with the incident OA. MRI may identify

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bone structure changes more sensitively than radiographic findings (37). Schiphof *et al.* compared the findings between MRI and plain radiograph in a population-based study, and concluded the definition of knee OA based on MRI more sensitively detected structural knee OA than the definition based on plain radiograph (37). Zhu *et al.* performed a prospective cohort study of 895 participants, and showed that 85% had MRI-detected osteophytes at baseline while only 10% were detected by radiographs (38).

It is widely known that meniscal extrusion due to meniscal injuries or degeneration can accelerate the initiation and progression of knee OA. Even absent a discrete tear, meniscal extrusion has shown to be associated with the incidence of knee OA; therefore, meniscal extrusion on MRI would suggest risk for developing knee OA (39-42). In patients age 50–90 years old with asymptomatic knees, Englund *et al.* found the prevalence of meniscal tear was 60% on MRI, yet 23% of patients had no radiographic evidence of OA (43). Others also reported that meniscal lesions were frequently observed in MRI even in the knees from 50 to 90 years old asymptomatic subjects without radiographic findings of OA (44,45).

From the Multicenter Osteoarthritis Study (MOST), Javaid et al. have reported that MRI features of OA in only a few specific locations occurred prior to clinical symptoms in the knees without significant symptoms or radiographic OA, suggesting that bony changes may be associated with early knee pain development (46). Using the MOST data, Felson et al. also reported that a substantial volume of synovitis in the knee was an independent cause of the incident OA (47). Moreover, several studies from the Osteoarthritis Initiative have showed the associations between MRI findings and incident OA (48-51). Roemer et al. reported that the presence of synovitis and medial meniscal lesion in MRI 2 years prior to incident radiographic OA increased the risk for incident radiographic OA (48). Liebl et al. showed that increased baseline T2 values in articular cartilage, which was assessed when radiographic changes are not yet apparent, may be useful in predicting the development of radiographic tibiofemoral OA. Sharma et al. showed that worsening MRI findings were associated with concurrent incident radiographic OA and subsequent symptoms (50). Katsuragi et al. reported that the knees with osteophyte formation at the intercondylar notch, even those of KL grade 0 or 1 in radiographic assessments, had a risk for the radiographic OA development within 4 years.

#### Conclusions

MRI is a tool that provides useful information for early OA diagnosis. Although MRI is not recommended for now to diagnose early knee OA in daily clinical practice, because of lack of validated consensus criteria and the frequent prevalence of structural knee joint changes with MRI, the literature suggests that such MRI-detected lesions may represent early knee OA, and add support for the investigation of intervention effectiveness at the early stage of OA. Further investigations using MRI will be warranted.

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# References

- Liu Q, Niu J, Huang J, et al. Knee osteoarthritis and all-cause mortality: the Wuchuan Osteoarthritis Study. Osteoarthritis Cartilage 2015;23:1154-7.
- Luyten FP, Denti M, Filardo G, et al. Definition and classification of early osteoarthritis of the knee. Knee Surg Sports Traumatol Arthrosc 2012;20:401-6.
- Luyten FP, Bierma-Zeinstra S, Dell'Accio F, et al. Toward classification criteria for early osteoarthritis of the knee. Semin Arthritis Rheum 2018;47:457-63.
- 4. Guermazi A, Roemer FW, Haugen IK, et al. MRIbased semiquantitative scoring of joint pathology in osteoarthritis. Nat Rev Rheumatol 2013;9:236-51.
- Hunter DJ, Zhang W, Conaghan PG, et al. Responsiveness and reliability of MRI in knee osteoarthritis: A metaanalysis of published evidence. Osteoarthritis Cartilage 2011;19:589-605.
- 6. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957;16:494-502.
- 7. Peterfy CG, Guermazi A, Zaim S, et al. Whole-organ magnetic resonance imaging score (WORMS) of the knee in osteoarthritis. Osteoarthritis Cartilage 2004;12:177-90.
- Hunter DJ, Lo GH, Gale D, et al. The reliability of a new scoring system for knee osteoarthritis MRI and the validity of bone marrow lesion assessment: BLOKS (Boston Leeds Osteoarthritis Knee Score). Ann Rheum Dis 2008;67:206-11.
- Lynch JA, Roemer FW, Nevitt MC, et al. Comparison of BLOKS and WORMS scoring systems part I. Cross sectional comparison of methods to assess cartilage morphology, meniscal damage and bone marrow lesions on knee MRI: Data from the osteoarthritis initiative. Osteoarthritis Cartilage 2010;18:1393-401.
- Felson DT, Lynch J, Guermazi A, et al. Comparison of BLOKS and WORMS scoring systems part II. Longitudinal assessment of knee MRIs for osteoarthritis and suggested approach based on their performance: Data from the Osteoarthritis Initiative. Osteoarthritis Cartilage 2010;18:1402-7.
- Hunter DJ, Arden N, Conaghan PG, et al. Definition of osteoarthritis on MRI: Results of a Delphi exercise. Osteoarthritis Cartilage 2011;19:963-9.
- 12. Mullen PM. Delphi: myths and reality. J Health Organ

Manag 2003;17:37-52.

