Imaging of osteomyelitis: the key is in the combination

An accurate diagnosis of osteomyelitis requires the combination of anatomical and functional imaging techniques. Conventional radiography is the first imaging modality to begin with, as it provides an overview of both the anatomy and the pathologic conditions of the bone. Sonography is most useful in the diagnosis of fluid collections, periosteal involvement and soft tissue abnormalities, and may provide guidance for diagnostic or therapeutic interventions. MRI highlights sites with tissue edema and increased regional perfusion, and provides accurate information of the extent of the infectious process and the tissues involved. To detect osteomyelitis before anatomical changes are present, functional imaging could have some advantages over anatomical imaging. Fluorine-18 fluorodeoxyglucose-PET has the highest diagnostic accuracy for confirming or excluding the diagnosis of chronic osteomyelitis. For both SPECT and PET, specificity improves considerably when the scintigraphic images are fused with computed tomography. Close cooperation between clinicians and imagers remains the key to early and adequate diagnosis when osteomyelitis is suspected or evaluated.

KEYWORDS: computed tomography ■ hybrid systems ■ imaging ■ MRI ■ nuclear medicine ■ osteomyelitis ■ ultrasonography

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Osteomyelitis is inflammation of the bone that is usually due to infection. There are different classification systems to categorize osteomyelitis. Traditionally, it has been labeled as acute, subacute or chronic, depending on its clinical course, histologic findings and disease duration, but there is no consensual agreement on the temporal scale used or specific findings. As a result, some researchers have proposed more detailed classification systems, such as the Waldvogel classification system based on etiology of the infection (hematogenous spread of an organism, direct inoculation of an organism through trauma or contiguous spread from a soft tissue infection), and Cierny-Mader classification, a descriptive system that takes into account both anatomic factors and the host's physiologic status [1,2].

An inadequate or late diagnosis increases the degree of complications and morbidity; for these reasons, imaging techniques are essential to confirm the presumed clinical diagnosis and to provide information regarding the exact site and extent of the infection process [1].

Although a variety of diagnostic imaging techniques is available for excluding or confirming osteomyelitis, it is often difficult to choose the most appropriate technique to conclusively establish the diagnosis of osteomyelitis. Several imaging modalities have been used in the evaluation of suspected osteomyelitis. The ideal imaging technique should have a high sensitivity and specificity; numerous studies have been published concerning the accuracy of the various modalities in diagnosing chronic osteomyelitis [2–4]. Confirmation of the presence of osteomyelitis usually entails a combination of imaging techniques. Table 1 shows the main pathologic findings of osteomyelitis assessed by diverse imaging techniques.

Conventional radiography

Plain films are usually the first imaging test ordered by clinicians [5]. Conventional radiography should not be used to exclude acute osteomyelitis in a patient who has experienced symptoms for less than 10 days. Nevertheless, deep soft tissue swelling, joint effusion or early periosteal changes may be seen within days after onset of infection. Furthermore, conventional radiography helps to exclude fracture or tumor.

Destructive bone changes do not occur until 7–10 days after the onset of infection. During the first 2–3 days of symptoms, radionuclide bone imaging may be particularly useful in showing a well-defined focus of increased uptake on the dynamic perfusion, as well as early blood pool and delayed images corresponding to the area of hyperemia [6]. At this early stage, the main utility of plain film is to provide a global view

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Table 1. Imaging abnormalities in osteomyelitis.

