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REVIEW

Current and Future Advanced Imaging Modalities for the Diagnosis of Early Osteoarthritis of the Hip

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Abstract: Hip osteoarthritis (OA) can be idiopathic or develop secondary to structural joint abnormalities of the hip joint (alteration of normal anatomy) and/or due to a systemic condition with joint involvement. Early osteoarthritic changes to the hip can be completely asymptomatic or may cause the development hip symptomatology without evidence of OA on radiographs. Delaying the progression of hip OA is critical due to the significant impact of this condition on the patient's quality of life. Pre-OA of the hip is a newly established term that is often described as the development of signs and symptoms of degenerative hip disease but no radiographic evidence of OA. Advanced imaging methods can help to diagnose pre-OA of the hip in patients with hip pain and normal radiographs or aid in the surveillance of asymptomatic patients with an underlying hip diagnosis that is known to increase the risk of early OA of the hip. These methods include the delayed gadolinium-enhanced magnetic resonance imaging (MRI) of cartilage (dGEMRIC), quantitative magnetic resonance imaging (qMRI- T1rho, T2, and T2* relaxation time mapping), 7-Tesla MRI, computed tomography (CT), and optical coherence tomography (OCT). dGEMRIC proved to be a reliable and accurate modality though it is limited by the significant time necessary for contrast washout between scans. This disadvantage is potentially overcome by T2 weighted MRIs, which do not require contrast. 7-Tesla MRI is a promising development for enhanced imaging resolution compared to 1.5 and 3T MRIs. This technique does require additional optimization and development prior to widespread clinical use. The purpose of this review was to summarize the results of translational and clinical studies investigating the utilization of the above-mentioned imaging modalities to diagnose hip pre-OA, with special focus on recent research evaluating their implementation into clinical practice.

Keywords: hip, pre-osteoarthritis, dGEMRIC, 7T MRI, qMRI, OCT, delayed gadolinium-enhanced magnetic resonance imaging of cartilage, optical coherence tomography, quantitative magnetic resonance imaging

Introduction

The prevalence of degenerative joint disease (DJD) continues to increase, with more than 300 million individuals diagnosed with knee and hip osteoarthritis (OA) in 2017.[1] The hip is one of the largest human joints and is the second most affected site by OA. Hip OA can be idiopathic or secondary to conditions associated with deviation from the normal hip anatomy (such as trauma, developmental dysplasia of the hip) and/or systemic disease with involvement of the hip joint.

Although not clearly defined, pre-OA has been described as a modifiable disease process that is not detectable using conventional radiographic imaging and may or may not be associated with the presence of pain in the affected joint.[2,3] In regard to the hip, conditions including femoroacetabular impingement syndrome (FAIS),[4] developmental hip dysplasia (DDH) and slipped capital femoral epiphysis (SCFE) have been associated with early degenerative changes in the hip. They also have an increased likelihood for surgical intervention in the form of hip preservation or replacement surgery at a young age.[5] These patients can be completely asymptomatic or present with hip pain and dysfunction without evidence

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of OA on radiographs, computed tomography (CT), or magnetic resonance imaging (MRI) studies using conventional protocols.[5] The accurate diagnosis of early OA is paramount for the personalized treatment of disease, especially as new machine-learning database studies further elucidate the deleterious effects of non-steroidal anti-inflammatory drugs (NSAIDS).[6]

NSAID play an important role in the management of patient with early arthritis of the hip joint. Anti-inflammatory medications provide adequate pain control at the early stages of OA an allow for pain free participation in physical activity. Unfortunately, NSAIDS are mainly helpful for the reduction of inflammation and pain in patients with arthritic hip disease, but they are not effective against the disease progression which is associated with the viability of the articular cartilage. In certain patient populations, such as athletes, chronic use of NSAIDS may result in severe progression of OA over the years due to the mitigation of symptoms and the delay in seeking medical care.

During the last decade, research has focused on the development of advanced imaging modalities for the detection of pre-OA of the hip with the goal to diagnose OA at an early, modifiable stage.[3] Different methods for the detection of pre-OA of the hip have been investigated including delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC), quantitative magnetic resonance imaging (qMRI), 7-Tesla MRI, CT, and optical coherence tomography (OCT).[7–12] Our purpose was to summarize the results of translational and clinical studies investigating the utilization of the above-mentioned imaging modalities to diagnose hip pre-OA with a special focus on recent research evaluating their implementation into clinical practice.

