State of the art in the diagnostic evaluation of osteomyelitis: exploring the role of advanced MRI sequences—a narrative review

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Background and Objective: Osteomyelitis, a severe bone infection caused mainly by pyogenic organisms, poses diagnostic challenges due to its non-specific magnetic resonance imaging (MRI) manifestations. Conventional MRI, though the imaging modality of choice, often exhibits signal abnormalities with overlapping differential diagnoses, potentially leading to overestimation of infection extent and duration. To address these limitations, advanced MRI sequences, including dynamic contrast-enhanced (DCE) MRI, 1H magnetic resonance spectroscopy (MRS), diffusion-weighted imaging (DWI), and Dixon techniques have emerged as promising alternatives. This narrative review explores the potential role of these sequences in aiding the differential diagnosis of osteomyelitis.

Methods: We used the PubMed database to search for relevant articles using the MeSH keywords: (osteomyelitis) AND (advanced MRI sequences) and we manually selected the most suitable studies to include in our review. Articles outside of original studies were also included. Only records in English or French were considered.

Key Content and Findings: In particular, DWI is useful for characterizing fluid collections, distinguishing bone infarcts, and bacterial skull base osteomyelitis from neoplastic lesions. Moreover, DWI assists in differentiating diabetic foot osteomyelitis (DFO) from Charcot neuro-osteoarthropathy, facilitates the diagnosis of pediatric acute osteoarticular infections, and aids in distinguishing osteomyelitis from Modic I degenerative changes. Additionally, DWI proves valuable in monitoring spinal infections and distinguishing pedal osteomyelitis from other conditions, even in patients with renal impairment. DCE-MRI enhances MRI specificity by assessing contrast uptake over time, providing valuable insights into inflammatory microenvironments. It aids in detecting DFO, differentiating it from acute Charcot arthropathy, and distinguishing osteomyelitis from neuropathic arthropathy. Moreover, DCE-MRI shows potential in assessing response to antibiotic therapy in spinal infections. Dixon acquisition improves image quality and facilitates the detection of bone marrow abnormalities, aiding in the differentiation of diabetic foot from osteomyelitis. It also assists in distinguishing osteomyelitis from neuropathic arthropathy and provides valuable information in evaluating the diabetic foot. Proton MR spectroscopy, a well-established modality, offers metabolic information that can differentiate malignant from benign lesions.

Conclusions: The role of advanced MRI techniques in evaluating osteomyelitis remains to be fully defined, and further research is required to explore its potential utility in this context. In conclusion, the incorporation of advanced MRI sequences has shown promise in improving the differential diagnosis of

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osteomyelitis. Future investigations exploring combinations of these techniques and their clinical applications hold significant potential to enhance diagnostic accuracy and patient outcomes.

Introduction

Osteomyelitis is an acute or chronic inflammatory process involving the bone and its structures secondary to infection and can arise as a result of the spread of pathogens through the bloodstream from a remote location, through direct introduction following an injury, or by extending from a nearby soft tissue infection. It can be caused by viruses, bacteria, fungi, and parasites but the majority are caused by bacteria. The most common causative agent is *Staphylococcus aureus*, responsible for 80–90% of pyogenic osteomyelitis (1). In osteomyelitis, magnetic resonance imaging (MRI) remains the imaging modality of choice after initial evaluation through plain radiography (2,3). Conventional MRI sequences have long been the cornerstone in the diagnosis of osteomyelitis, offering notable advantages such as excellent soft tissue contrast and multiplanar imaging capabilities (4). It has high sensitivity and specificity in the diagnosis of osteomyelitis as described in the recent works by Weaver *et al.* and Llewellyn *et al.* showing that in adults, MRI had a sensitivity of 95.6% and a specificity of 80.7% in the diagnosis of osteomyelitis (1,5). T1-weighted and T2-weighted sequences, along with gadolinium-enhanced T1-weighted imaging, have been instrumental in visualizing bone marrow edema, soft tissue abscesses, and periosteal reactions, facilitating the accurate assessment of osteomyelitis (4).

However, these conventional sequences come with limitations, such as reduced sensitivity in the early stages of the disease and the inability to differentiate between infectious and non-infectious causes of bone marrow edema (4). Indeed, bone marrow signal abnormalities on MRI are known to be non-specific findings (differential diagnosis includes contusion, fracture, postsurgical change, arthritis, neoplasm, Charcot arthropathy, etc.) and can overestimate the extent and duration of infection on fluid-sensitive images due to the coexistence of reactive marrow edema with true marrow infection (2,3).

In contrast, innovative approaches like diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) have emerged as potential game-changers in osteomyelitis diagnosis. DWI provides insights into tissue cellularity and can detect subtle changes even before structural alterations become apparent. DCE-MRI, on the other hand, aids in assessing perfusion dynamics, offering valuable information about the inflammatory process (6). In this review article we investigate the role of such advanced MR sequences such as DCE-MRI, DWI, magnetic resonance spectroscopy (MRS), and Dixon in the evaluation of osteomyelitis. We present this article in accordance with the Narrative Review reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1138/rc).

Methods

The systematic literature search conducted on March 26, 2023, aimed to identify relevant studies pertaining to advanced MRI techniques in the context of osteomyelitis. The primary database searched was PubMed, utilizing a comprehensive set of search terms including "(advanced MRI techniques) AND (osteomyelitis)". The search timeframe spanned from 1988 to 2023 to ensure a comprehensive coverage of relevant literature. Inclusion criteria were established to encompass a broad spectrum of evidence, comprising all types of studies such as reviews, letters, and case reports. Additionally, reports written in either English or French were eligible for review, and human studies were considered. Conversely, exclusion criteria were defined to refine the focus, excluding animal studies and articles not written in English or French. The selection process involved both reviewers independently screening the identified records. After the independent selection, the reviewers compared their choices, and any disparities were resolved through discussion, emphasizing a consensus-based approach. This method was employed to

Table 1 The search strategy summary

Items	Specification
Date of search	26 March 2023
Databases and other sources searched	PubMed
Search terms used	(advanced MRI techniques) AND (osteomyelitis)
Timeframe	1988–2023
Inclusion and exclusion criteria	Inclusion criteria: (I) all types of studies including reviews, letters, and case reports; (II) reports written in English or French; and (III) human studies were eligible for review. Exclusion criteria: (I) animal studies and (II) articles not written in either English or French were excluded
Selection process	Both reviewers selected the records independently and compared afterwards. Any disagreements were resolved through discussion

enhance the reliability and objectivity of the study selection process. For a summary of the review process see *Table 1*.