Technique	Main findings	
	Acute	***Chronic***
Conventional radiography	Radiolucent areas associated with periostitis Cortical resorption identified as endosteal scalloping, intracortical lucent regions or tunneling Lytic lesions Focal osteopenia Loss of trabecular architecture	Single or multiple radiolucent abscesses (Brodie's abscess) Cortical sequestration New bone apposition
Computed tomography	Blurring of fat planes Increased density of fatty bone marrow sequestra, involucra and intraosseous gas	Periosteal thickening Cortical erosion or destruction
Ultrasonography	Soft tissue abscess (if present) Surrounding fluid collection	Elevated periosteum Fistulous tracts Cortical discontinuity
MRI	T1-weighted: low signal intensity medullary space T2-weighted: high signal intensity contiguous to inflammatory processes and edema Gadolinium: enhances areas of necrosis Subacute: Evidence of Brodie's abscess, single or multiple radiolucent abscesses T1-weighted: central abscess cavity with low signal intensity T2-weighted: high signal intensity of granulation tissue surrounded by low signal intensity band of bone sclerosis (double-line effect)	T1- and T2-weighted: low signal intensity areas of devascularized fibrotic scarring in the bone marrow

of the suspect part of the skeleton and to provide information regarding differential diagnosis in a patient complaining of pain.

Structural bony changes and periosteal reaction consist first of subperiosteal resorption or scalloping, which creates radiolucencies within cortical bone that may progress to irregular destruction with areas of periosteal new bone formation. However, hematogenous osteomyelitis in children typically arises within cancellous bone, mostly in the vicinity of physeal plates, and secondarily involves cortical bone and periosteum.

In general, osteopenia becomes evident on conventional radiographs after the loss of approximately 30–50% of bone mineralization. Follow-up radiographs may be normal if therapy is successful, or in some instances periosteal new bone formation may be apparent.

The search for sequestra is a common and important diagnostic challenge in chronic osteomyelitis. The presence of a sequestrum may lead to a decision of surgery. A bone sequestrum manifests on conventional radiographs as a piece of calcified tissue within a lucent lesion. The increased density of the sequestrum relative to the surrounding bone is a consequence of its absence of blood supply. As a result of this devascularization, the sequestrum does not participate in the reactive hyperemia and therefore does not exhibit the osteopenia of the adjacent living bone. A wide scope of bone lesions may present with an image suggestive of sequestrum including osteoid osteoma, eosinophilic granuloma and primary lymphoma [7].

A lucent circumscribed lesion (Brodie's abscess) in the metaphyses of long bones predominantly abutting the growth plate with well-defined dense margins is commonly seen in the tibia and femur of children with subacute osteomyelitis.

Periostitis, involucrum formation and sinus tracts are due to a subperiosteal abscess with lifting of the periosteum, new bone formation and soft tissue fistulas. All of these findings are indicative of the protracted nature of the infection process.

Special situations

Diabetic foot

In a recent meta-analysis of the accuracy of diagnostic tests for osteomyelitis in diabetic patients with foot ulcers, the sensitivity of plain radiography for diagnosis of osteomyelitis was highly variable, ranging from 0.28 to 0.75. The wide variation may be attributable to the timing of performance of the radiograph in relation to the chronicity of the ulcer. The pooled sensitivity was 0.54 and the pooled specificity was 0.68. The diagnostic odds ratio

(OR) for radiography was 2.84 (the value of a diagnostic OR ranges from 0 to infinity; higher values indicate better discriminatory test performance) [5].

In summary, plain radiography is helpful as a first step, as it is widely available and may reveal soft tissue changes and alternative diagnoses (e.g., bone metastases or a fracture) can be made; however, it is not a sensitive test for acute osteomyelitis. Radiographs, when positive, are helpful, but negative radiographic findings are unreliable to exclude the diagnosis of osteomyelitis in patients who have violated bone [8].

Tuberculous osteomyelitis & arthritis

Tuberculous osteomyelitis can remain localized to bone or involve adjacent joints. In general, tuberculosis confined to bone is relatively infrequent. Virtually any bone can be affected, including the pelvis, phalanges and metacarpals, long bones, ribs, sternum, skull, patella, carpal and tarsal bones, although tuberculous osteomyelitis has predilection for the spine (thoracic and lumbar segments) and weight-bearing joints (i.e., hip and knee joints) [9].

