The Image Study of Articular Cartilage in China

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Abstract The purpose of this article is to review the current image study of articular cartilage in China, the conventional and new MRI sequences to be used in cartilage, the clinical application of MRI, Our team's achievements, and future directions and developments in cartilage imaging. In conclusion, articular cartilage plays an important role in the function of the joints of the body. MRI is a noninvasive method for the assessment of cartilage and it can reveal the morphological and biochemical changes in cartilage.

Keywords Cartilage · Articular cartilage · MRI · Osteoarthritis · Joint · Quantitive MR imaging

Introduction

Cartilage is one of the most important markers in degenerative and traumatic joint diseases, and the integrity of

cartilage is an important factor to the normal movement of the joint, but before the application of MRI technology in clinic, articular cartilage imaging is almost blind. Therefore, before the use of MRI, the thesis of imaging of articular cartilage and its diseases can be said to be very rare.

Current Status in China

In 1996, a review article [1] “MR Imaging Study Of Articular Cartilage” summarized early experience with MRI of articular cartilage by stating that “although the role of MRI in the evaluation of articular cartilage remains undefined, the ideal sequences may be fat suppression or MTC 3D-GRE”. So far, about 116 articles concerning cartilage image study had been published on the nucleus journals in China since 2000. And research in this field is steadily increasing since 2003 (Fig. 1). Statistically, there are 73 clinical application articles, 31 experimental articles, and 12 reviews.

Cartilage pathology may be the result of degeneration or injury. Many imaging methods are available to assess cartilage, and MRI of cartilage articles accounts for 89.7 %, while ultrasound only accounts for 9.5 %. There is no doubt that MRI is the most important method for cartilage evaluation at present. Conventional radiography can be used to detect gross loss of cartilage, evident as narrowing of the distance between the two adjacent bones of a joint, but it does not show cartilage directly. CT provides information limited to the contour of the cartilage surface, while MRI, with its excellent soft-tissue contrast, is the best imaging technique currently available for the assessment of articular cartilage [2].

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Fig. 1 Published articles on cartilage imaging in China

In recent years, articles published in the journal of China on cartilage mainly involve three aspects: (1) the MR sequences of cartilage; (2) MRI manifestations and diagnosis of cartilage disease; and (3) using MRI to reveal the biochemical composition, histological characteristics, and biomechanical structure of cartilage. A large number of researches that are invested in the development of these morphologic and quantitative imaging techniques are motivated by new therapeutic modalities, such as cartilage repair and pharmacological therapy.

Conventional MRI Methods

2D Fast Spin-Echo Imaging

T₁WI, T₂WI, PDWI with or without suppression (There were 50 articles on this sequence in recent years).

Yin Jingjing et al. [3] found that sagittal fat saturation T₁ sequence can depict the knee meniscus and articular cartilage better than other scan sequences, but it provided poor contrast between cartilage and joint effusion, while T₂WI provided better contrast than T₁. FS-T₂WI could be used to detect cartilage defects; FSE PD/T₂WI sequences provide excellent SNR and CNR of cartilage defects [4]. In osteoarthritis, these conventional sequences were suited for morphologic assessments and of articular cartilage and other structures around it [5–7].

3D Gradient-Echo Techniques

Three-dimensional spoiled gradient-recalled echo imaging with fat suppression (**3D-FS-SPGR**) (There were 25 articles on this sequence in recent years).

Dual-echo steady state (**DESS**) (There were 3 articles on this sequence in recent years).

3D-FS-SPGR

Plenty of research showed that 3D-FS-SPGR is the standard sequence for morphologic imaging of cartilage, and it offers higher SNR and CNR than 2D techniques [8, 9] (Fig. 2); meanwhile, it is useful for cartilage volume and thickness measurement [10–16]. But, it also has disadvantages; it does not adequately highlight surface defects with fluid and does not allow thorough evaluation of other joint structures such as ligaments or menisci [17].

DESS

Studies have demonstrated that the usefulness of 3D DESS imaging for the morphologic assessment of cartilage provided higher SNR and CNR compared with other sequences [18] (Fig. 3). The acquisition time for DESS is shorter than that for 3D-FS-SPGR, besides, it allowed quantitative assessment of cartilage thickness and volume with good accuracy [19].

New MRI Methods

T₂ Relaxation Time Mapping (There were 16 articles on this sequence in recent years)

The T₂ relaxation time of cartilage is sensitive to its matrix [20]. It reflects the interactions among water molecules and surrounding macromolecules. It may reveal the areas of increased or decreased water content that correlate with cartilage damage [21]. It also can indicate component abnormality of articular cartilage without morphology

Fig. 2 Human cartilage of knee

Fig. 3 The lateral condyle of knee joint [18] (Color figure online)

change of early OA. Chen Qichun et al. found that “ T_2 mapping imaging (Fig. 4) of articular cartilage can monitor early cartilage degeneration prior to morphologic changes, which has a high value to diagnose and detect early cartilage injury in the early stage of OA. The T_2 value of cartilage is influenced by the weight-bearing condition, and the T_2 value of weight-bearing site is higher than that of non-weight-bearing site” [22•]. The T_2 value of the articular cartilage could increase significantly with cartilage deterioration, which was highly related to the degree of cartilage degeneration and could be considered as a sensitive method to detect early cartilage degeneration [23–27].

