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SYSTEMIC REVIEW

Recent Advances in MRI of the Articular Cartilage of the Knee

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ABSTRACT

Background: Articular cartilage is a vital component of the joint, as it is frequently exposed to trauma and is affected by several conditions and diseases such as osteoarthritis and hemophilic arthropathy. Therefore, its evaluation and assessment are crucial. Magnetic resonance imaging (MRI) plays a critical role in its evaluation. With the recent advances in MRI imaging, multiple techniques and modalities allow both morphological and physiological evaluation of articular cartilage. Morphological methods allow the evaluation of articular cartilage structural integrity, and physiological methods allow the evaluation of chemical changes in its components even prior to degeneration. This aids in the early detection and improved assessment of articular cartilage pathology. Therefore, it permits a more accurate evaluation of patients with articular cartilage issues and defects, allowing for prompt treatment and high better quality of life. This article reviews recent and innovative MRI techniques and sequences for morphological and functional evaluation of the cartilage.

Methods: A broad-based internet search, utilizing multiple academic search engines, Google Scholar, and PubMed, using the keywords for title and abstract. We found 17500 results and excluded 1700 papers from the title and abstract. Furthermore, papers emphasizing the imaging of specific peripheral joints without discussing the main techniques were excluded. Finally, our search yielded 15 articles highlighting the most recent imaging and evaluation techniques for articular cartilage. Recent advancements and new MRI techniques aid in elucidating the anatomical and physiological details of articular cartilage, allowing for the early detection and treatment of the articular cartilage.

Conclusions: Multiple recent advances and new MRI techniques help better delineate the anatomical and physiological details of the articular cartilage, so early interference and treatment of cartilage defects.

Keywords: MRI; Recent advances; articular cartilage; 3D

INTRODUCTION

Articular cartilage is a type of hyaline cartilage with a low number of chondrocytes and a significant number of extracellular matrices surrounding them. The extracellular matrix is composed of collagen and water. It is surrounded by fluid produced by the synovial membrane adjacent to it, or it is immediately adjacent to the subchondral bone plate [1]. The primary function of hyaline cartilage is to absorb and distribute loading forces and, to a lesser extent, tension forces. It must also have low surface friction in order to facilitate smooth movement [2]. MRI is

primarily utilized to examine joint cartilage. Due to its high-water content, it appears uniform on standard MRI scans and has a signal strength comparable to or slightly greater than muscle. It has a medium signal strength at T1, a low signal strength at T2, and a medium to slightly high signal strength at PD. At PDFS/STIR: signal strength is relatively high [3]. There are different practical ways to evaluate articular cartilage that focus on the following extracellular matrix components. Before these procedures can be implemented in practice, additional research is necessary. This is due to strict technical conditions (such as a unique RF pulse and a 7T magnet) and contrast media issues. This comprehensive study discusses the new MRI techniques for measuring articular cartilage [4].

Evaluation of the morphology of the joint cartilage

The morphological measurement of cartilage reveals the size and structure of the tissue. There are numerous methods for capturing images of fissures and localized or extensive cartilage loss [5], including 3D MRI sequences [6].

Several different 3D MRI images have been made. The strength and size of the scanner have determined the feasibility of 3D images [6].

3D MRI sequences include 3d FSE and 3d GRE [7]: **Fig (2) [6]**

The benefits of 3D MRI imaging include less Partial Volume Averaging, Multi-planar Reconstructions in any plane with any slice thickness, Segmentation and Quantitative Assessment, and Metal Artefact Reduction. Still, there are limitations, such as the lengthy acquisition time. The 3D sequences have only one image contrast weighting, as opposed to 2D sequences, which have PD (for assessing the menisci and cartilage), T2 (for assessing the tendons and ligaments), and T1 (for better assessing the marrow) contrast weightings [6].

The gradient recalled echo sequence (GRE) was the first 3D sequence for studying joint cartilage. Traditionally, they are divided into dark fluid sequences (e.g., flash gradient echo or FLASH) and bright fluid sequences (e.g., double echo steady-state or DESS) [8]. (Fig 3) [8].

They are available widely on most machines, even those with weaker magnetic fields, and thereby frequently utilized in clinical practice [6].

The main concept behind this method is spoiled gradient recalled echo (SPGR), Fig (4) [6] which has relative T1-weighting. shows a relative T2-weighted dual-echo steady state (DESS) MRI [5]. Moreover, these pulse patterns are frequently produced by inhibiting fat or stimulating water [9].

The 3D GRE MRI is an effective method for determining the cartilage's thickness and size [5]. However, GRE sequences cannot assess other joint components, such as the menisci, tendons, ligaments, and bones. It requires a long acquisition time [6] and susceptibility artefact [5]. Moreover, these sequences cannot be used to determine sites prone to this artefact, such as hardware or bone marrow [6].

Additionally, a low edema signal in the bone marrow on GRE images makes it difficult to determine anomalies in the bone and cartilage (6).

3D FSE sequences (Fig. 5) [10]:

Scanners and coils have advanced, and the 3D FSE sequence can make signals appear as 2D FSE proton density (PD) (Fig. 2) or T2 sequence. Even though these processes can provide a full image of the joint, they are not available on all older scanners and function most effectively on 3-T scanners [9].