Delayed Gadolinium-Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC)

dGEMRIC is an imaging technique that can assess the cartilage in a joint by using the negatively charged contrast agent gadolinium diethylene triamine pentaacetic acid ($Gd(DTPA)^{2-}$) to reflect against the negatively charged glycosaminoglycan (GAG) distribution in cartilage.[13] T_1-weighted conventional MRI, either 1.5T or 3T, is then used to quantitatively evaluate cartilage degradation by measuring post-contrast T1 relaxation time (T1Gd), known as the dGEMRIC index. This information is used in 3D T1 or T2 mapping.[13] A lower dGEMRIC index has been shown to correlate with more severe OA in in vivo, in vitro and ex vivo histologic specimens.[13] In an animal study on ovine femoral heads, the dGEMRIC index was successfully used to detect cartilage damage in young sheep that was not appreciated on macroscopic evaluation and that correlated with histological analysis.[14] Tiderius et al compared the dGEMRIC index between healthy volunteers and patients with early hip OA and found decreased dGEMRIC index in the latter group (Figure 1).[15]

With regards to dGEMRIC technique, MRI of the joint is performed prior to intra-articular or intravenous contrast injection and repeat images are taken at various time intervals post-injection after allowing a time period for the contrast to disperse and washout.[16] This process can be time-consuming due to it necessitating two MRIs being performed with wait time in between for contrast to circulate. To improve this process, Xu et al and Bittersohl et al investigated whether pre-contrast MRI could be omitted.[16,17] The authors found that pre-contrast values were not necessary when using dGEMRIC protocol for evaluating cartilage degeneration in patients with early hip OA, allowing for a more efficient imaging protocol.[16,17] Schmaranzer et al performed a retrospective diagnostic study comparing manual two-dimensional (2D)-MRI to automatic 3D-MRI methods of cartilage thickness measurement and dGEMRIC index in 25 symptomatic hips who had not undergone previous hip surgery (Figure 1).[5] The authors found both techniques to be accurate and reliable, presenting an efficient method to characterize pre-arthritic cartilage change that reduces user-dependent variation in image processing time.[18]

In regards to clinical practice, dGEMRIC is currently being used for the diagnosis of osteoarthritic changes in various hip abnormalities including but not limited to DDH, FAIS, and SCFE (Table 1).[8–11] Kim et al examined the association of dGEMRIC index with hip pain but also joint space and lateral center edge angle measurements (index of acetabular dysplasia) on the standing anteroposterior pelvic radiograph.[19] The authors showed that the dGEMRIC index correlated with the degree of hip dysplasia (mild, moderate, severe) and the presence of hip pain but found no correlation with joint space. Based on these results, the authors concluded that dGEMRIC index may be a sensitive measure of OA development in dysplastic hips.[19] In a retrospective study, anterior hip degeneration was the strongest predictor of osteotomy failure, and

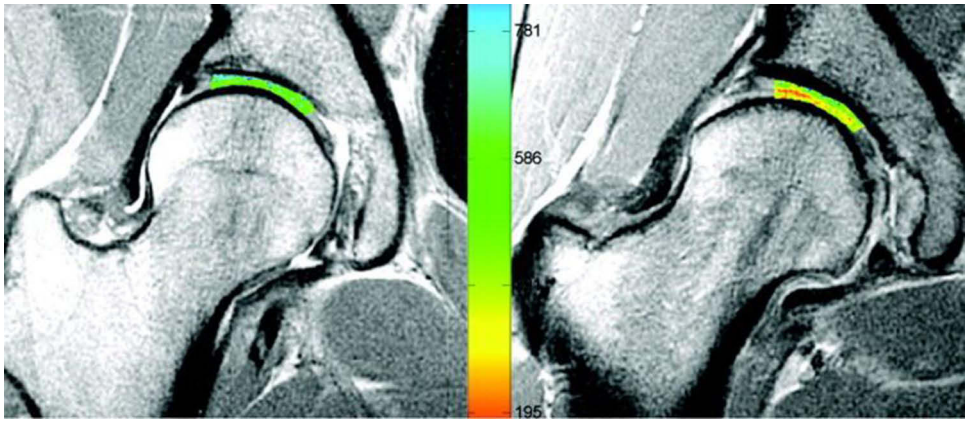

Figure 1 dGEMRIC images of weight-beating Hip cartilage in a healthy volunteer (left) and a patient with early osteoarthritis (right).
Note: Reproduced from Tiderius CJ, Jessel R, Kim Y-J, et al. Hip dGEMRIC in asymptomatic volunteers and patients with early osteoarthritis: the influence of timing after contrast injection. Magnetic Resonance in Medicine. 2007;57(4):803–805. Copyright © 2007 Wiley-Liss, Inc.[15]

patients who prematurely failed peri-acetabular osteotomy (PAO) had lower pre-operative dGEMRIC indices.[20] Cunningham et al also found that patients with DDH who failed PAO surgery had a preoperative dGEMRIC index of 370ms compared with 489ms in the group with "satisfactory" PAO outcomes ($p < 0.001$).[21] Significant decreases in dGEMRIC indices in both the deep and superficial zones of hip cartilage were detected at 12 and 24 months post-PAO compared to the pre-operative dGEMRIC values. These results indicate that PAO surgery may accelerate molecular pathways that lead to cartilage degradation.[22] Based on the above, dGEMRIC indices appear to be positively predictive in assessing early cartilage change in DDH patients and may help anticipate corrective surgery outcome status.

