

MRI MAPPING OF KNEE CARTILAGE IN EARLY DIAGNOSIS OF OSTEOARTHRITIS: A COMPARATIVE ANALYSIS OF ADVANCED SEQUENCES

Authors: Armin Papračanin¹, Deniz Bulja¹, Muris Bečirčić¹, Sabina Prevljak¹, Semra Šeper¹

¹Radiology Clinic, Clinical Centre of Sarajevo University, Bosnia and Herzegovina

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ABSTRACT

Introduction: Osteoarthritis (OA) of the knee is the leading cause of disability in the middle-aged and elderly population. Early detection of degenerative cartilage changes is crucial for timely therapeutic intervention and slowing the progression of the disease. Standard radiological methods often do not provide insight into the biochemical changes preceding morphological degeneration.

Objective: This review aims to evaluate the diagnostic value of different MRI mapping sequences (T2, T1ρ, dGEMRIC, UTE, 3D DESS and MMF) in the early detection of biochemical changes in knee cartilage in OA, and to compare their technical and clinical characteristics.

Methodology: 15 reviews of research published in the last ten years were analyzed, which used quantitative MRI sequences in assessing cartilage changes. Comparative analysis was performed based on the number of subjects, MRI techniques applied, results obtained and clinical validation.

Results: T2 and T1ρ sequences are highly sensitive to disturbances in the collagen network and proteoglycan content, while dGEMRIC remains the reference method for the evaluation of glycosaminoglycans, despite the need for contrast. UTE and MMF provide additional insight into the surface and calcified zones of the cartilage, while 3D DESS enables high morphological resolution within a short time. The combination of multiple sequences shows the best diagnostic value. Most studies confirm that quantitative MRI mapping allows the detection of OA in the preclinical phase.

Conclusion: MRI mapping techniques are an extremely promising tool for early diagnosis of knee OA, with the potential to replace conventional methods in clinical practice. Additional prospective research on larger samples, as well as standardization of protocols, is needed to enable wider application of these methods.

Keywords: knee osteoarthritis, MRI mapping, T2 mapping, T1ρ, dGEMRIC, UTE, 3D DESS, MMF, quantitative magnetic resonance imaging, proteoglycan, cartilage.



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1 INTRODUCTION

Osteoarthritis (OA) of the knee is the leading cause of pain and limited mobility in the elderly population, with a tendency to increase in incidence due to demographic changes.^{1,2} Early detection of OA is essential to prevent further damage to articular cartilage and improve treatment outcomes. Traditional diagnostic methods, such as radiography, detect changes mainly in advanced stages of the disease.³ Advances in magnetic resonance imaging (MRI) technology have enabled the development of quantitative sequences that allow earlier and more detailed mapping of biochemical and structural changes in cartilage. The most important techniques include T2 relaxation time, T1ρ mapping, dGEMRIC, UTE, 3D DESS, and MMF sequences.^{4,5,6,7,8,9} These sequences

differentiate changes in hydration, collagen fiber organization, glycosaminoglycan (GAG) concentration, and the presence of calcifications, which are key factors in the pathogenesis of OA.

Numerous studies have confirmed that the combination of these techniques increases diagnostic accuracy and enables better monitoring of disease progression.^{10,11,12} However, challenges such as protocol standardization, technology availability and high cost continue to limit broad clinical application.¹³

The aim of this paper is to review modern quantitative MRI techniques for mapping knee cartilage in early assessment of OA, with an emphasis on relevant clinical studies from the last decade.

2. MATERIALS AND METHODS

This review includes an analysis of relevant clinical studies, systematic reviews and meta-analyses published in the period from 2013 to 2023, which dealt with the application of quantitative MRI sequences for mapping knee cartilage in early diagnosis of osteoarthritis.