DWI

DWI is a molecular method for evaluating bone marrow edema that makes use of the random (Brownian) movement of free water molecules inside a tissue voxel to produce an indirect estimate of cellularity and cell membrane integrity (7). The accuracy of DWI also increases as the level of diffusion weighting (b value or diffusion moment) increases (7). The measurement of diffusion in the form of apparent diffusion coefficient (ADC) involves data acquisition with two distinct b values. Unlike conventional DWI, which inherently carries T2-weighting, ADC values are devoid of this property, and they are presented in the form of a parametric map, commonly referred to as an ADC map (7). Each voxel within the ADC map represents a distinct numerical diffusion value, expressed in units of mm^2/s. By selecting a region of interest (ROI) on the ADC map, we can ascertain the average ADC values (3).

DWI could have a valuable role in osteomyelitis by assisting in the characterization of associated fluid collections. In cases where purulent material is present within an abscess, the free diffusion of water molecules will be restricted. This restriction will be reflected in high diffusion signals on fractional anisotropy/trace images and low signal intensity on ADC maps, resulting in an improved image with excellent background suppression, as illustrated in *Figure 1* (7-9). This use case becomes especially important for individuals who are unable to be administered gadolinium-based contrast agents because of compromised renal function or an allergy to contrast agents (9-13).

Another valuable application of DWI is its potential to differentiate bone infarct from osteomyelitis in sickle cell patients, which is considered one of the most challenging issues both radiologically and clinically when evaluating acute bone pain in this patient population (14,15). In these scenarios, achieving an early diagnosis holds significant therapeutic and prognostic implications, as it permits the implementation of specific treatments at an initial stage, thereby circumventing the unnecessary use of intravenous broad-spectrum antibiotics, minimizing the requirement for multiple diagnostic assessments, reducing morbidity, shortening hospital stays, and resulting in substantial cost savings (14,15). While both bone infarct and osteomyelitis can manifest restricted diffusion, characterized by a bright DWI signal and a low ADC value, Tuna *et al.* proposed that during the initial stages of a vaso-occlusive crisis (within 24 hours), there may be restricted diffusion associated with a dark DWI signal and diminished T2 signal. This distinction could prove beneficial in discerning between a bone infarct and an infectious process (14). Additional supporting factors for diagnosing bone infarction instead of infection include the lack of edema on T2-weighted images, the lesion's geographical pattern, poor enhancement of the infarcted bone, and the absence of permeative or erosive changes. *Figure 2* illustrates this differentiation (14). It's crucial to recognize that the presence of sickling and sequestration can result in an exceptionally low signal on T2-weighted images, primarily due to the paramagnetic influence of intracellular deoxyhemoglobin (14). Given that diffusion-weighted images inherently incorporate T2 weighting, the tissue's T2 properties can impact their appearance, irrespective of tissue diffusivity. This can give rise to T2 shine-through and T2 blackout effects (14). The
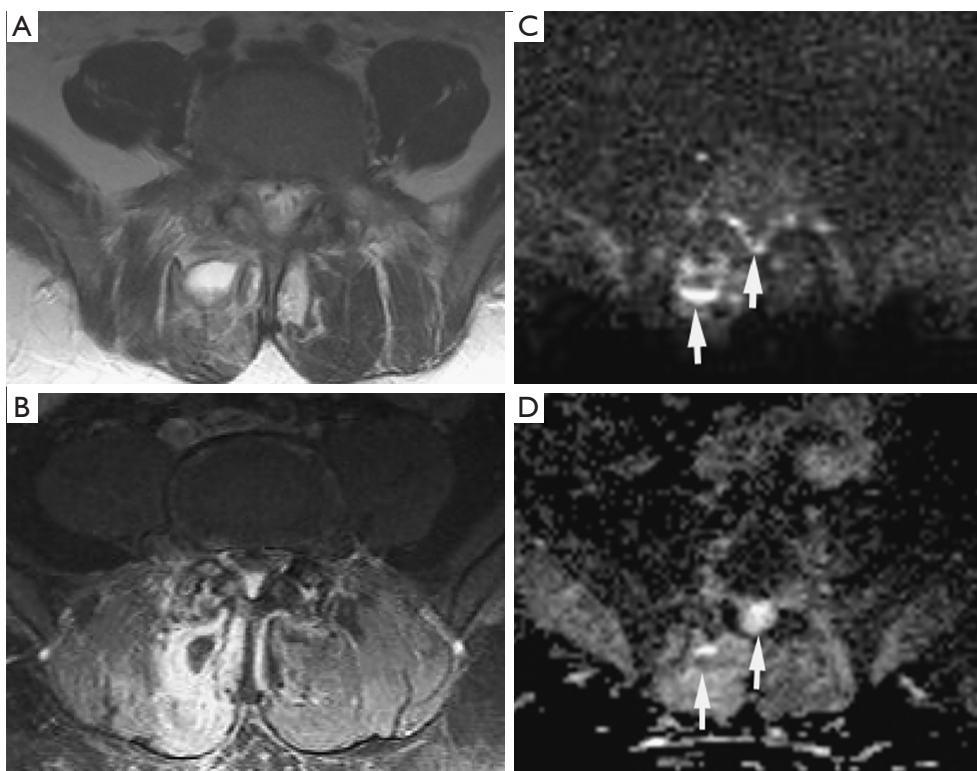
Figure 1 Epidural and paraspinal abscesses with septic facet joint infection. Methicillin-susceptible *Staphylococcus aureus* was proven by surgical drainage. (A) On axial T2 weighted image, high signal intensity in the right spinous muscle at L4–L5. It is difficult to detect small epidural abscesses. (B) Axial post-contrast T1 weighted image with fat saturation reveals the paraspinal abscess and epidural enhancement with associated facet joint infection. (C,D) Diffusion-weighted imaging (C) demonstrates the paraspinal abscess and small epidural abscesses as hyperintense with partially increased apparent diffusion coefficient values (D) likely due to dilution by exudates and/or partial volume artefacts (arrows).