Furthermore, 3-D Fast SE Imaging includes bSSFP balanced FFE (fast field echo) and DEFT (Driven equilibrium Fourier transform). Both increase the signal from the joint fluid while keeping the signal from the cartilage, making the difference between the fluid and the tissue more explicit. SPACE combines SPACE Imaging (perfect sampling with application-optimized contrast using different flip angles) [11].

Therefore, it improves SNR by enhancing SNR's functionality; nevertheless, it cannot accurately measure subchondral bone

[5]. Joint cartilage can be effectively evaluated in 3D. Other tissues, such as menisci, tendons, and bone marrows, can be evaluated more effectively in 2D [6].

Physiological evaluation of the cartilage:

Changes in the matrix's water and macromolecular structures, such as the PG and collagen network, are the first indications of cartilage breakdown. These physiological changes can be measured with quantitative MRI mapping [12].

The most effective methods for early cartilage loss detection are those sensitive and specific to these changes [12]. MRI numeric maps, which convert MRI relaxation times into numeric values of tissues, can detect slight changes in cartilage composition (13).

Quantitative MRI methods for cartilage matrix biochemistry can be put into four groups: (i) methods based on relaxometry, such as T1 (with and without contrast agent), T2, and T1 relaxation time quantification; (ii) methods based on diffusion measurement; (iii) methods based on magnetization transfer measurements, such as conventional magnetization transfer and chemical exchange saturation transfer (CEST); and (iv) sodium imaging (Li).

The role of water and collagen in the joint cartilage matrix is based on the T2 relaxing time. It varies based on the width of the joint cartilage and the distribution of water and proteoglycans in the ECM. T2 relaxation measurements reveal areas with water, directly proportional to cartilage degradation severity. It is crucial to select an MRI technique that can measure T2 relaxation with high precision [14].

Delayed gadolinium (gd)-enhanced proton mri of cartilage (dgemric)

When proteoglycans in the extracellular matrix (ECM) degrade, joint cartilage starts to degrade prematurely [14].

This method measures the amount of PG in cartilage by measuring T1 in the presence of the contrast agent. It is based on the fact that PG contains numerous negatively charged groups or the GAG. In addition, the contrast agent Gd-DTPA2 (Magnevist; Berlex Laboratories, Wayne, NJ) is administered directly (or into the joint) and diffuses throughout the cartilage. The time required for diffusion depends on the thickness of the cartilage; in weight-bearing femur cartilage, the process takes approximately two hours. Because Gd-DTPA2 has a negative charge, it will be distributed in low concentrations in areas with abundant GAG (normal cartilage) and higher concentrations in areas with less GAG (degenerated cartilage) [12].

T2 mapping:

T2 measurement is an effective method for identifying the biology of cartilage matrix the cartilage matrix's biology [7].

The underlying concept is that individuals with localized or extensive cartilage damage have locations with longer T2 relaxation times. In addition, a correlation has been established between damaged cartilage and elevated T2 levels. Since PGs do not significantly alter T2-mapping. The most precise and well-planned of these studies is T2 mapping (Fig. 6) [15].

This sequence has a short collection time, allowing it to be utilized in clinical imaging both now and in the future [15].

T1rho imaging

It is a sensitive MRI method that can detect early proteoglycan loss in the ECM, which is achieved through T1rho mapping. It searches for variations in the loosening of magnetic field spins. This method differs from T2 mapping, which examines changes in the collagen structure (Fig. 7 [16]) [14]. The loss of PG in cartilage was linked to lengthening T1 opening time [12].

The primary advantage of T1rho is that it is more accurate than T2 mapping at detecting small changes in cartilage [17], but it does require a specific MR machine [17].

Quantitative sodium MRI:

The amount of salt in cartilage is significantly higher than that of the adjacent joint fluid or bone. It has been demonstrated that quantitative sodium MRI is a highly accurate method for detecting glycosaminoglycans in cartilage. Normal cartilage is sodium-rich and rich in proteoglycans. In contrast, injured cartilage

contains proteoglycan but is low in sodium and FCD (Fig. S1 [18]) [17].

There is an abundance of sodium in articular cartilage. Sodium MRI has been utilized to examine cartilage due to this fact. The absence of proteoglycans is indicated by the presence of excessive salt. This method is viewed as an alternative to dGEMRIC or measuring a focal cerebral defect [14]. This method is characterized by its sensitivity [17]; however, it has a low signal-to-noise ratio (SNR), a low spatial precision, requires special gear, and takes a long time to scan. It is best for ultrahigh fields (7 T) [19].

DWI

Depending on the rate at which water molecules can move around the proteoglycans and collagen structure of cartilage. DWI can provide vital information about the shape of tissues because it can detect water movement within tissues. The apparent diffusion coefficient (ADC) signal is low because the surviving cartilage components impede water movement. Conversely, damage to cartilage and alterations to its normal structure facilitate the movement of water and strengthen the cartilage signal of the ADC. These changes in ADC readings are depicted in (Fig. S2 [20]) [17].