- 13. Jones J, Hunter D. Consensus methods for medical and health services research. BMJ 1995;311:376-80.
- Kornaat PR, Ceulemans RYT, Kroon HM, et al. MRI assessment of knee osteoarthritis: Knee Osteoarthritis Scoring System (KOSS) - Inter-observer and intraobserver reproducibility of a compartment-based scoring system. Skeletal Radiol 2005;34:95-102.
- Hunter DJ, Guermazi A, Lo GH, et al. Evolution of semiquantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). Osteoarthritis Cartilage 2011;19:990-1002.
- Roemer FW, Hunter DJ, Crema MD, et al. An illustrative overview of semi-quantitative MRI scoring of knee osteoarthritis: Lessons learned from longitudinal observational studies. Osteoarthritis Cartilage 2016;24:274-89.
- Runhaar J, Schiphof D, van Meer B, et al. How to define subregional osteoarthritis progression using semiquantitative MRI Osteoarthritis Knee Score (MOAKS). Osteoarthritis Cartilage 2014;22:1533-6.
- Guermazi A, Roemer FW, Hayashi D, et al. Assessment of synovitis with contrast-enhanced MRI using a whole-joint semiquantitative scoring system in people with, or at high risk of, knee osteoarthritis: the MOST study. Ann Rheum Dis 2011;70:805-11.
- Pakin SK, Xu J, Schweitzer ME, et al. Rapid 3D-T1rho mapping of the knee joint at 3.0T with parallel imaging. Magn Reson Med 2006;56:563-71.
- Regatte RR, Akella SVS, Lonner JH, et al. T1rho relaxation mapping in human osteoarthritis (OA) cartilage: comparison of T1rho with T2. J Magn Reson Imaging 2006;23:547-53.
- Duvvuri U, Reddy R, Patel SD, et al. T1rho-relaxation in articular cartilage: effects of enzymatic degradation. Magn Reson Med 1997;38:863-7.
- Li X, Benjamin Ma C, Link TM, et al. In vivo T1ρ and T2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. Osteoarthritis Cartilage 2007;15:789-97.
- 23. Menezes NM, Gray ML, Hartke JR, et al. T2 and T1rho MRI in articular cartilage systems. Magn Reson Med 2004;51:503-9.
- Dunn TC, Lu Y, Jin H, et al. T2 Relaxation Time of Cartilage at MR Imaging: Comparison with Severity of Knee Osteoarthritis. Radiology 2004;232:592-8.
- 25. Deichmann R, Adolf H, Nöth U, et al. Fast T2-mapping with snapshot flash imaging. Magn Reson Imaging

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1995;13:633-9.

- 26. McKenzie CA, Chen Z, Drost DJ, et al. Fast acquisition of quantitative T2 maps. Magn Reson Med 1999;41:208-12.
- Multanen J, Rauvala E, Lammentausta E, et al. Reproducibility of imaging human knee cartilage by delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) at 1.5 Tesla. Osteoarthritis Cartilage 2009;17:559-64.
- van Tiel J, Bron EE, Tiderius CJ, et al. Reproducibility of 3D delayed gadolinium enhanced MRI of cartilage (dGEMRIC) of the knee at 3.0 T in patients with early stage osteoarthritis. Eur Radiol 2013;23:496-504.
- Bashir A, Gray ML, Burstein D. Gd-DTPA2- as a measure of cartilage degradation. Magn Reson Med 1996;36:665-73.
- Bashir A, Gray ML, Boutin RD, et al. Glycosaminoglycan in articular cartilage: in vivo assessment with delayed Gd(DTPA)(2-)-enhanced MR imaging. Radiology 1997;205:551-8.
- MacKay JW, Low SBL, Smith TO, et al. Systematic review and meta-analysis of the reliability and discriminative validity of cartilage compositional MRI in knee osteoarthritis. Osteoarthritis Cartilage 2018;26:1140-52.
- Prasad AP, Nardo L, Schooler J, et al. T1ρ and T2relaxation times predict progression of knee osteoarthritis. Osteoarthritis Cartilage 2013;21:69-76.
- 33. Mosher TJ, Liu Y, Torok CM. Functional cartilage MRI T2 mapping: evaluating the effect of age and training on knee cartilage response to running. Osteoarthritis Cartilage 2010;18:358-64.
- Akella S V, Regatte RR, Gougoutas AJ, et al. Proteoglycaninduced changes in T1rho-relaxation of articular cartilage at 4T. Magn Reson Med 2001;46:419-23.
- 35. Wang L, Regatte RR. Quantitative mapping of human cartilage at 3.0T: parallel changes in  $T_2$ ,  $T_1\rho$ , and dGEMRIC. Acad Radiol 2014;21:463-71.
- Li X, Han ET, Ma CB, et al. In vivo 3T spiral imaging based multi-slice T1p mapping of knee cartilage in osteoarthritis. Magn Reson Med 2005;54:929-36.
- Schiphof D, Oei EHG, Hofman A, et al. Sensitivity and associations with pain and body weight of an MRI definition of knee osteoarthritis compared with radiographic Kellgren and Lawrence criteria: A population-based study in middle-aged females. Osteoarthritis Cartilage 2014;22:440-6.
- 38. Zhu Z, Laslett LL, Jin X, et al. Association between MRI-