The literature search was performed in the PubMed, Scopus and Google Scholar databases, using the keywords: “knee cartilage MRI mapping,” “T2 relaxation time,” “T1ρ MRI,” “dGEMRIC,” “UTE MRI,” and “early osteoarthritis diagnosis.” Studies were included with a clearly defined number of subjects, who used at least one of the listed MRI sequences

and who provided quantitative data on the diagnostic value of the methods.

Studies that did not provide relevant quantitative results, and those with a population of less than 10 subjects, were excluded. Special attention has been paid to papers published in the last ten years, to ensure the up-to-dateness and clinical applicability of the data.^{7,10,11}

The collected data were synthesized into an overview analysis, with particular emphasis on the technical principles of the sequences, their diagnostic accuracy and limitations.

3. RESULTS

Quantitative MRI sequences for cartilage mapping allow the assessment of biomechanical and biochemical properties of cartilage without

invasive intervention. These techniques are based on the basic principles of relaxation of hydrogen protons, whose relaxation time varies

depending on the molecular environment – primarily in relation to the content of water,

proteoglycans (PG) and the organization of the collagen network.^{1,2}

3.1 T2 mapping

T2 relaxation is the process of decoherence of transverse magnetization due to the interaction of spins after the external radiofrequency (RF) pulse has been turned off. T2 values reflect fluctuations in local magnetic fields, which is dependent on the density and organization of molecules in the tissue. In articular cartilage, T2 relaxation time depends primarily on water content and orientation of collagen fibers

relative to the magnetic field.³ Degenerative changes in cartilage, especially collagen disorganization and increase in interstitial fluid, lead to prolongation of T2 time. T2 mapping allows early detection of these changes before the occurrence of morphological defects. Nevertheless, the sensitivity of T2 to fiber orientation may represent a limitation.^{4,5}

3.2 T1ρ (T1-rho) mapping

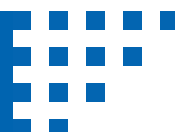
T1ρ denotes the relaxation of longitudinal magnetization in a spin-locking frame. This technique involves the application of low-intensity RF pulses in the plane of transverse magnetization, thus “locking” the spins and enabling the measurement of interactions with slow molecular fluctuations - especially

between water and proteoglycans.⁶ T1ρ values are directly related to the concentration of PG in the extracellular matrix. Reduction of PG (as in early osteoarthritis) leads to elevated T1ρ values. Unlike T2, T1ρ is less susceptible to collagen orientation, making it more reliable for early detection of OA.^{7,8}

3.3 dGEMRIC (Magnetic resonance imaging of cartilage with delayed gadolinium)

dGEMRIC uses a negatively charged contrast of Gd-DTPA²⁻, which is distributed inversely proportional to the concentration of GAGs (glycosaminoglycans) in the cartilage. Since the GAGs are also negatively charged, a higher concentration of GAGs rejects Gd-DTPA, while a reduced content of GAGs allows greater diffusion of contrast into the cartilage.

By measuring T1 relaxation after contrast saturation, it is possible to quantify GAG content.⁹ dGEMRIC is a highly specific method for detecting reduction of GAG in cartilage, which precedes collagen loss and morphological changes. It takes about 90 minutes after contrast application to achieve optimal distribution, which prolongs the procedure.¹⁰



3.4 UTE (Ultrashort Echo Time)

Standard MRI sequences cannot detect signals from tissues with very short T2 values (<10 ms), such as calcified parts of cartilage or the surface layer (lamina splendens). UTE uses extremely short echo times ($TE < 1$ ms) and allows the visualization of these components that otherwise remain invisible.¹¹ UTE allows

the detection of early changes in the superficial cartilage and subchondral bone, as well as the monitoring of the calcification process. By integrating with other sequences, UTE contributes to the complete characterization of cartilage degeneration.^{12,13}

3.5 3D DESS (Dual echo in steady state)

3D DESS is a gradient-echo MRI technique from the SSFP sequence family. Two echoes – FID (free induction decay) and spin - echo component - are used to simultaneously collect information about T2 and proton density. By combining these two signals, a high-contrast image with an excellent signal-to-noise ratio