DTI

It can also be used to examine the directions of water in cartilage's extracellular matrix. Water moves unevenly through normal cartilage because of its construction. Therefore, changes in anisotropy are likely caused by changes in how cartilage is constructed on a microscopic scale. The concept behind DTI is related to the layered arrangement of collagen fibers [17].

The primary advantage of DTI is that it can be used as a measurement for joint degeneration and can reveal how well the articular cartilage is still in good shape [17]. However, DWI and DTI have some limitations, such as the inability to visualize the inner structures of T2, such as tendons, ligaments, menisci, deep hardened layers of cartilage, and the bone cortex [12, 17]. Low SNR and how sensitive diffusion MRI is to motion.

Glycosaminoglycan chemical exchange saturation transfer (gag cest) imaging

GagCEST is an innovative technique for determining the composition of cartilage matrix. It is peculiar to GAG concentration and does not require a contrast agent dose (Fig. S3 [21]) [14].

When GAG is lost, the gag CEST score is reduced [17]. The primary advantage is that it is sensitive and specific to PG changes. However, it has a low signal-to-noise ratio (SNR), low spatial resolution, needs special gear, and takes a long time to scan, and it performs optimally in an ultrahigh field (7 T) [19].

Gadolinium hyaluronic acid nano particles MRI (Gd-HA MRI):

It is a novel MRI contrast agent with excellent longitudinal relaxation time and high biocompatibility. Moreover, it may simultaneously reach the inner portion of joint tissues (Fig. S4 [22]).

The significant advantage is that they work well as MR imaging probes to detect cartilage damage because they are the proper size and resemble ECM. It exits the body through urine without affecting organ function. However, injecting the contrast agent can cause side effects and tissue formation, and it can take a long time for the contrast agent to spread through the cartilage [19].

Magnetic resonance fingerprinting (MRF):

It is a fast and accurate method for mapping the knee joint cartilage using numerous parameters. It could distinguish between individuals with mild arthritis and healthy individuals. Because it is difficult to obtain, it is rarely used in clinical settings (Fig. S5 [23]) [24].

(CS) Compressed sensing:

Compressed sensing is a method of under sampling that has been used to lower the scan time of 3D FSE and composed mapping sequences (Fig. S6 [6]) [6, 17].