detected osteophytes and changes in knee structures and pain in older adults: a cohort study. Osteoarthritis Cartilage 2017;25:1084-92.

- 39. van der Voet JA, Runhaar J, van der Plas P, et al. Baseline meniscal extrusion associated with incident knee osteoarthritis after 30 months in overweight and obese women. Osteoarthritis Cartilage 2017;25:1299-303.
- 40. Teichtahl AJ, Cicuttini FM, Abram F, et al. Meniscal extrusion and bone marrow lesions are associated with incident and progressive knee osteoarthritis. Osteoarthritis Cartilage 2017;25:1076-83.
- Zhang F, Kumm J, Svensson F, et al. Risk factors for meniscal body extrusion on MRI in subjects free of radiographic knee osteoarthritis: Longitudinal data from the Osteoarthritis Initiative. Osteoarthritis Cartilage 2016;24:801-6.
- Badlani JT, Borrero C, Golla S, et al. The effects of meniscus injury on the development of knee osteoarthritis: Data from the osteoarthritis initiative. Am J Sports Med 2013;41:1238-44.
- 43. Englund M, Guermazi A, Gale D, et al. Incidental Meniscal Findings on Knee MRI in Middle-Aged and Elderly Persons. N Engl J Med 2008;359:1108-15.
- Hayashi D, Felson DT, Niu J, et al. Pre-radiographic osteoarthritic changes are highly prevalent in themedial patella and medial posterior femur in older persons: Framingham OA study. Osteoarthritis Cartilage 2014;22:76-83.
- 45. Guermazi A, Niu J, Hayashi D, et al. Prevalence of abnormalities in knees detected by MRI in adults without knee osteoarthritis: Population based observational study (Framingham Osteoarthritis Study). BMJ 2012;345:e5339.
- 46. Javaid MK, Lynch JA, Tolstykh I, et al. Pre-radiographic MRI findings are associated with onset of knee symptoms: the most study. Osteoarthritis Cartilage 2010;18:323-8.
- 47. Felson DT, Niu J, Neogi T, et al. Synovitis and the risk of knee osteoarthritis: the MOST Study. Osteoarthritis Cartilage 2016;24:458-64.
- 48. Roemer FW, Kwoh CK, Hannon MJ, et al. What Comes First? Multitissue Involvement Leading to Radiographic Osteoarthritis: Magnetic Resonance Imaging-Based Trajectory Analysis Over Four Years in the Osteoarthritis Initiative. Arthritis Rheumatol 2015;67:2085-96.
- 49. Liebl H, Joseph G, Nevitt MC, et al. Early T2 changes predict onset of radiographic knee osteoarthritis: data from the osteoarthritis initiative. Ann Rheum Dis 2015;74:1353-9.

### Page 6 of 6

- 50. Sharma L, Chmiel JS, Almagor O, et al. Significance of preradiographic magnetic resonance imaging lesions in persons at increased risk of knee osteoarthritis. Arthritis Rheumatol 2014;66:1811-9.
- 51. Katsuragi J, Sasho T, Yamaguchi S, et al. Hidden

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osteophyte formation on plain X-ray is the predictive factor for development of knee osteoarthritis after 48 months - data from the Osteoarthritis Initiative. Osteoarthritis Cartilage 2015;23:383-90.