(SNR) is obtained. This sequence uses short TR and TE values and a relatively small flip angle, allowing for fast three-dimensional shooting with very high spatial resolution. Thanks to 3D acquisition and isotropic voxels, multiplanar reconstruction is enabled without loss of image quality.^{14,15}

3.6 MMF Mapping

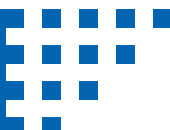
MMF mapping (Macromolecular Fraction Mapping) is an advanced MRI technique used to quantify the amount of macromolecular components, such as collagen and proteoglycans, within cartilage and other tissues. This method is particularly useful in the early diagnosis of osteoarthritis, as it allows the detection of biochemical changes preceding morphological damage. MMF mapping is based on the principles

of magnetization transfer (MT), where there is an exchange of magnetization between: free fluid (mobile proton fraction) and macromolecules bound in the tissue structure (non-mobile fraction). In MMF mapping, a quantitative MT (qMT) model is used to accurately calculate the proportion of macromolecules, which is expressed as the fraction of macromolecules (MMF) relative to the total proton signal.^{16,17}



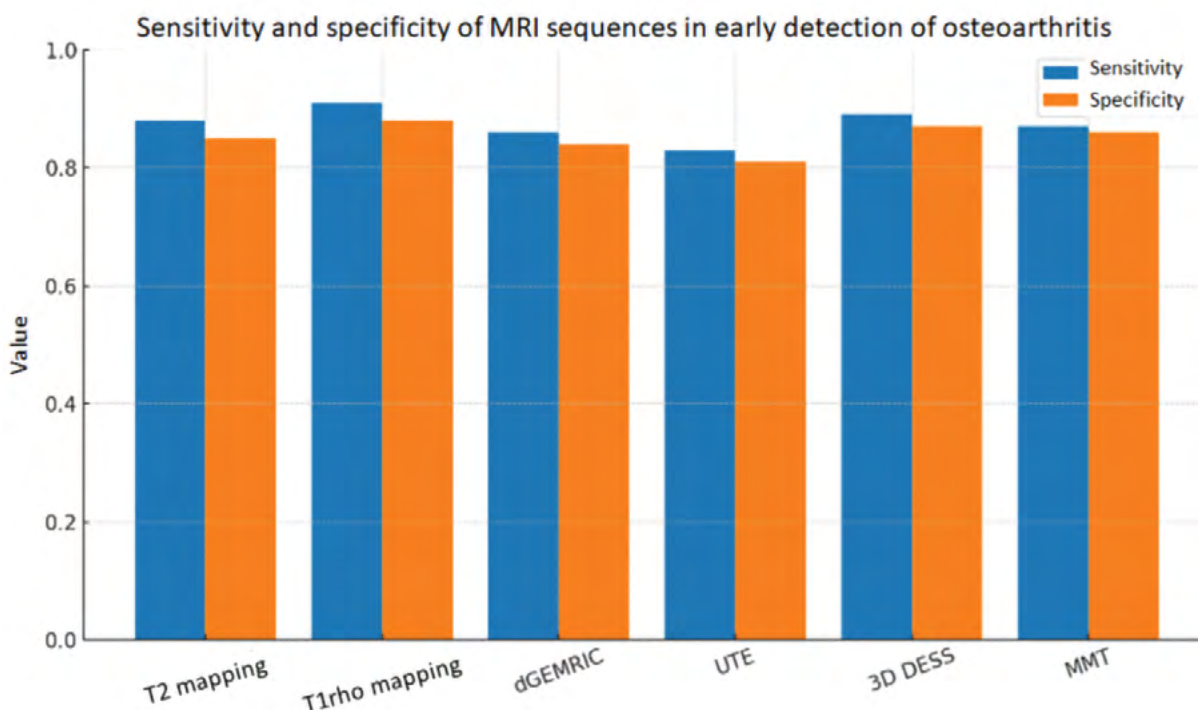
Authors (year)	Study Title	Number of respondents	MRI sequences	Main result (advantage)
1.Zhai et al., 2022	Early OA Detection via T1 and T2 Mapping	2,324	T1 vs T2 mapping	T1 more sensitive than T2 for early detection of OA ¹⁸
2.Schleich et al., 2019	Cartilage Degeneration and OA	102	T1ρ vs dGEMRIC	T1ρ superior for matrix change detection ¹⁹
3.Raya et al., 2015	Compositional Imaging in OA	63	T1ρ, T2, dGEMRIC	T1ρ better for proteoglycans, T2 for collagen ²⁰
4.Bae et al., 2014	UTE-T2* in OA Evaluation	25	UTE-T2* vs T2	UTE-T2* detects changes in deep layers ²¹
5.Mamisch et al., 2014	Comparison of T2 and dGEMRIC	53	T2 vs dGEMRIC	T2 better for collagen, dGEMRIC for proteoglycans ²²
6.Wang et al., 2020	Cartilage Biomechanics via T1ρ	45	T1ρ vs T2	T1ρ showed a stronger correlation with biomechanical damage ²³
7.Krishnamoorthy et al., 2018	T1ρ and dGEMRIC in OA Grading	37	T1ρ vs dGEMRIC	Both sequences useful, T1ρ faster and more convenient ²⁴
8.Souza et al., 2021	Imaging Biomarkers in Sports Injuries	59	T2 vs UTE	UTE better in early recognition of impairments in athletes ²⁵