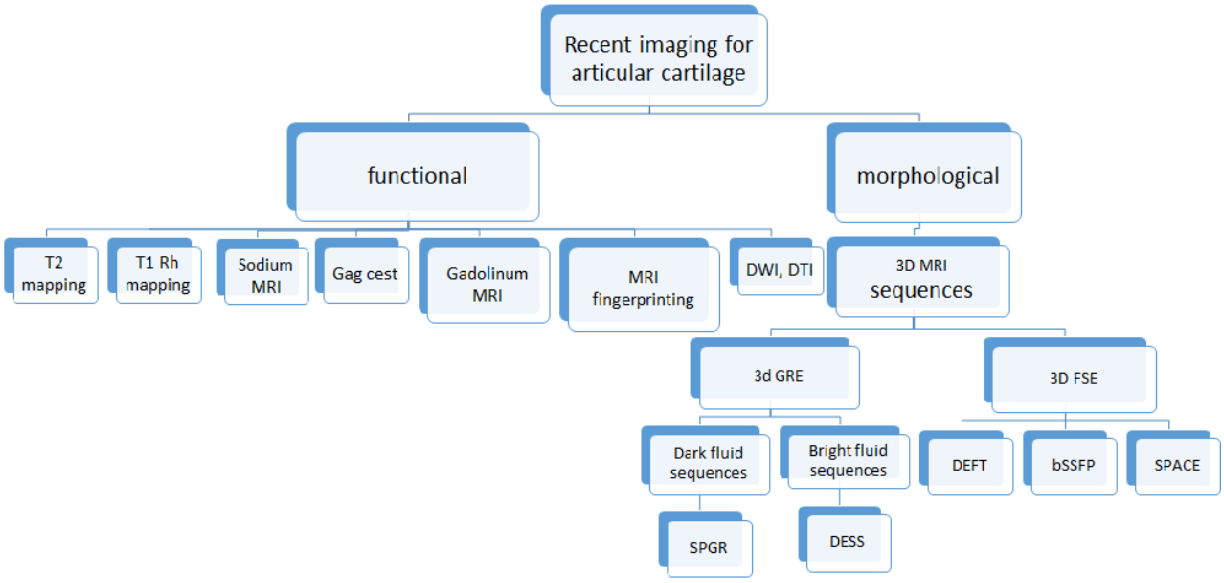

Figure 1: Study design

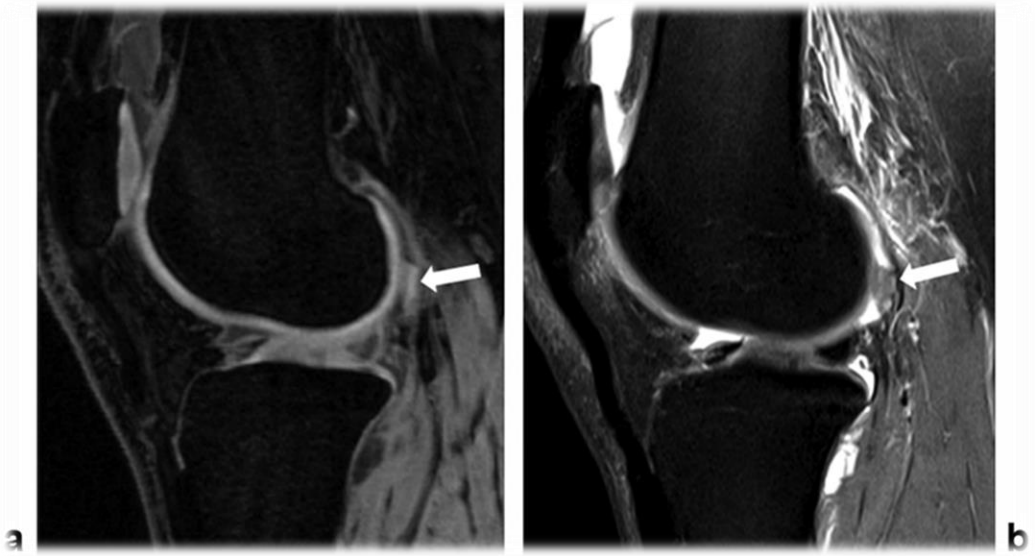

Fig 2:a) Displaced intra-articular cartilage fragment (arrow) from a lateral femoral condylar full-thickness chondral defect (not shown) is easily identified on the dark fluid three-dimensional gradient-recalled echo sagittal image due to the large contrast difference between the high signal of cartilage fragment and the dark fluid. (**b**) Two-dimensional proton-density fast spin-echo sagittal image also demonstrates the fragment (arrow), but it is slightly less distinct because it is partially averaged with adjacent synovial proliferation of similar intensity and is somewhat less distinct in bright fluid [6].

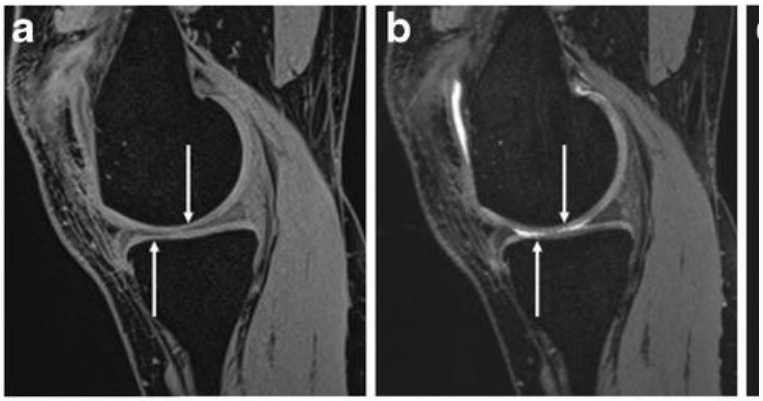

Fig 3: 32-year-old female marathon runner with episodes of medial knee pain. Comparison of sagittal FLASH (**a**), DESS (**b**) [8].

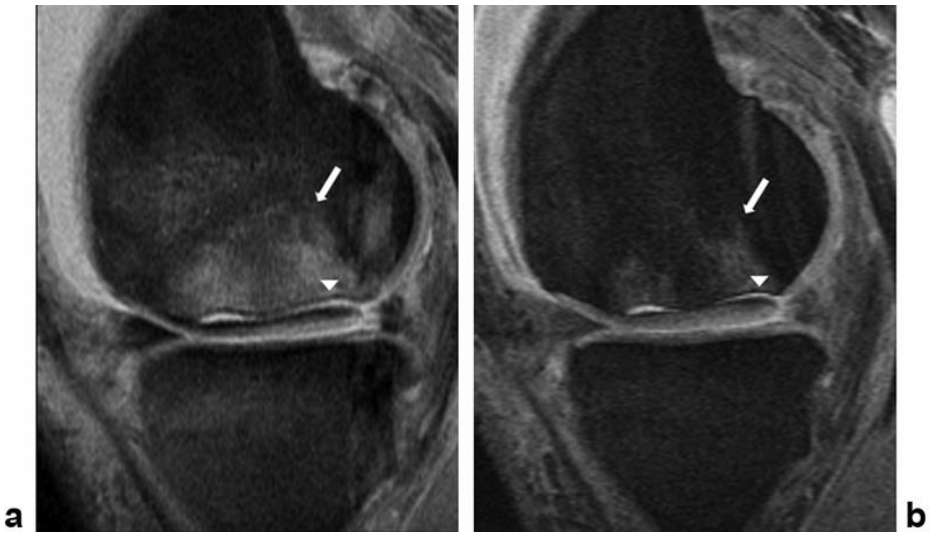

Fig. 4 A large osteochondral lesion of the medial femoral condyle with bright fluid (white arrowhead) undercutting an intra-articular osteochondral fragment is well visualized (**a**) on the sagittal fat-saturated two-dimensional (2D) proton-density (PD) fast spin-echo (FSE) and (**b**) on the bright fluid three-dimensional (3D) gradient-recalled echo (GRE) double-echo steady-state sequences. Associated bone marrow edema (white arrow) is prominent (a) on the 2D PD FSE image but is less conspicuous (b) on the 3D GRE image [6].