phenomenon of DWI T2 blackout occurs when lesions with extremely low T2 values diminish the signal intensity in the diffusion-weighted image, potentially concealing or eliminating its sensitivity to diffusion. In severe instances, this may have implications for the accuracy of the ADC map calculations, rendering it unreliable (14,16).

Chaturvedi (8) highlights that DWI is also valuable in distinguishing between bone malignancy and aggressive osteomyelitis. Similarly, a study by Leclair *et al.* showed a substantial elevation of the ADC values in inflammatory bone lesions due to chronic recurrent nonbacterial osteomyelitis (17). These studies highlighted DWI as a promising technique that may help to distinguish between malignant lesions and benign inflammatory processes (8). Furthermore, in cases of bacterial Skull Base Osteomyelitis (SBO), DWI aids in its differential diagnosis with lymphoma or nasopharynx carcinoma (18). Ozgen *et al.* demonstrated that using an ADC value cutoff equal to

or higher than 1.08×10^{-3} mm^2/s can effectively rule out lymphoma and nasopharynx carcinoma with an accuracy of 96% (19). Similarly, this ADC cutoff can be utilized to distinguish between patients with SBO and patients with neoplastic lesions of the skull base (specifically lymphoma, nasopharynx carcinoma, and metastasis), achieving an accuracy of 86%, with a sensitivity and specificity of 89% and 85%, respectively (19). In bacterial SBO, ADC values tend to be high, whereas in malignant diseases, ADC values tend to be relatively reduced due to factors such as reduced extracellular matrix, enlargement of nuclei, and hypercellularity (18). However, the presence of restricted diffusion, increased signal on DWI, and low ADC values should raise suspicion of associated abscess formation in SBO (similar to intraosseous abscesses) (18,20). One limitation of DWI is its inability to differentiate between abscess formation in SBO and malignant neoplasms (21). Nevertheless, on postcontrast imaging, focal abscesses may
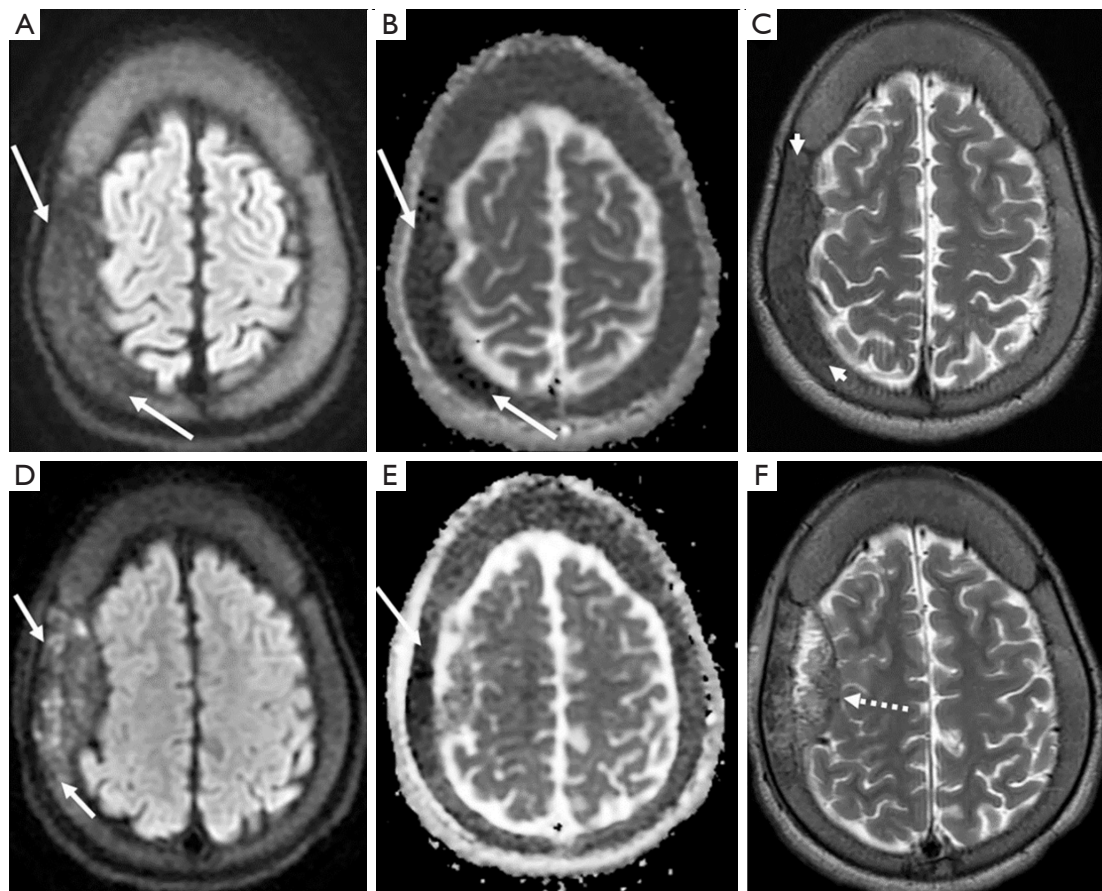
Figure 2 Axial MRI of a 63-year-old patient with right parietal bone infarct represented by an arrow in each figure. (A-C) The imaging findings within 6 h of presentation demonstrating decreased (A) DWI as well as (B) ADC signal and (C) decreased signal on T2 weighted image in the affected bone marrow. (D-F) Follow up contrast enhanced axial MRI of the same patient 3 days later demonstrating (D) increasing heterogenous DWI trace, and (E) decreased ADC signal, and (F) lack of enhancement on T2 weighted sequences. MRI, magnetic resonance imaging; DWI, diffusion weighted imaging; ADC, apparent diffusion coefficient.

exhibit a peripheral rim of enhancement, whereas neoplasms generally show homogenous or heterogenous enhancement within the diffusion-restricting tissue. Refer to *Figure 3* for an illustration (21). A significant hurdle encountered with diffusion-weighted images in the skull base region pertains to susceptibility artifacts stemming from the non-uniform tissues in this region (18). Nevertheless, the utilization of non-epi DWI imaging can offer a solution to mitigate these artifacts (18).