The use of dGEMRIC index to evaluate progression of cartilage damage in patients with FAIS has also been reported.[23–25] Two different studies used T1gD values to evaluate the degree and distribution of cartilage damage in FAIS. They found more anterior superior cartilage damage in cam-based FAIS and a more global distribution of degradation in pincer-based FAIS patients.[23,26] Palmer et al reported that a combined variable of alpha angle, superior anterior acetabulum cartilage dGEMRIC ratio and positive impingement test was able to best predict progression of OA in patients with cam deformities.[27] Similarly, Jessel et al looked at the alpha angle in FAI hips and reported good correlation between dGEMRIC index, pain and radiographic OA measures.[25] Similar dGEMRIC indices were reported in patients with DDH (531 ms) and FAIS (551 ms) in a comparative study. In the subgroup of patients with radial T1 index <500ms, a more global pattern of cartilage degradation was noted in the DDH compared with FAIS subjects.[24] In patients with FAIS, dGEMRIC index may be used alongside alpha angle to identify early cartilage change, guiding clinical management of the pre-arthritic condition. This is particularly important in the athletic population, where activity modification protocols and regular hip screening protocols can be implemented in athletes with hip pain and signs of early chondral damage on dGEMRIC study.

Limited evidence is available on the utilization of dGEMRIC technique in patients with SCFE. Zilkens et al assessed the GAG content in hip joint cartilage in mature hips with SCFE. The authors found dGEMRIC and T1Gd values to be significantly correlated with the severity of hip alpha angles in the patients with normal femoral head–neck offset (alpha angles<50°) and those with severe femoral head–neck offset decrease (alpha angle>60°). This study also showed statistically significant differences in regionality of cartilage damage, specifically central and lateral hip regions.[28] Based on these findings, dGEMRIC may be useful in the detection of OA onset in patients with SCFE who have no evidence of joint space narrowing on hip radiographs but further studies are necessary to evaluate the diagnostic capability of dGEMRIC in patients with SCFE.

While dGEMRIC allows relatively fast imaging acquisition with 3D segmentation, it requires the administration of intravenous and, ideally, intraarticular contrast. Kim et al and Cunningham et al exemplified promising data concerning dGEMRIC index in the characterization of hip OA,[20,21] yet their data has been difficult to reproduce. This may be accounted for by the transition from 1.5T to 3T MRI in more recent studies. 3T MRI provides better image resolution via

Table 1 Studies Investigating the Use of dGEMRIC in the Diagnosis of Pre-Arthritic Hip

Study (First Author, Year)	Study Design (Population, Methodology)	Conclusion
Bashir, A et al, 1999[13]	• 23 discs of human cartilage from 7 knee joints. • GAG concentration was assessed using T1 values in the presence and absence of $Gd(DTPA)^{2-}$ contrast.	GAG in human cartilage can be measured and quantified using T1 MR imaging after equilibrium with $Gd(DTPA)^{2-}$ contrast
Bittersohl, B; Hosalkar, H et al, 2009[16]	• 25 symptomatic FAI patients. • Sought to determine the necessity of pre-contrast assessment in evaluating dGEMRIC post-contrast T1 values.	Only post contrast T1 values are sufficient for dGEMRIC analysis making the process more efficient.
Bittersohl, B, Steppacher, S et al, 2009[23]	• 26 patients with symptomatic FAI. • dGEMRIC images were obtained and patients were grouped based on type of FAI: CAM, Pincer, mixed type.	T1 mapping based on dGEMRIC imaging can assess regional variations of cartilage damage in hips with FAI pathology.
Cunningham, T et al, 2006[21]	• 40 patients who underwent Bernese PAO for DDH. • Evaluated correlations between radiographs, patient outcome scores and dGEMRIC analysis.	dGEMRIC imaging can be a useful tool to decrease morbidity from PAO for DDH with improved patient selection.
Domayer, S et al, 2010[24]	• 20 DDH patients were compared to 20 FAI patients. • Authors evaluated demographics, WOMAC score, XR and dGEMRIC in different ROIs (radial, peripheral, central).	DDH and FAI have different patterns of cartilage degeneration and radial dGEMRIC can be used to assess such patterns.
Hingsammer, A M ert al, 2015[22]	• 37 patients treated with PAO for DDH. • Patients underwent preoperative and 1-year follow up dGEMRIC studies.	PAO surgery can alter hip cartilage distribution and may accelerate joint damage due to post-surgical inflammation.
Jessel, R, et al, 2009[25]	• 30 patients with FAI and radiographic impingement. • WOMAC scores, radiographs and dGEMRIC index were assessed. Subgroup analysis done based on alpha angles.	Tonnis grade and joint space narrowing did not correlate with patient pain symptoms, but dGEMRIC index did correlate with pain and deformity (alpha angle).
Kim, S. D. et al, 2012[20]	• 41 patients who underwent Bernese PAO for DDH • Pre-operative radiographic parameters for DDH were obtained along with dGEMRIC index and WOMAC scores.	Success after PAO is correlated with OA and DDH severity. Specific regions of cartilage degeneration can predict PAO failure.
Kim, Y. J. et al 2003[19]	• 43 patients with mild, moderate and severe dysplasia. • WOMAC scores, lateral center edge angle, joint space and dGEMRIC index were used to evaluate the patients.	dGEMRIC has the ability to discriminate among patients with different levels of pain and severity of dysplasia.
Lazik-Palm, A et al, 2016[42]	• 11 healthy volunteers evaluated with 7T MRI using dGEMRIC technique to quantitatively assess cartilage relaxation times and T1, T2 and T2* mapping.	dGEMRIC index and mapping can be performed with no interference from gadolinium contrast, image quality improved with 7T MRI.
Mamisch, T. C et al, 2011[26]	• 33 patients with symptomatic FAI divided into 3 groups: asymptomatic controls, CAM FAI and pincer FAI. • Patients were evaluated with radiographs and dGEMRIC index w/ T1 mapping in 7 ROIs.	dGEMRIC mapping allows for more specific analysis of cartilage wear in patients with FAI which can be helpful in patient selection and surgical planning.
Palmer, A et al, 2017[27]	• 34 patients with CAM deformity evaluated over 5 years. • Evaluated with XR and MR dGEMRIC technique assessing indices of various regions of interest (ROIs).	The severity of the CAM deformity correlated with severity and location of cartilage degeneration on dGEMRIC imaging.
Schmaranzer, F er al, 2019[18]	• 23 symptomatic patients who had contrast-enhanced MRI. • Compared the gold standard technique of manual 3D analysis with new software assisted 3D analysis.	Automatic 3D imaging of dGEMRIC MRI images shows no difference from manual 3D segmentation of cartilage data.
Xu, L et al, 2012[17]	• 21 patients with acetabular dysplasia were grouped based on Tonnis grade. • Evaluated with dGEMRIC index in 7 regions of interest (ROI).	Radial dGEMRIC without pre-contrast measurements is useful for evaluating patterns of cartilage degeneration in patients with hip dysplasia.