When the joint is affected, monoarticular disease is the likely cause, although polyarticular disease is also reported. Multiple imaging modalities, such as conventional radiography, computed tomography (CT), MRI and ultrasound, may play a role in suggesting the diagnosis and aiding in the recovery of culture material through directed biopsies (FIGURE 1).

On radiographs, tuberculous arthritis is manifested as soft tissue swelling, foci of osteolysis accompanied by varying amounts of eburnation and periostitis. Corner defects simulating the erosions of inflammatory noninfectious arthritides are reminiscent of this. The combination of regional osteoporosis, marginal erosions and relative preservation of joint space is suggestive of tuberculous arthritis. Other changes include bony proliferation, subcondral eburnation and periostitis generally parallel to the osseous contour. Sequestrum is less frequent than in pyogenic arthritis. The eventual result in tuberculous arthritis is usually fibrous ankylosis of the joint [10].

Sinography

Opacification of a sinus tract can produce important information that influences the choice of therapy. In this technique, a small flexible catheter is placed within a cutaneous opening. Retrograde injection of contrast material defines the course and extent of the sinus tract and its possible communications with neighboring structures. Sinography or fistulography may be combined with CT for better delineation of the anatomical relationships of the contrast-filled track [8]. Sinography is not widely used in clinical practice.

Ultrasonography

During recent years, ultrasonography has had an expanding role in the investigation of infectious processes of the soft tissues and in early detection of subperiosteal fluid collections that are seen in acute osteomyelitis in childhood [11].

A constellation of grayscale and color Doppler ultrasound findings can be highly indicative of bone infection including: fistulous tracts, periosteal thickening, cortical discontinuity, soft tissue abscess and cellulitis, juxta-cortical fluid collections, distension of the pseudocapsule in arthroplasties and periosteal vascularity in patients with long-standing chronic post-traumatic/postoperative osteomyelitis [12]. The presence of joint effusion may be a diagnostic clue to the existence of septic arthritis.

Power Doppler ultrasonography detects the increased microvascular flow associated with infectious collections [13]. Furthermore, ultrasonography has been demonstrated to be useful in assessing therapeutic response and as a guide for accurate aspiration of material for culture [14–16].

MRI

MRI provides excellent delineation between bone and soft tissue as well as abnormal and normal bone marrow. Furthermore, it can detect osteomyelitis as early as 3–5 days after infection. MRI is used to evaluate the extent of abnormalities and in cases of surgical treatment, it is valuable for planning an accurate surgical strategy or clinical follow-up [8].

MRI helps to detect early stages of osteomyelitis owing to its ability to identify bone and soft-tissue edema. It is particularly useful for detecting osteomyelitis of the spine and pelvic bones. In addition, it is helpful for excluding complications. It may be instrumental in difficult differential diagnosis (infection vs tumor). Disadvantages of MRI are its occasional inability to distinguish infectious from reactive inflammation and its limited resolution in areas with metallic implants, such as joint prostheses or fixation devices.

MRI has the potential to differentiate a true avascular sequestrum surrounded by necrotic tissue from a piece of residual vascularized