DWI (There were 2 articles on this sequence in recent years)

Diffusion-weighted imaging is based on the motion of water molecules. It can detect water molecular diffusion state of tissue (degrees of freedom and direction). The diffusion of

water in cartilage reflects tissue’s biochemical structure and architecture. The apparent diffusion coefficient (ADC) is low in healthy cartilage because the diffusion of water molecules is restricted by cartilage matrix. However, disruption of the cartilage matrix results in an enhanced water mobility, which increases the ADC of cartilage. This research also confirmed that the ADC av of the healthy people was lower than that of OA group (Fig. 5). DWI is a useful method in detecting early cartilage injury which cannot be shown on routine sequences [28]. ADC value of patellar cartilage in early CMP was obviously increased, and DWI had a high clinic value in diagnosis and follow-up of CMP [29].

Delayed Gadolinium-Enhanced MRI of Cartilage (dGEMRIC) (There were 8 articles on this sequence in recent years)

After intravenous injection of Gd-DTPA, it penetrates cartilage and concentrates where the cartilage

Fig. 4 T₂ mapping colored map of the lateral condyle cartilage [22] **a, b** female, 35, normal volunteer; the cartilage signal was uniform, showed *light green* in color; **c, d** male, 52, early OA patient; the cartilage signal was inhomogeneous, showed *yellow* or *reddish yellow* in color

Fig. 5 ADC map of patella cartilage. **a.** healthy people: ADC av: $(4.36 \pm 6.09) \times 10^{-4} \text{ mm}^2/\text{s}$; **b.** OA people: ADC av: $(13.7 \pm 6.21) \times 10^{-4} \text{ mm}^2/\text{s}$

Fig. 6 Bovine cartilage (dGEMRIC). The upper cartilage was treated by trypsin, and the second half was treated as control [52••]

glycosaminoglycan content is relatively low. Subsequent T1 imaging, which is reflective of Gd-DTPA concentration, therefore yields an image depicting glycosaminoglycan distribution. This technique is referred as delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) [30–32] (Fig. 6).

An animal research had revealed that “SIR on early and delayed Gadolinium-enhanced MRI has the ability in evaluating the early stage change of cartilage degeneration” [33]. Doses of Gd-DTPA had important effect on cartilage T₁ value, contrast ability, and delay time of dGEMRIC [31]. In 2009, a clinical study indicated that “dGEMRIC can be used to diagnose whether the biochemical ingredients of cartilage were lost by means of quantitating the GAG. It has a potential feasibility to diagnose the early stage of cartilage degeneration” [34].

T₁ρ Mapping (There were 5 articles on this sequence in recent years)

T₁ρ relaxation time is similar to T₂ relaxation time. The interactions between motion-restricted water molecules and their local macromolecular environment can be monitored by measuring T₁ρ value, making this a promising technique for assessing the composition of cartilage, since its extracellular matrix provides a motion-restricted environment for the water molecules. Thus, the changes to the extracellular matrix, such as proteoglycan depletion, may alter T₁ρ values measured in cartilage [35]. In the damaged

hyaline cartilage, it demonstrates higher T₁ρ value than normal cartilage, thus, T₁ρ measurement could be used as a noninvasive early evaluation method for cartilage disease [36].

Clinical Application

The most important clinical applications for MRI are the assessment of cartilage in osteoarthritis, chronic or acute osteochondral injury, osteochondritis, chondromalacia patellae, and inflammatory arthropathies. In addition, cartilage imaging is required to monitor the treatment’s effect after invasive cartilage repair procedures or conservative therapies (including pharmacological therapies).

Degenerative Disease

Osteoarthritis is an important cause of disability in China and is marked by degeneration of articular cartilage. Early degenerative lesion may be seen on conventional MRI [37]. It appears to be the changes of cartilage contour (such as fibrosis and irregular surface) and cartilage thickness (including thinning or thickening) [38]. While, advanced degenerative lesion shows multifocal thinning or missing of the cartilage [39]. By comparing articular cartilage thickness between OA cases and healthy volunteers, the articular cartilage thickness in a bulk of cartilage weight-loading surface attenuated gradually, following with the aggregated OA disease [40].

Cartilage lesions on MRI are often graded on Noyes scale: **0** Normal; **1** Signal change (increased T₂); **2** Partial-thickness defect <50 %; **3** Partial-thickness defect ≥50 %; and **4** Full-thickness defect [41, 42].