(*Continued*)

Table 1 (Continued).

Study (First Author, Year)	Study Design (Population, Methodology)	Conclusion
Zilkens C et al, 2011[28]	• 28 young adults (32 hips) with history of moderate SCFE. • Assessed for correlation between dGEMRIC and radiographic parameters in regions of interest (ROIs) in the hip	dGEMRIC can demonstrate cartilage damage in SCFE patients with no joint space narrowing on radiographs.
Zilkens C et al, 2013[14]	• 20 femoral head cartilage specimens from 10 lambs and 10 sheep. • Evaluated with histologic analysis and dGEMRIC T1 mapping.	dGEMRIC imaging can reveal early cartilage damage in morphologically normal joints.

greater magnetic field strength with a drawback of greater field inhomogeneity. As dGEMRIC mapping uses a dual-flip-angle (DFA) gradient echo-method, these flip angle variations are increased at 3T versus 1.5T.[29] Patient-specific factors, such as implanted metallic hardware and body mass index, have also been shown to impact field inhomogeneity.[30,31] A new magnetization-prepared 2 rapid gradient-echo dGEMRIC sequence was developed to minimize the impact of flip angle variations, demonstrating more accurate T1 mapping of hip cartilage versus original DFA techniques.[32]

In the effort to quantitatively measure pre-arthritic cartilage change, dGEMRIC seems to provide a sensitive and increasingly efficient method to detect early cartilage abnormalities in patients with hip pain but without radiographic evidence of OA. This method can be of significant benefit to young patients with DDH, FAIS, and SCFE where delaying the progression of chondral damage and the need for hip replacement surgery at a young age is critical. To establish this as the standard of care, research is necessary to elucidate the clinical feasibility of routine dGEMRIC use in identifying early cartilage degradation. Diagnostic standardization will require larger studies in healthy volunteers and patients with hip pathologies.

Ultra-High Field 7-Tesla (7T) Magnetic Resonance Imaging (MRI)

7-Tesla (7T) MRI, or ultra-high field MRI, is an evolving imaging technique that offers an increased signal to noise ratio compared to conventional 1.5 or 3T MRI and results in increased image resolution.[8,33,34] Technical challenges associated with the use of this imaging modality include increased inhomogeneity and relaxation parameters such as T1, T2, and T2*. These significantly change field strength and values, which can make imaging of more central regions of the musculoskeletal system difficult to interpret.[35] As a result, 7T MR imaging of the hip requires technical optimization and robust pulse sequence development before it can be widely used clinically to assess hip cartilage.

Several studies assessed protocols to resolve technical challenges, with different sequences and shimming techniques used in 7T MR imaging of hip cartilage (Figure 2). In a study of 12 hips, Theyson et al compared the clinical feasibility between different 7T MRI techniques and reported that second-order circularly polarized (CP2+) transmit mode was more feasible than individualized shimming due to better resolution and decreased acquisition time.[36] Kraff et al evaluated quantitative MRI at 7T in eight healthy patients and three patients with FAIS. The authors found that triple-echo steady state (TESS) T2 mapping offered shorter acquisition times with comparable image quality when compared to convention multi-echo-spin-echo (CPMG).[37] Further studies and implementation into practice are needed to fully establish an efficient clinical workflow for use of 7T MRI in imaging hip cartilage.