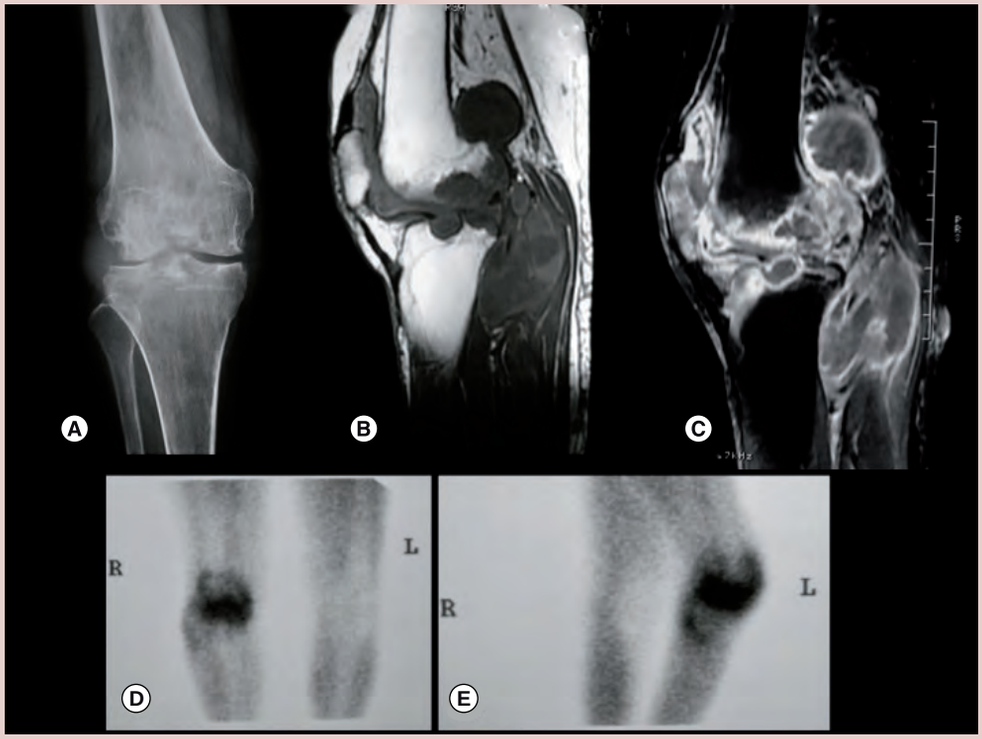

Figure 1. Tuberculous arthritis. (A) Conventional radiography frontal view of the right knee displaying diffuse soft tissue swelling, osteopenia, lateral joint space narrowing and medial and lateral compartment 'corner defects'. **(B)** Sagittal T2-weighted MRI demonstrates hypointense thickened synovium covering the posterior aspect of lateral condile affecting the articular joint space, tibial plateau and suprapatellar bursae. **(C)** Sagital T2 fat-saturation MRI with enhancement of the liquid collection and cortical defects. **(D & E)** Anterior and lateral view of a methoxyisobutylisonitrile-technetium-99m showing diffuse captation in the right knee.

normal bone. Nonenhanced and gadolinium-enhanced MRI sequences are required to fully characterize a sequestrum in chronic osteomyelitis [7].

The typical appearance of acute osteomyelitis in an MRI scan is a localized area of abnormal bone marrow with decreased signal intensity on T1-weighted images and increased signal intensity on T2-weighted images [17].

Special situations

Diabetic foot

One devastating complication in diabetic patients is foot osteomyelitis; early diagnosis is required in order to give adequate treatment. Recently, a meta-analysis examined the accuracy of MRI as a diagnostic test in patients with diabetic foot ulcers and osteomyelitis; the authors found the pooled sensitivity was 0.90 (95% CI: 0.82–0.95) and the pooled specificity was 0.79 (95% CI: 0.62–0.91). The diagnostic OR was 24.36. The measurement of accuracy was the highest among all of the diagnostic tests that were studied [5,18].

Vertebral osteomyelitis

In those patients with neurologic impairment, MRI should be the first diagnostic step, to look for spinal epidural abscess and to rule out a herniated disk. MRI has a high accuracy (90%) for diagnosing spinal osteomyelitis [19,20].

In a different scenario, the differential diagnosis between intervertebral degenerative osteochondrosis and septic discitis is difficult. In degenerative disk-related inflammatory end plates, the magnetic resonance pattern of bone marrow edema, including low signal on T1-weighted and high signal on T2-weighted images, reflects the development of a highly vascular fibrous tissue inside end-plate bone marrow. Similarly, infected tissue presents increased vascularity reflected by substantial enhancement on gadolinium-enhanced T1-weighted sequences. Gadolinium contrast agents, as markers of the extracellular space, induce pronounced enhancement of tissues, presenting increased vascularity, and are therefore not specific to infection or sterile inflammation.