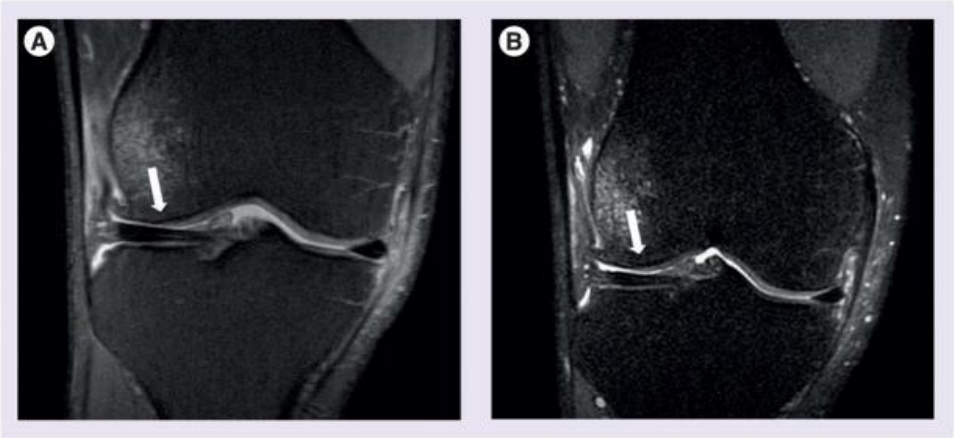

Fig 5: 2D and 3D imaging using fast spin echo [10]**.**

(a) Depicts traditional 2D fast spin echo (FSE) coronal proton density imaging of the knee with high signal-to-noise ratio and impressive tissue contrast. **(b)** An example of 3D FSE proton density imaging in the coronal plane.

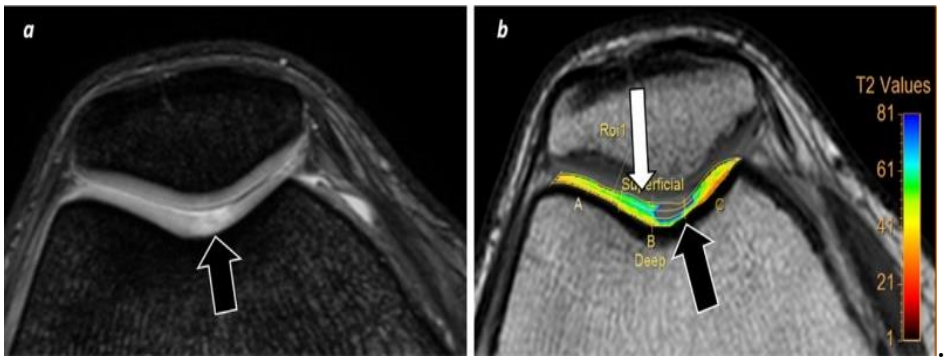

Fig 6 : **(a)** A focal area of signal intensity increase is identified (arrow) at trochlea on morphological axial FFE T2W sequence. **(b)** T2-mapping confirms a focal defect of signal with severe increase of T2 relaxation times at trochlear sulcus as well as early cartilage damage changes at superficial cartilage layer (white arrow), which not clearly seen on morphological sequence. FFE [15, 16].

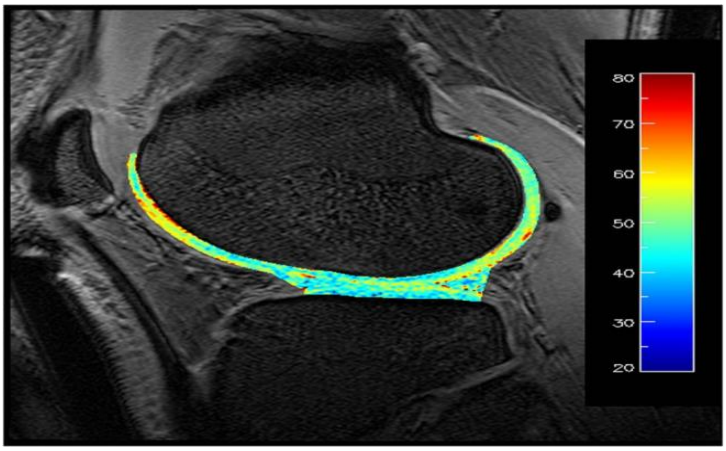

Fig 7: Normal T1rho color map. This color-coded T1rho map of the knee articular cartilage in a healthy research subject shows normal variation of T1rho signal across the articular surface of the lateral femoral condyle and lateral tibial plateau [17].

CONCLUSION

Recent advances and new MRI techniques make it easier to see the structural and physiological features of joint cartilage. In addition, 3D MRI images are used in morphological methods. The majority of quantitative MRI mapping consists of gradient patterns and physiological methods.