DWI is also utilized for distinguishing between diabetic foot osteomyelitis (DFO) and Charcot neuro-osteoarthropathy (CN). In a study conducted by Diez *et al.*, the researchers aimed to compare the diagnostic accuracy of functional MRI with that of ^{18}F-FDG PET/CT in differentiating between DFO and CN (22). Their findings indicated that analyzing the high b-value signal

pathological-to-normal bone ratio on DWI (DWIr) and measuring the volume transfer constant (K^{trans}) and internal area under the gadolinium curve at 60 s ($iAUC_{60}$) allowed for a reliable differentiation of DFO and CN, especially for large regions of interest (ROIs) (22). While ^{18}F-FDG PET/CT was identified as the most accurate diagnostic modality for differentiating these conditions, the novel combined PET/MRI, which integrates morphological, functional, and metabolic evaluations, shows great promise as a pivotal tool in DFO imaging (22-26). This integrated approach may provide valuable insights and improved accuracy in distinguishing between DFO and CN, benefiting patients and clinicians in managing these complex conditions more effectively.

In a comparative study conducted by Habre *et al.* (27), the diagnostic performance of standard contrast-enhanced

Figure 3 A 76-year-old man with central skull base osteomyelitis. Isotropic diffusion-weighted image shows hyperintensity within ring-enhancing lesion at preclival region (arrow) raises suspicion of a skull base osteomyelitis associated abscess.

MRI was compared to an unenhanced DWI protocol (11). The results revealed that emergency unenhanced DWI alone is adequate for establishing the diagnosis of pediatric acute osteoarticular infections, eliminating the need for gadolinium contrast. Specifically, for septic arthritis and osteomyelitis in long bone metaphyses/diaphyses or metaphyseal equivalents, DWI did not provide additional diagnostic value since all cases were effectively identified using standard unenhanced MRI sequences (11). On the other hand, when it comes to the diagnosis of bone and soft tissue abscesses, DWI significantly improved sensitivity to 100%. The imaging protocol, which included short tau inversion recovery (STIR), water-only T2 Dixon, T1, and DWI, proved sufficient for enabling prompt medical and surgical management of these conditions (27). However, it's important to note that static contrast-enhanced MRI remains crucial for evaluating the femoral head chondroepiphysis in children below the age of 30 months, especially considering their increased propensity for this site (27,28). In this particular age group, DWI has limited sensitivity, which is partly explained by the low epiphyseal fat content in younger individuals, leading to higher enhancement that may affect the effectiveness of DWI in this specific area (27). Overall, the study suggests that an unenhanced DWI protocol can be highly valuable in the diagnosis of pediatric acute osteoarticular infections, offering a reliable alternative to standard contrast-enhanced MRI, while still recognizing the importance of using contrast-enhanced MRI for specific scenarios, such as evaluating the femoral head chondroepiphysis in young children.

DWI also proves advantageous in distinguishing acute discitis-osteomyelitis from Modic I degenerative alterations, as these two conditions can exhibit similar MRI appearances (1). Modic type 1 degenerative signal changes can occasionally resemble infections, prompting invasive diagnostic procedures and incurring additional costs (1). However, in a retrospective study by Patel *et al.*, the accuracy and utility of a novel DWI "claw sign" were analyzed to distinguish vertebral diskitis/osteomyelitis from symptomatic type 1 degeneration (1,29). The study revealed that the presence of a "claw sign" is highly suggestive of degenerative disease, with a very high likelihood (97–100%) of being associated with degeneration rather than infection. Conversely, the absence of the "claw sign", which refers to a pattern of diffusely increased diffusion signal, strongly suggests diskitis/osteomyelitis in individuals displaying type 1 signal changes in the vertebral bodies exhibiting a notably high accuracy, ranging from 93% to 100%, in effectively discerning infection from disk degeneration associated with Modic type 1 endplate alterations (1,29). *Figure 4* illustrates this finding. This differentiation is valuable in clinical practice as it helps avoid unnecessary invasive procedures and reduces healthcare costs by guiding appropriate management based on the underlying condition, whether it is degenerative changes or infection.

Diagnosing spinal infections can be challenging as MRI results frequently trail behind the onset of clinical symptoms, and may also take time to normalize during the healing phase. This uncertainty can make it difficult to initiate treatment and determine when treatment has been adequate to be stopped (30). In a study conducted by Dumont *et al.*, they proposed standards for ADC values that are representative of spinal infection (30). Their research revealed that in individuals suspected of having a spine infection, the ADC values obtained from DWI were notably lower in those with positive microbiological sampling (indicating the presence of infection) as opposed to individuals with negative microbiological sampling (indicating the absence of infection) (30). In accordance with their investigation, an ADC value falling below $1,250 \times 10^{-6}$ mm^2/s could be a cause for concern when evaluating the possibility of spine infection. Furthermore, their observations indicated that ADC values may return to normal levels during successful treatment of spinal infections, implying that DWI can serve as a valuable tool for monitoring the response to antibiotic therapy (30,31). This

Figure 4 An 81-year-old woman with degenerative vertebral end plate changes. From left to right: T1 FLAIR; contrast-enhanced, fat-suppressed T1 FLAIR; T2; diffusion weighted imaging. The claw sign (arrows) compatible with Modic type I degenerative changes, is identified on trace/combined diffusion-weighted images as well-marginated, linear, typically paired regions of high signal situated within the adjoining vertebral bodies at the boundaries between the normal bone marrow and vascularized bone marrow that lies close to the affected disk, presumed to represent a form of physiologic reactive response or induration. FLAIR, fluid attenuated inversion recovery.

information can complement conventional MRI, especially when the clinical picture is equivocal, helping in more accurate and timely decision-making regarding the diagnosis and management of spinal infections (30). By utilizing DWI as an adjunct to conventional MRI, healthcare professionals can potentially improve the accuracy of diagnosing spinal infections and assess treatment response more effectively, ultimately leading to better patient outcomes.