A study designed to evaluate cellular MRI for the differentiation of infectious and degenerative vertebral disorders using superparamagnetic iron oxide (SPIO) contrast (marker of macrophages that infiltrate the infected tissue), concluded that MRI of the spine with SPIO injection differentiates infection from aseptic inflammation on quantitative analysis (signal-to-noise ratio) where significant signal loss evokes the presence of infection, but the use of SPIO makes direct visual evaluation less satisfactory. Further studies are underway to determine whether this new tool is useful for diagnosis in patients with spinal infections [21].

In addition, MRI is more sensitive than CT for the early detection of osteomyelitis [8]. Therefore, CT is generally indicated only if the patient has a contraindication to MRI or if CT is needed to guide a percutaneous biopsy. Neither CT nor MRI has 100% specificity.

Computed tomography

Computed tomography provides a good definition of cortical bone damage, periosteal reaction and soft tissue changes and is the best method for detecting small foci of gas within the medullary canal, areas of cortical erosion or destruction, tiny foreign bodies, and to define the presence and extent of sinus tracts and sequestra [4].

In chronic osteomyelitis, CT demonstrates abnormal thickening of the affected cortical bone, with sclerotic changes, encroachment of the medullary cavity and chronic draining sinus. In a systematic review and meta-analysis assessing the accuracy of different imaging techniques for the evaluation of chronic osteomyelitis, CT yielded a sensitivity of 0.67 (95% CI: 0.24–0.94), and a specificity of 0.50 (95% CI: 0.03–0.97) [3]. CT is not recommended for routine use in diagnosing osteomyelitis; however, it is the imaging modality of choice when MRI is not available or contraindicated [8]. It is particularly useful in the evaluation of flat and irregular bones, such as vertebrae, the pelvis and sternum.

Spiral CT with multiplanar reconstruction is superior to standard CT. The currently available multidetector CT provides the best multiplanar reconstructions, and is particularly important in the diagnosis of sternoclavicular osteomyelitis and its complications.

The definition of soft tissue changes with CT is suboptimal. Contrast-enhanced CT is better, but still inferior to conventional MRI. A major limitation of CT, as well as MRI, is the artefact produced by the presence of orthopedic hardware [2].

Nuclear medicine imaging

Early diagnosis of osteomyelitis and prosthetic joint infection is essential for successful therapy and prevention of complications. Nuclear medicine offers a variety of modalities for this aim. Advantages and disadvantages of different nuclear medicine and hybrid imaging systems are shown in TABLE 2. Nuclear medicine imaging techniques can detect osteomyelitis 10–14 days before changes are visible on plain radiographs. Several agents have been studied, including technetium-99m-labeled methylene diphosphonate (^{99m}Tc-MDP), gallium-67 citrate (^{67}Ga-citrate) and indium-111-labeled white blood cells (^{111}In-labeled WBCs). These techniques are highly sensitive [22] and depending on the clinical situation have a moderate-to-high specificity [23].

Three-phase bone scintigraphy

Bone scintigraphy is performed with ^{99m}Tc-labeled diphosphonates, usually ^{99m}Tc-MDP and hydroxy-methylene diphosphonate, which are the most commonly used radiopharmaceuticals to image osteoblastic activity.

In three-phase bone scan, areas of bone turnover and increased osteoblastic activity are detected using a radionuclide tracer (^{99m}Tc-diphosphonate). There are three phases to the test: nuclear angiogram or blood flow phase (immediately after injection), blood pool phase (within 5 min after injection) and bone phase (~3 h after injection). Cellulitis is characterized by high uptake in the blood flow and blood pool phase with normal uptake in the osseous phase, whereas osteomyelitis gives progressively increasing uptake over the course of the study.