Chang et al looked at the feasibility of 7T MRI to assess hip articular cartilage in 15 patients (mean age = 60.6 years), as well as bone microarchitecture and clinical imaging.[38] Five patients had no history of hip pathology, four had a diagnosis of osteopenia, five had a diagnosis of osteoporosis, and one had a history of labral debridement and femoral neck osteochondroplasty for FAI.[38] Different sequences such as T1-weighted 3D fast low angle shot (FLASH), volumetric interpolated breath-hold examination (VIBE), and 2D intermediate-weighted fast spin-echo (FSE) sequences were recommended for characterization of articular cartilage. They were found to effectively visualize all aspects of the hip joint and concluded that 7T MRI with these sequences is clinically feasible.[38] Greaves et al used 7T MRI to assess the changes in cartilage thickness in human hips with simulated physiologic loading provided by a pneumatic hip loading

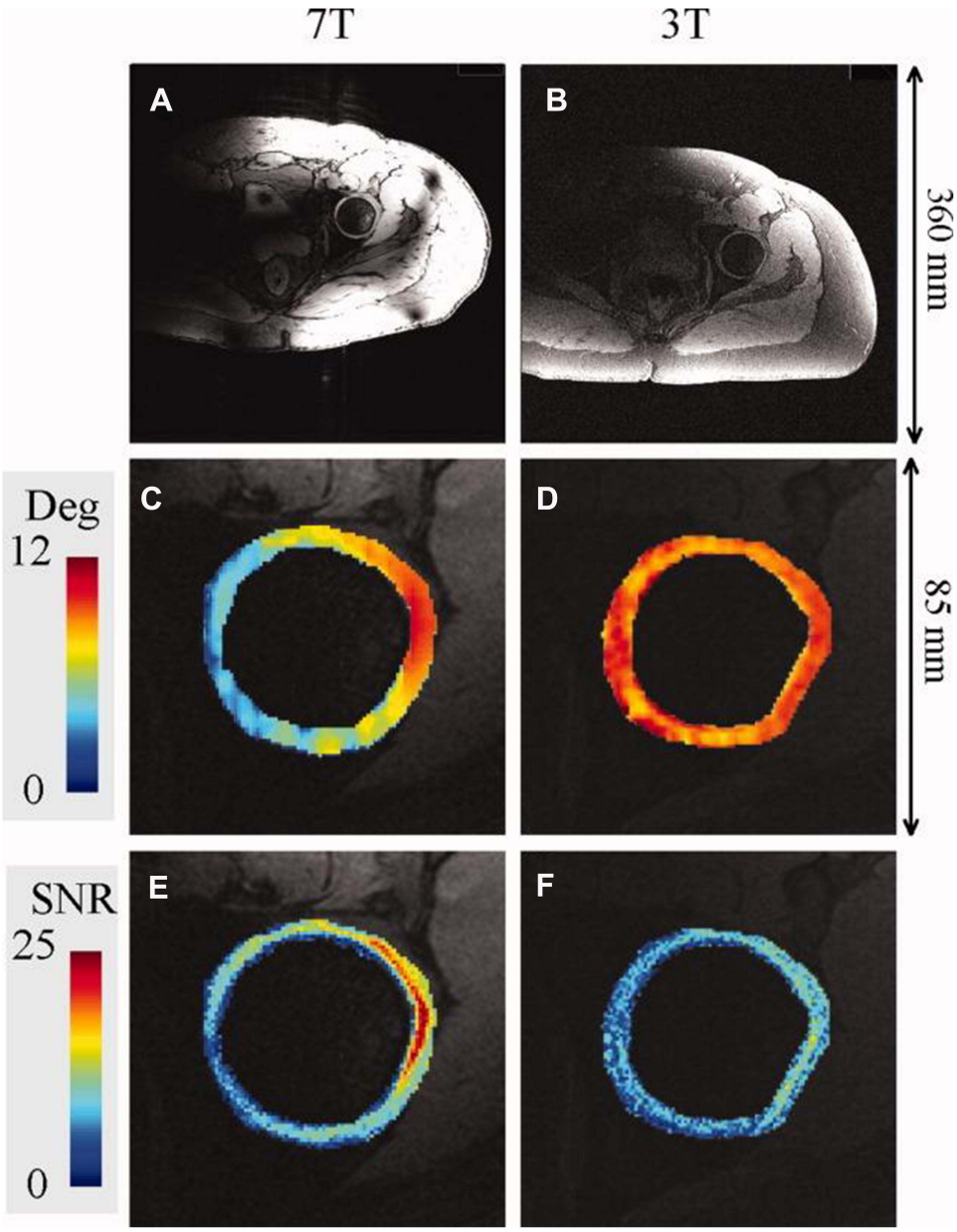

Figure 2 High resolution axial spoiled gradient echo (GRE) images of the Hip region with 3 Tesla (left) and 7 Tesla (right) MRI (**A** and **B**) with flip angles (**C** and **D**). Quantitative signal-to-noise ratio maps of GRE images are shown in (**E** and **F**).
Note: Reproduced from Deniz CM, Brown R, Lattanzi R, et al. Maximum efficiency radiofrequency shimming: theory and initial application for Hip imaging at 7 tesla. Magnetic Resonance in Medicine. 2013;69(5):1379–1388. Copyright © 2012 Wiley Periodicals, Inc.[41]