Non contrast DWI sequences have been found to improve specificity of conventional MR sequences in diagnosing pedal osteomyelitis, as conventional MR sequences alone can lead to false positive results (6). By using an ADC value cut-off of 1.57×10^{-3} mm^2/s, the sensitivity for diagnosing pedal osteomyelitis was 88.2%±10.3%, while the specificity was 80.0%±19.4% (6). This increased specificity is especially beneficial for patients with pedal osteomyelitis, as they often have impaired renal function that may prevent the use of contrast agents in conventional MR sequences. Non-contrast diffusion-weighted sequences provide valuable diagnostic information without the need for contrast, offering a safer and more reliable imaging option in this specific patient population (6). By incorporating non-contrast diffusion-weighted sequences in addition to conventional MR sequences, healthcare professionals can more accurately distinguish pedal osteomyelitis from other conditions, leading to improved diagnoses and better patient care.

DCE-MRI

The increasing body of research in the realm of MRI physics has brought forth the development of novel sequences that incorporate functional imaging to enhance the specificity of this imaging modality. DCE-MRI is an example of such an approach, which evaluates the progression of contrast agent uptake in a lesion over a period of time (6,32).

IV gadolinium contrast is recommended when there is suspicion of epiphyseal infection because unenhanced images may not show any abnormalities, potentially leading to a false-negative diagnosis. By using post-contrast fat-saturated T1 sequences, any sinus tract or abscess can be better visualized and characterized, enhancing the detection and evaluation of the infection. Moreover, IV gadolinium contrast is essential for distinguishing between an abscess and a phlegmon. The contrast agent aids in highlighting areas with increased vascularity, allowing for a clearer differentiation between these two conditions. This differentiation is crucial for appropriate treatment planning and management decisions.

Raj *et al.* conducted a study focused on examining the contrast uptake patterns in two groups of patients suffering from diabetic foot ulcers and suspected DFO (6). They utilized semi-quantitative parameters from the DCE-MRI sequence, which had not been previously assessed
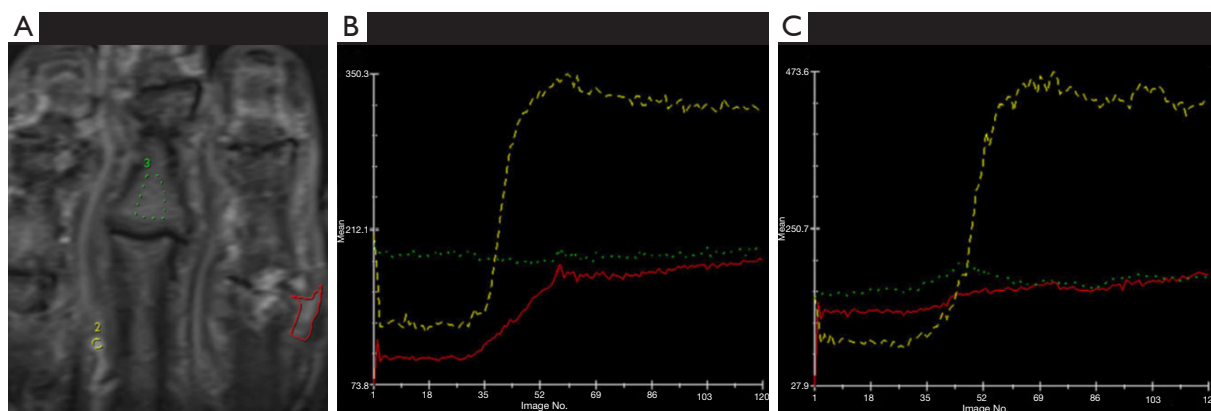
Figure 5 Synovitis assessment in a 61-year-old woman with an erosive osteoarthritis. (A) Coronal T1 gradient-echo MRI shows ROIs for DCE-MRI evaluation. Within ROIs delineating the thickened and inflamed synovium (1, red solid line), unaffected bone marrow (2, green dotted line) and artery (3, yellow dashed line) enhancement curves are calculated. DCE-MRI curves (B) at baseline compared to curves (C) after 12 months of treatment show a decrease in enhancement slope of the synovium (solid lines). The relative enhancement of the synovium (dashed lines) compared to the unaffected bone marrow (dotted lines) also decreased after treatment. MRI, magnetic resonance imaging; ROIs, regions of interest; DCE, dynamic contrast-enhanced.

for diagnosing DFO. Additionally, they compared the differences in ADC values between these patient groups. The study findings demonstrated that the sensitivity of MRI for diagnosing DFO can be enhanced by incorporating DCE-MRI alongside conventional MRI sequences (6). The DCE parameters, including tissue signal intensity on unenhanced T1 images (SI_0), maximum absolute contrast enhancement (SImax), wash-in rate (WIR), and the type of contrast enhancement curve, were found to be valuable in detecting DFO. WIR and the presence of a type II enhancement kinetic curve (observed in 94.1% of positive cases) were particularly advantageous for diagnosing osteomyelitis (6). This approach can enhance the overall sensitivity and specificity of MRI in distinguishing DFO from acute Charcot arthropathy, thereby addressing diagnostic challenges (6). WIR provided insights into the rate of contrast uptake within a lesion, and it was significantly higher in cases of biopsy-confirmed DFO compared to biopsy-negative cases. This difference was attributed to increased vascularity, hyperemia, and vasodilation resulting from the presence of various inflammatory cytokines that promote transudation across capillaries during infection (6). In contrast, the lower levels of inflammation and hyperemia in acute Charcot led to a distinct contrast uptake pattern. The higher tissue signal intensity on unenhanced T1 images (SI_0) and maximum absolute contrast enhancement (SImax) observed in affected bones were likely due to the presence of more inflammatory

cells and heightened hyperemia resulting from the infection (6).