In patients with osteomyelitis and infected orthopedic prostheses, increased osteoblastic activity occurs. Detection of osteomyelitis with ^{99m}Tc-MDP is highly sensitive (90%) when the bone has not been violated. In post-traumatic patients and after surgery, specificity is dramatically lower (35%) [23].

Gallium scintigraphy

Radiogallium attaches to transferrin and lactoferrin, which leaks from the bloodstream into areas of inflammation showing increased isotope uptake in infection, sterile inflammatory conditions and malignancy.

Although ^{67}Ga-citrate scintigraphy has a high sensitivity for both acute and chronic infection and noninfectious inflammatory conditions, the technique has several limitations: the need for delayed imaging (>48 h),

Table 2. Advantages and disadvantages of different nuclear medicine and hybrid imaging systems.

Nuclear medicine	Advantages	Disadvantages
Bisphosphonates ^{99m}Tc-MDP, ^{99m}Tc-HDP	Highly sensitive (~90%)	Low specificity (~35%)
Gallium scintigraphy ^{67}Ga-citrate	Reasonable sensitivity (73%) for both acute and chronic infection	Low specificity (61%) Need for delayed imaging Limited spatial resolution Bowel excretion High radiation dose [23]
Radiolabeled leukocytes (^{99m}Tc-WBC)/radiolabeled specific antigranulocyte FDG	High sensitivity and specificity (~95%) Provides excellent localization of inflammatory focus Sensitive for detecting infection in patients with metallic implants Adequate discrimination between osseous and soft tissue infection	Laborious preparation Requires special equipment Sensitivity decreases when infection is located closer to the spine
Hybrid imaging systems		
^{99m}Tc-HDP-SPECT/CT	Increases specificity (~85%) Better anatomical localization	Availability
^{111}In-WBC SPECT	Sensitivity (~84%), higher specificity near 100%	
^{99m}Tc-MDP	Sensitivity 94–100% Specificity 87–100%	
FDG-PET/ FDG-PET/CT	Useful to discriminate osteomyelitis in diabetic feet with ulcers	

^{67}Ga: Gallium-67; ^{99m}Tc: Technetium-99m; CT: Computed tomography; FDG: Fluorine-18 fluorodeoxyglucose; HDP: Hydroxymethane diphosphonate; MDP: Methylene diphosphonate; WBC: White blood cells.

limited spatial resolution, low specificity, physiological bowel excretion and the high radiation dose [23].

Gallium scans may reveal abnormal accumulation in patients who have active osteomyelitis when technetium scans reveal decreased activity ('cold' lesions) or perhaps normal activity. ^{67}Ga-citrate has been used with reasonable sensitivity (73%) and relatively low specificity (61%). ^{67}Ga-citrate is now less frequently used owing to the availability of more favorable compounds and techniques [23].

Radiolabeled leukocytes

White blood cell scan was performed originally with ^{111}In-WBC and more recently with ^{99m}Tc hexamethylpropyleneamine oxime-labeled white cells. The principle is that the labeled WBCs concentrate in areas of inflammation, and the specificity of the study is improved to 80–90% compared with bone scans, particularly when complicating conditions are superimposed. In a review and meta-analysis, the sensitivity for extra-axial chronic osteomyelitis was 84% compared with 21% for the detection of chronic osteomyelitis in axial skeleton [3,8]. Combined ^{111}In-WBC and bone marrow imaging with ^{99m}Tc-sulfur colloid demonstrated a 100% sensitivity and 98% specificity in 50 patients with suspected infected total-hip arthroplasty [24].

Today, labeled leukocyte imaging is the procedure of choice for diagnosing prosthetic joint infection [25].

The main disadvantages of ^{111}In-WBC and ^{99m}Tc-WBC are their laborious preparation, requirement of specialized equipment, and the handling of potentially infectious blood [23].

Radiolabeled specific antigranulocyte monoclonal antibodies

Considerable effort has been devoted to the search for *in vivo* methods of labeling leukocytes, including peptides and antigranulocyte antibodies.