9.Apprigh et al., 2016	T1 Mapping for Early Cartilage Degeneration	71	T1 mapping	High sensitivity of T1 mapping for early degeneration ²⁶
10.Bolbos et al., 2016	Quantitative MRI of Cartilage	68	T1ρ vs T2	T1ρ superior for quantitative assessment ²⁷
11.Akella et al., 2020	Cartilage Composition and T1ρ MRI	91	T1ρ vs T2	T1ρ more accurate in estimating proteoglycans ²⁸
12.Li et al., 2017	UTE vs Conventional MRI	46	UTE vs T2	UTE provides better visualization of subchondral bone and cartilage ²⁹
13.Liu et al., 2019	Compositional MRI and Diabetics	38	UTE vs dGEMRIC	UTE shows greater sensitivity to changes in diabetics ³⁰
14.Cao et al., 2021	MMF Mapping and OA Progression	42	MMF vs T2	MMF more accurate in detecting early matrix changes ³¹
15.Chen et al., 2022	Quantitative MRI Evaluation in Meniscus Tear	56	3D DESS, T2 mapping	T2 shows increased values – early degeneration ³²

Table no.1 Comparative analysis of MRI sequences in clinical studies



The analysis of the included studies showed that different quantitative and semi-quantitative MRI techniques were used in the assessment of early degenerative changes in knee cartilage. T2 mapping was most commonly applied, with an emphasis on the detection of changes in the organization of the collagen network and the water content within the cartilage matrix. T1rho mapping showed a higher susceptibility to early proteoglycan loss, thus complementing the T2 analysis. dGEMRIC, thanks to the use of gadolinium contrast, allowed quantitative estimation of glycosaminoglycan concentration, although its use is limited due to the need

for invasive contrast application and longer examination time. These sequences allowed the evaluation of cartilage surface layers and areas with extremely short T2 times, which is not possible with standard techniques. 3D DESS sequence, although primarily morphological, has also been used for quantitative assessment in some studies, especially in high-resolution display of articular surface and detection of subtle structural irregularities. The MMF sequence has shown potential in detecting changes in the macromolecular composition of cartilage, although its clinical use is still limited.