DCE-MRI offers the advantage of providing quantitative assessments of perfusion and permeability, making it an effective tool for investigating microcirculation in living tissues that conventional MRI cannot evaluate. Notably, a previous study conducted by Jans *et al.* illustrated that in cases of osteomyelitis, the time-intensity curve (TIC) displayed an initial rapid rise followed by a progressively slower increase, potentially indicating the presence of an inflammatory process. In contrast, in areas affected by oedema in neuropathic arthropathy, a lower enhancement rate was observed with a slightly progressive increase in the TIC slope relative to the baseline, as depicted in *Figure 5* (33). Differentiating between regions presenting simultaneous osteomyelitis and acute neuropathic arthropathy poses an extremely challenging task for both clinicians and radiologists (34). In a study by Liao *et al.* aimed at evaluating the possibility of using DCE-MRI to differentiate between these two conditions, it was shown that the DCE-MRI parameters of the osteomyelitis group included greater transfer constant K^{trans} (related to wash-in), rate contrast K_{ep} (related to washout), and extracellular extravascular space volume fraction V_e values than those of the acute neuropathic arthropathy group (34). This distinction can be elucidated by considering the distinct pathological characteristics of these lesions. Acute neuropathic arthropathy is primarily

associated with bone marrow edema, characterized by relatively lower cellularity. In contrast, osteomyelitis involves the presence of white blood cells, deceased microorganisms, inflammatory cells, and, consequently, higher cellularity, leading to greater permeability (34). Furthermore, Pearson correlation analysis demonstrated a significant correlation between these DCE quantitative permeability parameters and the CRP and ESR levels in osteomyelitis patients (34). One possible explanation for this phenomenon may be the presence of microvascular irregularities within the inflammatory regions (35). In fact, Ertugrul *et al.* emphasized the significance of erythrocyte sedimentation rate (ESR) as a key inflammatory factor in diagnosing osteomyelitis (36). Furthermore, Van Asten *et al.* highlighted the importance of ESR and C-reactive protein (CRP) levels as crucial inflammatory markers for monitoring the effectiveness of therapy in osteomyelitis treatment (37). Consequently, the observed correlations between DCE-MRI parameters and inflammatory markers suggest that DCE-MRI parameters could serve as valuable imaging biomarkers, offering insights into the inflammatory microenvironment of osteomyelitis (since ESR and CRP are non-specific and may be positive even in other concomitant inflammatory conditions) and might be predictive of patient prognosis (38). This is because, apart from being non-specific to osteomyelitis, CRP and ESR do not give enough information on soft tissue involvement in chronic osteomyelitis, and thus could be useful in certain situations, it could serve as an alternative to performing an ^{18}F-FDG PET exam or a painful bone biopsy (39).

Dixon acquisition

The main types of MRI fat suppression techniques include chemical shift selective fat saturation pulse sequences (CHESS), STIR sequences, SPectral Attenuated Inversion Recovery (a hybrid technique combining features of both CHESS and STIR and based on chemical selective inversion and an adiabatic pulse), and chemical shift-based water/fat separation sequences like Dixon sequence techniques (40). These techniques exploit the chemical shift phenomenon, which allows the separation of water and fat signals based on their different resonant frequencies (7,41). In recent years, technical advancements have improved the optimization of the chemical shift phenomenon in Dixon acquisitions, enabling the generation of water-only signal images (by adding both in-phase and out-of-phase signal intensities) and fat-only signal images (by

subtracting the in-phase signal intensity from that of the out-of-phase image) within a single acquisition using multiple echoes in the same sequence, with the assistance of mathematical postprocessing of data (42). Unlike other MR fat suppression techniques that suppress fat during image acquisition, the Dixon technique suppresses fat in post-processing (43). Additionally, the Dixon method is relatively less sensitive to susceptibility artifacts, resulting in better detection of bony vertebral pathologies (44,45). The application of Dixon sequences enhances image quality and increases the detection of both soft tissue and osseous abnormalities, such as intraosseous sequestrums, sinus tracts, fistulas, cortical destruction, and periostitis. This improved visualization facilitates the differentiation between diabetic foot and osteomyelitis, as illustrated in *Figure 6* (10,46). By utilizing Dixon sequences, healthcare professionals can obtain clearer and more detailed images, leading to better diagnostic accuracy and more effective management of foot and bone conditions.

Dixon sequences could be used to distinguish between osteomyelitis from neuropathic arthropathy since neuropathic arthropathy shows a signal loss in the opposed-phase (OP) in the evaluation of bone marrow edema whereas there is no significant signal loss in osteomyelitis. This is because in OP, the signal is the difference between the signals from water and fat molecules (water signal-fat signal), OP images show a reduced signal from voxels that contain both fat and water. Thus, the increased edema in neuropathic arthropathy explains the signal loss on OP imaging compared to osteomyelitis which shows a severe increase in both water content and fat content (due to the high cellularity given predominantly by inflammatory cells) early in the course of the disease (10). In cases where only neuropathic arthropathy is present, genuine bone destruction occurs, resulting in the relative disappearance of bone contours on T1-weighted images. These contours do not reappear on fat-suppressed images. However, when both osteomyelitis and neuropathic arthropathy coexist, the bone contours also tend to disappear on T1-weighted images, but they have a tendency to re-emerge on fat-suppressed images, a phenomenon commonly referred to as the "ghost sign" (47). Dixon imaging is also a fundamental component of adequate evaluation of the diabetic foot.