device that applied 1980 N of axial compression.[26] Five human cadaver hip joints were imaged at 15-minute intervals after loading.[39] They found that hip cartilage reached a steady state thickness distribution after 225 minutes of loading, and the mean change in thickness on a day-to-day basis was 0.10 mm. Their results support that 7T quantitative MRI is useful for assessing hip cartilage strain.[39] Both in vivo and ex vivo studies support the use of 7T MRI in clinical practice to evaluate hip cartilage, possibly providing a high field strength technique that is adaptable to quantitative and morphological studies of pre-OA hip cartilage.

Three studies compared 7T MRI to 3T MRI to characterize hip articular cartilage.[6,27,28] Lazik-Palm et al evaluated 9 patients with history of autologous acetabular cartilage transplantation and found superior contrast ratios and significantly shorter relaxation times of T1 and T2* at 7T compared to 3T MRI.[10] Theyson et al evaluated subjective image quality,

soft tissue contrasts, B1 homogeneity, and depiction of femoral head abnormalities using both 7T and 3T MRI in 13 patients with avascular necrosis treated with advanced core compression.[40] They found that 7T MRI showed similar results in all parameters to 3T MRI with greater contrast detail and fluid detection.[40] Deniz et al imaged four healthy volunteers in an axial plane through the left hip articular cartilage using a maximum efficiency radiofrequency shimming technique for 7T MRI and found that it produced an increased signal to noise ratio as compared to 3T MRI, leading to improved hip joint imaging.[41] These studies further support the clinical feasibility of 7T MRI in assessment of hip cartilage morphology and composition suggesting that 7T MRI may be superior to 3T MRI in identifying pre-arthritic joint change.

A German multi-center study by Lazik-Palm et al sought to evaluate the image quality of dGEMRIC technique with 7-T MRI sequence, compared to 3T MRI. T1, T2 and T2* mapping techniques were validated for use in 7-T MRI in 9 patients with history of autologous acetabular cartilage transplantation. They were able to show 7T MRI has superior image quality to 3T MRI.[10] A separate study in 11 healthy volunteers by Lazik-Palm et al reported accurate and reproduceable data when all protocols were done simultaneously. Using this technique, they were able to make morphologic and quantitative cartilage analysis more efficient.[42] Both studies were limited by small patient sample sizes, but present evidence suggests the clinical utility of dGEMRIC with 7T MRI sequences in evaluation of hip cartilage morphology.

Quantitative MRI (qMRI)

As discussed, characterization of pre-OA in the hip relies on identifying articular cartilage change before radiographic evidence of pathology presents.[43–45] The use of qMRI with T1rho, T2, and T2* relaxation time mapping has potential to non-invasively identify biochemical signs of pre-arthritic cartilage change through its sensitivity in detecting heterogeneity of water content, collagen matrices, GAG concentration, and proteoglycan concentration.[46,47] Such heterogeneities have been shown to correlate with articular cartilage degradation and associated symptoms determined by histology, arthroscopy, patient reported outcomes (PROMs), and radiography.[45–48] Additional correlations exist in known regions of cartilage degradation in pre-OA conditions such as DDH or FAI.[47–51]

Siebenrock et al evaluated the utility of T2 and T2* mapping in detecting biochemical cartilage change compared to histological evaluation by Mankin score in eight sheep with osteotomy-induced cam-type FAI.[46] The sheep were allowed to ambulate for 10–14 weeks after FAIS-induction, and then the hip was imaged with 3T MRI. T2 and T2* values were taken from six different points throughout the hip joint and compared to histology.[46] T2 and T2* mapping corresponded to regional cartilage degradation, leading the authors to conclude that qMRI is useful in detecting early cartilage damage in this ovine FAI model.[46]

Longitudinal clinical studies have demonstrated increased T1rho and T2 relaxation times over the course of 18 months without radiographic evidence of morphologic change, indicating the ability to detect subtle cartilage composition.[43–45] Pedoia et al found that increased T1rho and T2 relaxation times correlated to worsening PROMs over an 18-month period in a 16-subject cohort (mean age = 46 years, range 23–69 years) with mild or moderate hip OA (Kellgren-Lawrence grade 2 or 3).[45] These increased T1rho and T2 patterns suggest increases in cartilage water content, decreased proteoglycan concentration, and rearrangement of the collagen matrix.[43–45] Both Siebenrock et al and Nishii et al showed that decreases in T2 and T2* relaxation times corresponded to cartilage degradation when compared to histology or radiography.[46,47] These studies suggest that the pattern of relaxation time relating to biochemical cartilage change varies by patient age, activity type, and disease stage. Further large cohort studies are needed to explore these confounding variables.