Radiolabeled antigranulocyte antibodies have been developed for *in vivo* labeling of white blood cells. Antibodies accumulate in infectious and inflammatory foci mainly by nonspecific extravasations, because of the enhanced vascular permeability in combination with specific targeting of infiltrated granulocytes. Overall sensitivity for infection detection with radiolabeled antibodies is approximately 80–90%. Peripheral bone infections are adequately visualized; however, sensitivity decreases when the infections are located near to the spine. ^{99m}Tc-anti-CD15 IgM and ^{99m}Tc-anti-NCA-95 IgG are some of the most effective antibodies to diagnose bone and joint infections.

Nonspecific IgG

Radiolabeled nonspecific human IgG also accumulates in infectious and inflammatory foci by nonspecific extravasation facilitated by enhanced vascular permeability [23]. ^{111}In-IgG has demonstrated excellent performance in the localization of musculoskeletal infection and inflammation.

Antibodies

BW 250/183 (Granuloscint; CISBio International, Gif sur Yvette, France) is a murine monoclonal IgGI immunoglobulin that binds to the nonspecific cross-reacting antigen-95 (NCA-95) present on leukocytes. Sensitivity for osteomyelitis ranges from 69% in the hips to 100% for the lower leg and ankle, probably reflecting easier detection with decreasing marrow distally [19]. Today, labeled leukocyte imaging is the procedure of choice for diagnosing prosthetic joint infection [25].

Sulesomab is a 50-kDa fragment antigen-binding (Fab) portion of a murine monoclonal antibody of the IgGI class that binds to the NCA-90 antigen on leukocytes [26]. Reported sensitivity, specificity and accuracy of the test were 90–93, 85–89 and 88–90%, respectively.

Immunoscintigraphy with ^{99m}Tc-fanolesumab, a murine M-class immunoglobulin that binds to the CD15 antigen expressed on human neutrophils, eosinophils and lymphocytes. Sensitivity reaches 91% with a lower specificity of 69%; nevertheless in 2004, it was withdrawn from the US market as a result of serious reports of cardiopulmonary events [27].

Fluorine-18 fluorodeoxyglucose-PET

Fluorine-18 fluorodeoxyglucose (FDG) is transported into cells via glucose transporters, and phosphorylated by hexokinase inside the cell to form fluorodeoxyglucose-6-phosphate. The phosphorylated deoxyglucose cannot be further metabolized and, thus, FDG accumulates in activated lymphocytes, neutrophils and macrophages with minimal decrease over time. FDG therefore concentrates in sites of infection, although it is a nonspecific tracer that also accumulates in regions of aseptic inflammation, as well as in malignant lesions [28].

This technique has several potential advantages: results are available within 30–60 min of tracer administration, imaging is not affected by metallic implant artifacts, and it has a distinctly higher spatial resolution than images obtained with single photon-emitting tracers. This imaging modality is highly specific for the diagnosis of osteomyelitis in diabetic foot [18].

PET systems are relatively novel techniques that are being applied in several medical fields. It has been demonstrated that FDG-PET has the highest diagnostic accuracy for confirming or excluding the diagnosis of chronic osteomyelitis in comparison with bone scintigraphy, MRI or leukocyte scintigraphy; FDG-PET is also superior to leukocyte scintigraphy for detecting chronic osteomyelitis in the axial skeleton [18,23,29].

Nawaz *et al.* assessed the diagnostic performance of FDG-PET to diagnose osteomyelitis in the diabetic foot, and compared it with that of MRI and conventional radiography in 110 patients with diabetic foot disease. They found that FDG-PET had a sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of 81, 93, 78, 94 and 90%, respectively; while MRI had a sensitivity, specificity, PPV, NPV and accuracy of 91, 78, 56, 97 and 81%, respectively. Conventional radiography had a sensitivity, specificity, PPV, NPV and accuracy of 63, 87, 60, 88 and 81%, respectively. They concluded that MRI is more sensitive and has the ability to provide anatomical details in addition to detecting abnormalities within the bone marrow, joint spaces and surrounding soft tissue; however, it is relatively less specific than FDG-PET. They propose to perform MRI first and if this results in a 'positive', then complete the follow-up of osteomyelitis in diabetic foot patients by performing FDG-PET imaging owing to its high specificity [18].