Proton MR spectroscopy

Proton MR spectroscopy is a well-established imaging modality that provides valuable chemical and metabolic
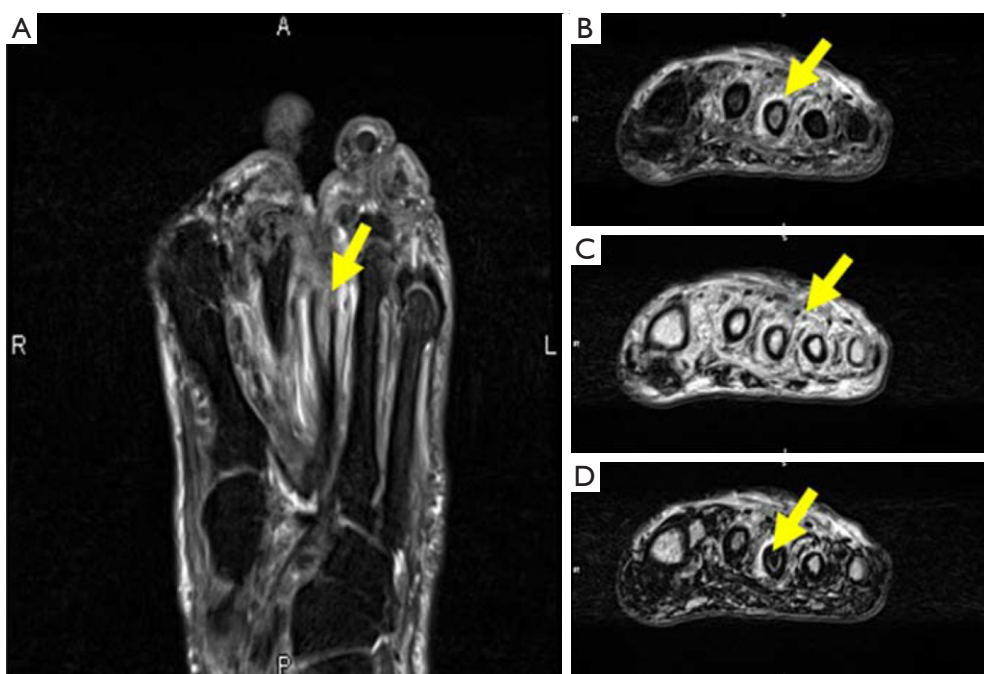
Figure 6 MRI of the foot of a 56-year-old male with DM and plantar ulcer below the 3rd metatarsal and suspected osteomyelitis. Prior fracture deformity of the second metatarsal head and surgical resection of the third metatarsal are also noted. (A) T2-weighted fat suppressed image and (B) T2 Dixon water map show marrow edema of the third metatarsal stump (arrows). (C) In-phase T2 Dixon map shows muscle fatty replacement from DM denervation change (arrow). (D) Opposed-phase T2 Dixon map shows marrow involvement by osteomyelitis (arrows). MRI, magnetic resonance imaging; DM, diabetes mellitus.

information about lesions by generating a spectrum of signal intensities emitted from different tissue metabolites. One essential capability of MR spectroscopy is its ability to reliably detect various lipid compartments (25,26,48,49). Notably, it can assess the unsaturation levels among triglycerides, which have proven useful in quantitatively assessing bone marrow inflammatory lesions (50). Another valuable aspect of proton MR spectroscopy is its ability to detect choline, a marker for cell membrane turnover. This enables differentiation between malignant and benign lesions (51,52). Amar *et al.* demonstrated that the absence of a choline peak on ^{1}H-MRS in focal bone lesions provides reliable assurance against malignancy (except for giant cell tumors), as illustrated in *Figure* 7 (53). However, using MR spectroscopy in bone lesions poses some challenges. The inherent heterogeneity of bone, with osseous trabeculae, fat, vessels, and muscle, along with magnetic susceptibility, makes adequate shimming (a process to optimize magnetic field homogeneity) a daunting task. This often leads to a high probability of obtaining inadequate spectra due to the abundance of lipids present in the musculoskeletal

system (54). Additionally, high levels of creatine in muscle can mask smaller metabolites, further complicating the interpretation of MR spectra (54). As of now, functional MRI imaging techniques such as MRI perfusion or MRS have not been widely utilized in the evaluation of osteomyelitis. While some studies suggest that these techniques could aid in making the differential diagnosis, more research should be encouraged before any definitive conclusions can be drawn (25,26). Further investigations and studies are necessary to determine the potential role of these functional MRI techniques in improving the evaluation and diagnosis of osteomyelitis.

Feasibility and challenges

It is crucial to note that these innovative sequences are not yet part of routine MRI examinations for osteomyelitis, and their incorporation into clinical practice requires careful consideration. As for the technical aspects, the feasibility of performing these sequences on standard MRI apparatus varies. While some, such as DCE-MRI and DWI, can

Figure 7 A 21-year-old female patient with left thigh pain. (A) X-ray image shows a dense sclerotic lesion in the metaphysis of the left proximal femur with an apparent sun-burst type of periosteal reaction along the lateral aspect (arrow) and matrix ossification. The radiographic diagnosis was osteosarcoma. (B) Metaphyseal lesion with a radiating type of periosteal reaction (arrow) is seen on coronal T1-W post-contrast image along with contrast enhancement within the periosteal component. (C) Magnetic resonance spectroscopy shows no discrete choline peak but a tall lipid lactate peak is noted. Histopathology was proven to be chronic osteomyelitis.