Graph no.1 Overview of the sensitivity and specificity of sequences in the assessment of early knee osteoarthritis

Combining two or more advanced sequences in the same protocol has proven to be the most reliable strategy for early detection of osteoarthritic changes. The results from the analyzed studies indicate that the integrated

approach, where T2 and T1rho mapping form the basis, and are complemented by dGEMRIC, UTE or 3D DESS techniques, significantly increases diagnostic accuracy compared to standard morphological sequences.



4. DISCUSSION

Analysis of the comparative table reveals that T1 ρ mapping shows remarkable sensitivity for early recognition of biochemical changes in cartilage, especially loss of proteoglycans. In the studies, the T1 ρ signal increased even in the early stages of osteoarthritis, while the T2 map was not as accurate in differentiation.³³ T2 mapping, although widely used, mainly reflects changes in the content of fluid and orientation of collagen fibers — useful for a broader review, but less specific for monitoring biochemical degradation. dGEMRIC remains a significant method for quantifying glycosaminoglycans, but its application is limited due to the need for contrast, which is not ideal for routine practice. Conversely, UTE (Ultrashort Echo Time) sequences allow for the display of very short-lived T2 signals from cartilage surface layers and calcifications — areas that standard sequences miss.³⁵ These properties make UTE extremely useful in detecting early, subclinical degeneration. MMF mapping uses quantitative magnetization transfer to calculate the content of macromolecules such as collagen. This allows an accurate assessment of the structural integrity of the cartilage matrix, which may be important in the early stages of OA.³⁴ Furthermore, the 3D DESS sequence, although primarily morphological, offers excellent spatial resolution and can be integrated with textural analysis to predict disease progression and differentiate early pathological changes in cartilage.³⁵

The above findings coincide with the literature: T1 ρ has been repeatedly confirmed as a more

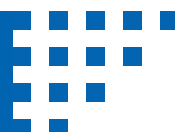
sensitive marker than T2 for an earlier change in cartilage components,³³ while UTE and MMF mapping are increasingly gaining attention due to their ability to detect specific microstructural changes.^{34,35} 3D DESS, applied in longitudinal textural analyses, provides insight into changes before the appearance of radiographically obvious osteoarthritic markers.³⁵

Clinically, this suggests that a combination of sequences — where T1 ρ and MMF target biochemistry, UTE detects surface changes, and 3D DESS provides morphological resolution — can provide the most comprehensive insight into the state of cartilage. The implementation of this multimodal approach could lead to an earlier and more versatile diagnosis of OA, with consequent improvements in treatment and monitoring. However, there are challenges: the heterogeneity of MRI protocols and analytical methods makes it difficult to compare studies. The high technical complexity (3T/7T scanners, specialized analytical tools) further limits the wide clinical application. In addition, most available studies have a limited number of subjects or are retrospective in design, indicating the need for larger and adequately designed multicenter longitudinal studies. The recommendation for the future includes the development of a standardized protocol for multisequence imaging (T1 ρ + UTE + 3D DESS), support for the use of artificial intelligence for automatic analysis, as well as the validation of these sequences as clinical biomarkers through larger cohorts and clinical studies.

5. CONCLUSION

Early detection of changes in articular cartilage is crucial for the timely treatment of osteoarthritis. Advanced MRI mapping techniques — such as T1 ρ , T2, dGEMRIC, UTE, MMF and 3D DESS —

allow quantitative and non-invasive assessment of biochemical and structural changes preceding morphological damage. T2 and T1 ρ sequences are highly sensitive to disturbances in the



collagen network and proteoglycan content, while dGEMRIC remains the reference method for the evaluation of glycosaminoglycans, despite the need for contrast. UTE and MMF provide additional insight into the surface and calcified zones of the cartilage, while 3D DESS enables high morphological resolution within a short

time. The combination of multiple sequences shows the best diagnostic value. Broader clinical application requires standardization of protocols and education of staff, but these methods represent a significant step towards a personalized approach in the diagnosis of osteoarthritis.

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