Many MRI sequences are sensitive to the biochemical changes within cartilage [43, 44]. More specifically, T₂ value was able to provide information about the change of cartilage collagen, and increased T₂ is most commonly associated with cartilage damage (collagen destruction); T₁Gd was mainly correlated with the content of GAG, and the lower GAG leads to decreased T₁ value [45]. ADC value of patellar cartilage in early chondromalacia patellae is obviously increased [29].

Traumatic Chondral Injuries

Acute injury to cartilage can be characterized by MRI [46, 47]. Cartilage injury lesions on MRI showed partial or full cartilage fracture, avulsion or subchondral bone marrow contusion, and edema or subchondral fracture [48, 49]. Discovery signal changes of subchondral bone marrow

should be alert to the corresponding articular cartilage injury or disease [50]. The isolated traumatic cartilage fracture does not exist in fact. And usually, the traumatic injury of articular cartilage should be combined with the subchondral bone contusion [51]. The assessment of MRI and arthroscopy in acute articular cartilage injury is consistent. Combined with arthroscopy, MRI can succeed in assessing the extension and degree of acute articular injury and allowing treatment planning [52•, 53]. An

experimental research revealed that the increase of MMP-13 expression of the covering cartilage of bone flap was of significance for clinical therapy [54].

Inflammatory Arthropathies

MRI can show the pathological changes of RA in early stages, such as chondral damage [55]. A research on animal

Our team's achievements:

2002-2003: Compared the advantage or shortage of several scan sequences in MRI of articular cartilage and determined the optimal series. From this we concluded that 3D-FS-SPGR could show the cartilage clearly than other sequences, the value of cartilage thickness with 3D-FS-SPGR was more accurate.

2003: Evaluated the diagnosis and differential diagnosis among chronic cartilage lesions on the plain films and MRI. A combination of the plain films and MRI was the best method for examining the joints and cartilages. 3D-FS-SPGR was the best sequence for the diagnosis of cartilage lesion.

2006: Evaluated the clinical significance of quantitative measurement ADC value of patella cartilage on MR diffusion weighted imaging (DWI). The ADC value of healthy people was lower than of the OA group, DWI was a useful method in detecting early cartilage injury which cannot be showed on routine sequences.

2007: 3D-FS-SPGR sequence is more sensitive than SE-T1-WI sequence in detecting the change of cartilage signal intensity. SIR on early and delayed Gadolinium-enhanced MRI has the ability in evaluating the early stage changing of cartilage degeneration.

2008: T2* map could give a quantitative criteria for abnormal microscopic content of water and the structure change of articular cartilage. T2* map is a useful method in detecting the cartilage injury.

2013: An animal study reveals that T₂ and T₁ mapping may be useful in the early diagnosis of cartilage degeneration. The changes in collagen content of the cartilage was related to T₂ relaxation time. Whereas T₁ relaxation time was affected by both collagen and proteoglycan.

2014: An animal research and clinical study reveals that T1ρ imaging technique has the better feasibility and sensitivity to the early diagnosis of articular cartilage degeneration, it might perform the prospective and quantitative evaluation to the prophase degenerative cartilage and the injuries should happen in further.

models of pyogenic arthritis induced by intra-articular injections of *Staphylococcus aureus* suspension revealed that diffuse signal increased on FSE T₂WI was the earliest sign of articular cartilage involvement in pyogenic arthritis. The changes of both signal intensity and morphology of articular cartilage can reflect histopathologic abnormality [56]. In addition, inflammatory infiltration in subchondral bone is the early sign of adjacent cartilage injury [57, 58].

Cartilage Repair Procedures

With the development of arthroscopic surgery and cartilage transplantation, all kinds of repair technologies about articular cartilage defect are getting matured. We should not only find the accurate location of articular cartilage abnormalities but also the MRI evaluation of operation effect. MRI also played an essential role in the assessment of cartilage volume [59]. Deng Xia et al. [60] got a conclusion that MRI provided a noninvasive way for monitoring the process of repair after AOT.

Whether the result is from degeneration or injury and inflammation, MRI offers a noninvasive means of assessing the degree of damage to cartilage and adjacent bone and of measuring the effectiveness of treatment.

Future Directions

- (1) Technologic advances in high-field imaging, pulse sequence development, and the application of MRI contrast agents.
- (2) To observe cartilage transplantation and drug therapeutic effect using MRI.
- (3) Molecular imaging: to observe cartilage structural and biochemical changes.

Compliance with Ethics Guidelines

Conflict of Interest Dr. Fei Wang, Dr. Si Shen, Dr. Lin Qiu, Dr. Cici Zhang, Dr. Meng Chen, and Dr. Sirun Liu each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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