The ability to detect biochemical changes in cartilage composition could enable therapeutic intervention in patients with DDH before morphological cartilage changes. Nishii et al used T2 mapping to evaluate cartilage matrix composition in 10 healthy volunteers (14 hips) and 23 DDH patients (26 hips)—14 hips were at the pre-arthritic stage (Kellgren-Lawrence grade 0) and 12 were at the early arthritic stage (Kellgren-Lawrence grade 1 or 2).[47] T2 mapping results revealed a gradient T2 pattern in all healthy volunteers, a low T2 pattern in the pre-arthritic group, and a high T2 pattern in the early arthritic group.[47] This indicates a drastic difference in T2 mapping patterns between pre-arthritic and early arthritic hip pathology. This is a promising sign in distinguishing the two conditions, but also prompts need for additional studies characterizing T2 mapping of pre-arthritis is DDH patients.

qMRI can also be utilized as a prognostic marker in DDH, predicting progression of OA in patients undergoing rotational acetabular osteotomy (RAO). Shoji et al reviewed 61 hips with early-stage OA that underwent RAO for DDH, with 16 patients having postoperative OA progression, defined as joint space narrowing of more than 1 mm at five years follow-up.[52] In this study, a robust, single-sliced 3T MR image was used that passed through the center of the femoral head and crossed the cartilage at a right angle.[52] Preoperative T2 mapping demonstrated significantly higher signal intensity to the center of the acetabulum's anterolateral portion and the femoral head in patients with OA progression versus those without OA progression.[52] Logistic regression analysis identified T2 values of the center to the anterolateral region of the acetabulum as independent predictors of subsequent OA progression ($p < 0.001$).[52] These data suggest that T2 preoperative mapping in DDH may prove superior to traditional radiological measures in predicting OA prognosis, with further study needed elucidate its role in long-term joint preservation.

Identification of subtle changes in cartilage composition may have a profound effect on the treatment of patients with FAI. Several studies have demonstrated significant elevation in T1rho, T2, and T2* mapping in the anterosuperior cartilage region. Hesper et al correlated T2* mapping of cartilage composition to arthroscopic findings in 29 patients (mean age = 35.6 years, range 22.8–48.4 years) with significant sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (83.5%, 67.7%, 78.4%, and 74.4%, respectively).[48] T1rho and T2 were further shown to be a sensitive measure in detecting cartilage delamination in 36 asymptomatic FAI patients compared to 36 age, gender, and BMI matched controls, suggesting the techniques' versatility in FAI characterization.[51] The quantitative effects of T1rho and T2 mapping have also been shown to enhance the diagnostic capability of magnetic resonance arthrography (MRA) by simultaneously assessing articular cartilage change and labral pathology in FAI.[50]

T1rho, T1, and T2 sequences have the advantage of being non-contrast techniques but they are time consuming, precluding availability of bilateral 3D reconstructions. T1rho image acquisition can be subject to vendor availability, further limiting widespread implementation. These logistical constraints may be addressed through simultaneous acquisition of T1rho, T1, and T2 imaging. Sharafi et al demonstrated the feasibility of magnetic resonance fingerprinting as a novel technique for simultaneous bilateral T1rho, T1, and T2 hip imaging, finding faster overall scan times for assessing femoral and acetabular cartilage.[53]

Overall, the use of qMRI appears to be a promising imaging modality to predict biochemical cartilage change in a hip that does not show radiographic signs of OA, indicative of the pre-arthritic condition. The aforementioned studies support clinical capabilities of the qMRI technique in assessing pre-OA, but further exploration of the effects of confounding variables and standardization of mapping values is needed for widespread application.

Computed Tomography (CT) and Optical Coherence Tomography (OCT)

CT, a radiologic workhorse in the clinical setting, has well-known limitations when evaluating articular cartilage without contrast enhancement.[11] It has continued to be essentially unrivaled when tasked to evaluate bony findings given its high spatial resolution and contrast from adjacent soft tissues.[11] In 193 patients with dysplastic hip joints (mean age = 35.5 years, range 15–61 years), degenerative changes, including subchondral cysts and osteophytes, were found primarily in the antero-lateral portion of the hip.[54] Although such findings are not necessarily apparent in pre-osteoarthritic hips, this study's findings spotlight the susceptibility of the watershed zone between the acetabular labrum and cartilage and the ability of CT to identify such pathologies.

CT is further empowered using intra-articular contrast. Tamura et al utilized CT arthrography to demonstrate that hip dysplasia patients (26 symptomatic Japanese females mean age = 32 years, range 16–52 years) have nonhomogeneous acetabular cartilage thickness.[55] Specifically, the lateral anterosuperior acetabulum showed increased cartilage thickness that was only apparent prior to the development of OA, providing a possible morphological marker for characterization of pre-OA.