REFERENCES

1. Tsai CC, Kuo SH, Lu TY, Cheng NC, Shie MY, Yu JJABS, et al. Enzyme-cross-linked gelatin hydrogel enriched with an articular cartilage extracellular matrix and human adipose-derived stem cells for hyaline cartilage regeneration of rabbits. ACS Biomater. Sci. Eng. 2020; 6(9):5110-9.
2. Milner PE, Parkes M, Puetzer JL, Chapman R, Stevens MM, Cann P, et al. A low friction, biphasic and boundary lubricating hydrogel for cartilage replacement. Acta Biomater. 2018;65:102-11.
3. Waller BJ, physical education, health. The effect of aquatic exercise on symptoms, function, body composition and cartilage in knee osteoarthritis. J. Phys. Educ. Sport. 2016 (250).
4. Gold GE, Chen CA, Koo S, Hargreaves BA, Bangerter NK. Recent advances in MRI of articular cartilage. AJR 2009; 193(3):628.
5. Braun HJ, Gold GE. Advanced MRI of articular cartilage. Imaging in medicine 2011;3(5):541.
6. Altahawi F, Pierce J, Aslan M, Li X, Winalski CS, Subhas N, editors. 3D MRI of the Knee. Semin. Musculoskelet. 2021; (Vol. 25, No. 03, pp. 455-467). 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA Thieme Medical Publishers, Inc.
7. Altahawi F, Subhas NJ. 3D MRI in musculoskeletal imaging: current and future applications. Curr. Radiol. Rep. 2018; 6:1-14.
8. Van Dyck P, Vanhevel F, Vanhoenacker FM, Wouters K, Grodzki DM, Gielen JL, et al. Morphological MR imaging of the articular cartilage of the knee at 3 T—comparison of standard and novel 3D sequences. Insights Imaging 2015; 6(3):285-93.
9. Naraghi A, White LM. Three-dimensional MRI of the musculoskeletal system. AJR. 2012; 199(3):W283-W93.
10. Braun HJ, Gold GE. Advanced MRI of articular cartilage. Imaging in medicine. Imaging in medicine 2011; 3(5):541.
11. Ibrahim SU, Musa HQ, Fadhil AA. Assessment of Articular Cartilage of Knee Joint by Magnetic Resonance Imaging in Comparison with Arthroscopy of the Knee. IPMJ, 2020;19(2).
12. Li X, Majumdar SJ. Quantitative MRI of articular cartilage and its clinical applications. J. Magn. Reson. Imaging, 2013;38(5):991-1008.
13. Mars M, Chelli M, Tbini Z, Ladeb F, Gharbi SJ, Practice. MRI T2 mapping of knee articular cartilage using different acquisition sequences and calculation methods at 1.5 Tesla. Med Princ Pract, 2018;27(5):443-50.
14. Paunipagar BK, Rasalkar DJ, Imaging. Imaging of articular cartilage. 2014;24(03):237-48.
15. Martín NT, Raya JG, Wessell DE, Vilanova JC, Rossi I, Luna AJ. Functional MRI for evaluation of hyaline cartilage extracelullar matrix, a physiopathological-based approach. Brit. J. Radiol. 2019;92(1103):20190443.
16. Le J, Peng Q, Sperling K. Biochemical magnetic resonance imaging of knee articular cartilage: T1rho and T2 mapping as cartilage degeneration biomarkers. Annals of the New York Academy of Sciences. Ann. N. Y. Acad. Sci. 2016;1383(1):34-42.
17. Banjar M, Horiuchi S, Gedeon DN, Yoshioka HJ. Review of quantitative knee articular cartilage MR imaging. Magn Reson Med Sci,2022;21(1):29-40.
18. Madelin G, Xia D, Brown R, Babb J, Chang G, Krasnokutsky S, et al. Longitudinal study of sodium MRI of articular cartilage in patients with knee osteoarthritis: initial experience with 16-month follow-up. Eur. J. Radiol. 2018;28(1):133-42.
19. Eck BL, Yang M, Elias JJ, Winalski CS, Altahawi F, Subhas N, et al. Quantitative MRI for evaluation of musculoskeletal disease: cartilage and muscle composition, joint inflammation, and biomechanics in osteoarthritis. Investig. Radiol. 2023;58(1):60-75.
20. Xu J, Xie G, Di Y, Bai M, Zhao X. Value of T2-mapping and DWI in the diagnosis of early knee cartilage injury. J. Radiol. Case Rep. 2011;5(2):13.
21. Schleich C, Bittersohl B, Miese F, Schmitt B, Müller-Lutz A, Sondern M, et al. Glycosaminoglycan chemical exchange saturation transfer at 3T MRI in asymptomatic knee joints. Acta radiol. 2016;57(5):627-32.

22. Lu R, Zhang Y, Tao H, Zhou L, Li H, Chen T, et al. Gadolinium-hyaluronic acid nanoparticles as an efficient and safe magnetic resonance imaging contrast agent for articular cartilage injury detection. Bioact. Mater. 2020;5(4):758-67.
23. Sharafi A, Zibetti MV, Chang G, Cloos M, Regatte RR. 3D magnetic resonance fingerprinting for rapid simultaneous T1, T2, and T1ρ volumetric mapping of human articular cartilage at 3 T. NMR Biomed. 2022;35(12):e4800.
24. Benjamin AJ, Gómez PA, Golbabaee M, Mahbub ZB, Sprenger T, Menzel MI, et al. Multi-shot Echo Planar Imaging for accelerated Cartesian MR Fingerprinting: an alternative to conventional spiral MR Fingerprinting. Magn. Reson. Imaging. 2019;61:20-32.