be executed on conventional scanners with appropriate parameter adjustments, others may necessitate specialized hardware configurations. In particular, performing MR spectroscopy and Dixon imaging in standard MRI machines is not possible without specialized hardware and software (55). Both of these techniques demand unique equipment and dedicated software for accurate results. For MR spectroscopy, specialized radiofrequency coils and pulse sequences are essential to target specific regions and measure chemical compounds. Post-processing software is required to analyze the acquired data and generate spectra. Dixon imaging, used for fat-water separation, relies on acquiring multiple images at different echo times and then applying complex mathematical algorithms during post-processing to create separate fat and water images. If an MRI machine lacks the necessary hardware and software for these techniques, upgrading the equipment or seeking access to a facility with specialized MRI capabilities should be considered. Thus, standard MRI software alone does not have the capabilities to perform MR spectroscopy or Dixon

imaging (55). In addition, the increased scan times and complexity associated with some of these sequences (such as DCE-MRI) may raise concerns regarding increased costs for healthcare providers and patient tolerability, which demand further evaluation. Regarding the expertise required, the latter sequences cannot be performed by all radiologists and their application is limited to specialized radiology departments (56,57). Adequate training and familiarity with these novel techniques are pivotal to ensure accurate and reliable results. While innovative MRI sequences hold promise in the diagnosis of osteomyelitis, their integration into standard practice necessitates addressing technical, logistical, and expertise-related challenges.

Conclusions and future outlook

Standard T1 and T2-weighted MRI is typically based on morphological sequences that provide purely structural information. It is clear that the above-discussed technical improvements (summarized in *Table 2*) have allowed the

Table 2 Summary of observations and findings indicating the patient group (if any), the application, imaging features, and relevant references

Application	Imaging findings and indications	Supplementary data	References
To characterize osteomyelitis associated purulent abscess	↑ DWI signal & ↓ ADC map signal	Patients with contraindication to gadolinium-based contrast agents	(3,4,7,13-16,25,26,58)
To differentiate bone infarct from osteomyelitis	Osteomyelitis: ↑ DWI signal & ↓ ADC map signal, ↓ T2 signal; in the early phases of vaso-occlusive crisis (within 24 h) of bone infarct: ↓ DWI signal & ↓ ADC map signal, ↓ post-contrast T2 signal	Sickle cell patients	(8)
To distinguish between abscess formation in SBO and malignant neoplasms of the skull base	Abscess formation in SBO: ↑ DWI signal & ↓ ADC map signal; post-contrast peripheral rim enhancement; malignant skull base neoplasms: ↑ DWI signal & ↓ ADC map signal; post-contrast enhancement within the diffusion-restricting tissue		(7,9,44,45)
To differentiate diabetic foot osteomyelitis from Charcot neuro-osteoarthropathy	DCE-MRI parameters such as DWIr, K^{trans}, iAUC60, WIR and type II enhancement (time-intensity) kinetic curve; utilize ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography whenever magnetic resonance imaging is unavailable or inconclusive		(10,18)
To differentiate acute discitis-osteomyelitis from Modic I degenerative changes	Modic type I degenerative changes: ↑ DWI signal + DWI claw sign; acute discitis/osteomyelitis: ↑ DWI signal + absence DWI claw sign		(1,9)
In treatment planning for spinal infections	ADC value <1,250×10^{-6} mm^2/s is indicative of ongoing spine infection; ADC values would normalize during effective treatment of spine infection	In patients with spinal infections whenever conventional MRI clinical picture is inconclusive	(17)

Table 2 (*continued*)

Table 2 (*continued*)

Application	Imaging findings and indications	Supplementary data	References
For more accurate diagnosis of pedal osteomyelitis	ADC value cut-off of 1.57×10^{-3} mm^2/s	In patients with deranged renal parameters	(18)
For suspected epiphyseal infection +/– sinus tracts or abscesses with normal unenhanced images	Post-contrast FS-T1 sequences will allow further characterization		(6)
To distinguish osteomyelitis from neuropathic arthropathy	In osteomyelitis: an initially fast-rising slope, followed by a progressively slow-rising phase observed on the time-intensity curve; no significant signal loss in Dixon sequence opposed-phase; in neuropathic arthropathy: a lower enhancement rate with a slightly progressive increase in the TIC slope relative to the baseline; significant signal loss in Dixon sequence opposed-phase	In patients whom an ^{18}F-FDG PET exam or a painful bone biopsy is not preferred	(4,32)
To differentiate malignant from benign lesions	Absence of choline peak on [1]H-magnetic resonance spectroscopy in focal bone lesions is a reliable assurance against malignancy (with exception of giant cell tumors)	In patients with suspected bone malignancy	(38-40,42)

DWI, diffusion weighted imaging; ADC, apparent diffusion coefficient; SBO, skull base osteomyelitis; DCE, dynamic contrast-enhanced; MRI, magnetic resonance imaging; DWIr, high b-value signal pathological-to-normal bone ratio on DWI; K^{trans}, the volume transfer constant; iAUC$_{60}$, internal area under the gadolinium curve at 60 s; WIR, wash-in rate; FS-T1, T1 fat-saturated; TIC, time intensity curve.

incorporation of functional quantitative information into structural information. As an illustration, a prior investigation conducted by Baba *et al.* demonstrated that quantitative parameters from DCE-MRI and normalized ADC values could be valuable in distinguishing between skull base osteomyelitis and nasopharyngeal cancer. Interestingly, when used in combination, these DCE-MRI parameters and normalized ADC values yielded better diagnostic performance compared to using each measure independently (59). Thus, a hypothesis worth being investigated in future is whether two or more advanced techniques in the setting of MR imaging could be combined to improve the diagnostic efficiency of osteomyelitis. Furthermore, one of the latest studies showed that Chemical shift imaging and related Dixon sequence were reliable tools for evaluating diabetic foot. They could distinguish between mimickers of bland edema of osteomyelitis and infectious edema-like changes of osteomyelitis-like changes with high sensitivity and specificity, particularly when using quantitative analysis of their signal abnormality (60).

Despite these recent developments, the role of these advanced techniques in the setting of osteomyelitis has not been fully defined and thus, further research is necessary to fully define their utility in this setting.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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