Three-dimensional (3D) and 4D CTs have demonstrated use in the workup and early diagnosis of conditions that predispose patients to early arthritis, including hip dysplasia and FAI. In patients with DDH, 3D CT scans were useful for surgical planning and estimation of femoral version in patients with positive impingement tests.[56] 3D CT scans did not demonstrate superiority to plain radiographs in diagnosing CAM deformities but may have some use to surgeons for

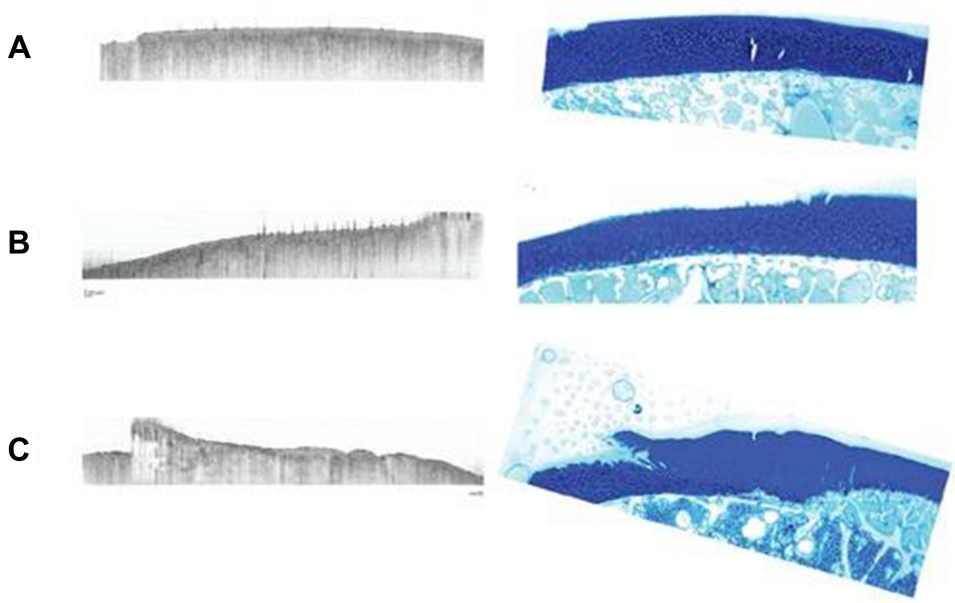

Figure 3 Optical Coherence Tomography (left) and equivalent histological sections (right) according to the graded classification system of Bear et al[59,60] Grade (**A**) indicates an intact surface and obvious birefringence, grade (**B**) represents an intact surface with no birefringence, and grade (**C**) corresponds to an irregular articular surface and/or subsurface voids.[59] This work is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported License. http://creativecommons.org/licenses/by-nc/3.0/.

preoperative planning.[57] It is important to note that such techniques are not widely used, and these studies did not examine the use of 3D CT scans in detecting pre-OA.

Fernquest et al demonstrated the use of 4D CT scans as a modality for studying the dynamics of FAI in patients with CAM deformities.[58] 4D CT scans were used to examine the hip kinematics and determine where in the arc of flexion each patient reached the point of impingement. This can allow surgeons to stratify patients based on risk of chondrolabral damage and intervene appropriately. This imaging modality should be used conservatively as 4D CT scans expose patients to 3 times as much radiation to the pelvis as a routine CT scan and obtaining views of additional hip motions besides flexion would further increase exposure.

OCT is a technique that utilizes reflected light across the spectrum to produce cross-sectional and 3D images.[59] It has been used in ocular imaging but is also applicable arthroscopically to detect grades of cartilage degeneration.[59] An in vitro study done by Pilge et al using resected femoral head specimens from 20 patients (mean age = 60.9 years, range 51.3–70.5 years) showed a high correlation between OCT images and histology for the detection of subsurface cartilage degeneration (Figure 3).[59] Birefringence can also be measured using polarization sensitive OCT (PS-OCT) to detect aberrances in the expected birefringence of articular cartilage, as reduced birefringence was found to be associated with cartilage degeneration and extracellular matrix remodeling.[12] Further studies are necessary to establish the role of OCT in the characterization of pre-arthritic hip cartilage.

Conclusion

Pre-OA of the hip is a newly recognized term to describe early, potentially modifiable degenerative changes in the hip that are often not detectable with conventional imaging modalities. Current research suggests that certain dGEMRIC and qMRI protocols could reliably diagnose pre-OA hip disease, but more research is necessary to allow for their implementation into clinical practice. CT has limited use in the detection of pre-OA, but it is a valuable tool in the work up and preoperative planning for associated conditions such as FAI and DDH. The benefits of using any CT imaging modality must be balanced with the risks of ionizing radiation in a young patient population.

Disclosure

Dr Jordan Gross reports being a consultant for Canon Medical Systems USA, outside the submitted work. The authors report no other conflicts of interest in this work.

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