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SUPPLEMENTARY FIGURES

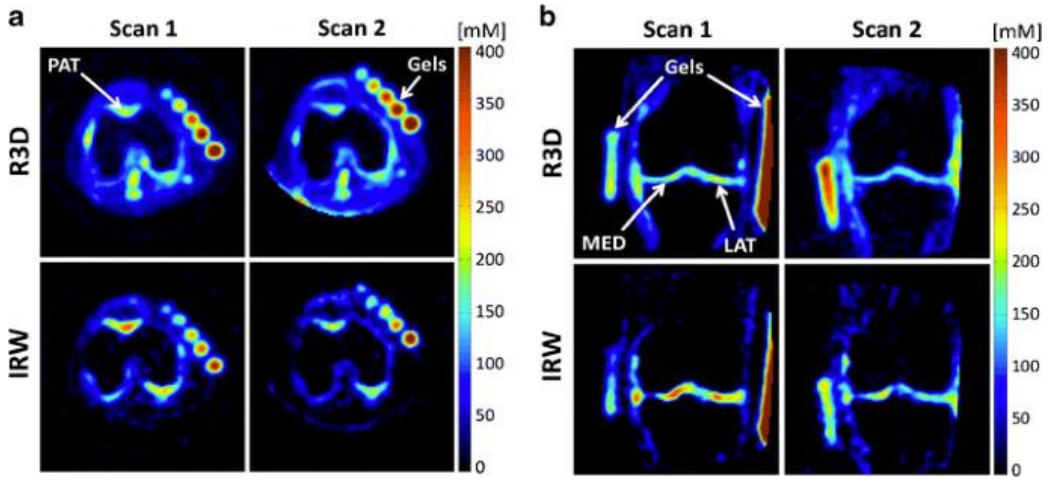

Fig S1: Sodium maps from one OA patient, reconstructed from data acquired with fluid suppression (sequence IRW) and without fluid suppression (sequence R3D), at baseline (scan 1) and 16-month follow-up (scan 2). A: Transverse slices showing patellar cartilage (PAT). b :Coronal slices showing femorotibial lateral (LAT) and medial (MED) cartilage [1]

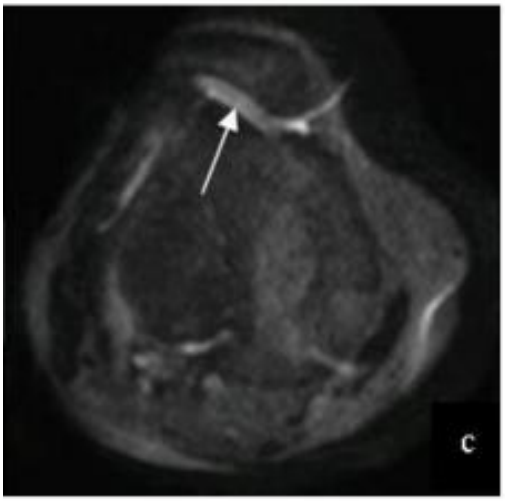

Fig S2: DWI (3.0 Tesla, TR/TE = 2000 msec/70 msec, Slice Thickness = 3mm) were expressed as a continuous cartilage and uniform signal (arrows) [2]

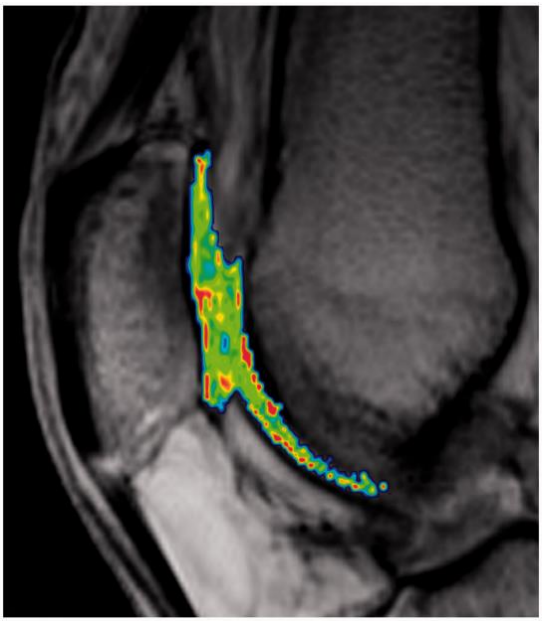

Fig S3: Fusion of morphological T1w image with CEST maps demonstrating high glycosaminoglycan content in patellar and trochlear cartilage [3]

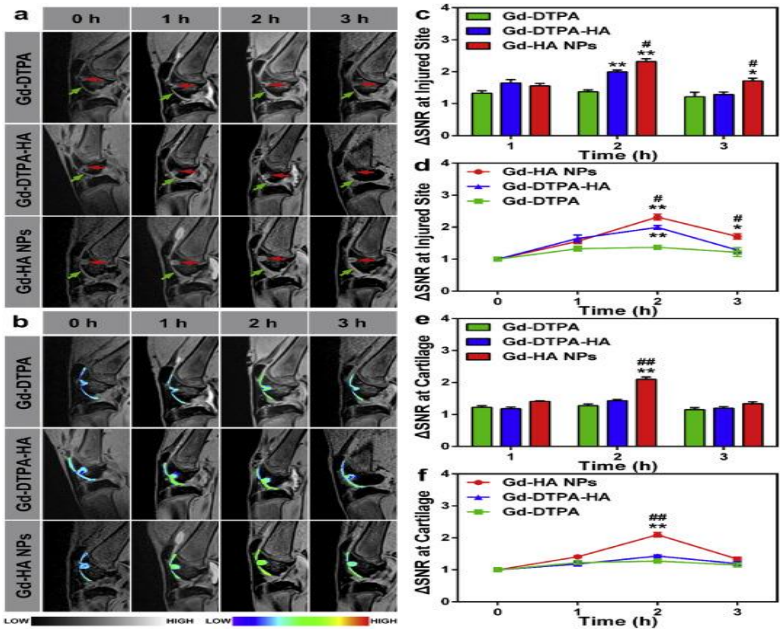

Fig S4: In vivo MRI detection of cartilage injuries by Gd-HA NPs. **(a)** T1-weighted MRI images of the knee of the cartilage-injured rabbit obtained before and after the intra-articular injections of Gd-DTPA (top), Gd-DTPA-HA (middle), and Gd-HA NPs (bottom). The cartilage and injured site were denoted by the green and red arrows, respectively. **(b)** Corresponding pseudo-colored images [4]

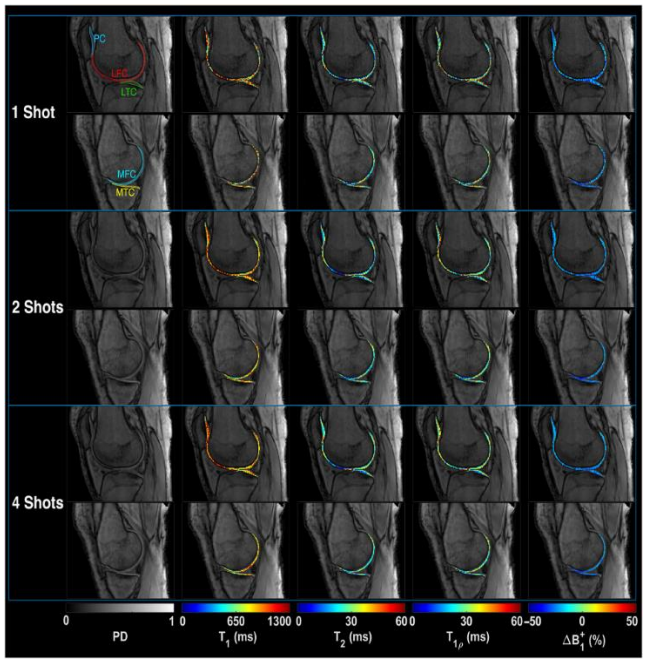

Fig S5: Representative maps for one, two, and four shots in medial and lateral knee cartilage for PD images, T1, T2, T1ρ, and ΔB1+ maps. Less variation was observed across cartilage by increasing the number of shots. The ROIs are shown in the shot 1 PD images. LFC, lateral femoral cartilage; LTC, lateral tibial cartilage; MFC, medial femoral cartilage; MTC, medial tibial cartilage; PC, patellar cartilage; PD, proton density; ROI, region of interest [2]

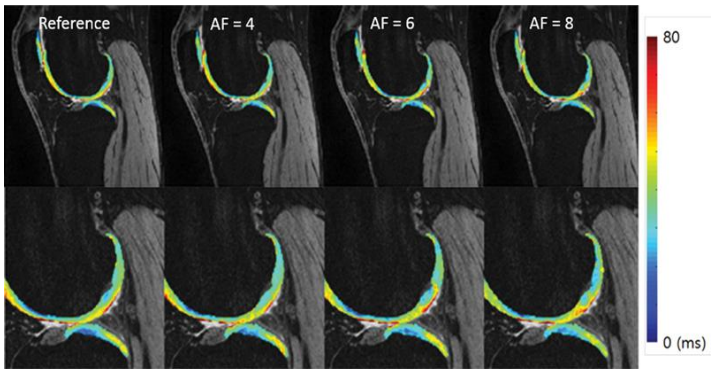

Fig S6: Compressed sensing can be used to decrease acquisition time of a three-dimensional T1ρ sequence without a clinically significant difference in accuracy. Reference acquisition using parallel imaging with an acceleration factor (AF) = 2 and a time of acquisition (TA) = 13:43 can be reduced to TA = 6:37 (AF = 4), TA = 4:24 (AF = 6), and TA = 3:18 (AF = 8), with < 4% difference in the average coefficients of variation between reference and accelerated sequences for all AFs. Top: whole image within field of view; bottom: zoomed-in images [5]