Hybrid imaging systems

It is well known that nuclear medicine images demonstrate function, rather than anatomy. Planar scintigraphy used to be the standard technique used to establish the diagnosis of osteomyelitis. However, the need for improved localization and precise definition of the infectious process extent has been facilitated by the recent development of hybrid systems (SPECT/CT and PET/CT devices), capable of performing functional and morphological images by exploiting the features of both techniques in the same scanning session. These systems allow more detailed 3D localization compared with planar imaging, and also provide useful information in both patients with osteomyelitis and in those with infected joint prostheses [23]. The process of image acquisition and fusion is of importance in accurately localizing radiopharmaceuticals, accumulation, detecting occult pathological sites, characterizing the

functionally active area of a known lesion and in precisely drawing regions of interest to perform quantitative studies [30].

Nevertheless, data are still very limited, especially for PET/CT in patients with arthroplasty, and further prospective studies are required to fully verify the clinical role and the added value of SPECT/CT and PET/CT in the diagnosis of osteomyelitis and prosthetic bone infection [31–33].

Some examples of these hybrid techniques include SPECT/CT ^{67}Ga- and ^{111}In-labeled leukocyte scintigraphy; a study by Bar-Shalom *et al.* demonstrated that this combination is useful to define the anatomical localization of foci and its extent [34].

Filippi *et al.*, using SPECT/CT and ^{99m}Tc-hexamethylpropyleneamine oxime-labeled leukocyte scintigraphy, suggested that this hybrid device could also improve localization and definition of the infection extent [35].

Conclusion

Osteomyelitis frequently requires more than one imaging technique for an accurate diagnosis. Conventional radiography still remains the first imaging modality. MRI and nuclear medicine are the most sensitive and specific methods for the detection of osteomyelitis. A CT scan can be a useful method to detect early osseous erosion and to document the presence of sequestrum, foreign body or gas formation; it is generally less sensitive than other modalities for the detection of bone infection. MRI provides more accurate information regarding the extent of the infectious process. Ultrasound represents a noninvasive method to evaluate the involved soft tissues and cortical bone and may provide guidance for diagnostic or therapeutic interventional, drainage or tissue biopsy. PET and SPECT are highly accurate techniques for the evaluation of chronic osteomyelitis, allowing differentiation from soft tissue infection.

Future perspective

An ideal imaging technique should demonstrate functional and anatomical definition, excluding inflammatory or tumoral pathologies. Currently, there is no perfect imaging technique for the diagnosis of osteomyelitis. The hybrid imaging systems are able to acquire functional and structural data in the same scanning session and, therefore, to limit the problems often observed with software approaches for image registration and fusion. Hybrid imaging systems represent the present and future of diagnostic imaging in osteomyelitis. However, technical improvements, widespread availability and lower costs in this computer-aided imaging techniques are encouraged.

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Executive summary

Conventional radiography

- First imaging technique used to gain an overview of the anatomy and pathology of bone.
- Changes are visible after several days from the beginning of the process.
- Main findings include osteopenia, lytic lesions, periosteal thickening and loss of trabecular architecture.

Sinography

- Useful to define the course and extent of the sinus tract and its possible communications with neighboring structures.

Ultrasonography

- Allows identification of early soft tissue changes: fistulous tracts, fluid collections, cortical discontinuity and abscess.
- Ultrasonography is accessible, low cost and noninvasive.

MRI

- Provides excellent delineation between bone and soft tissue as well as abnormal and normal bone marrow. Detects osteomyelitis as early as 3–5 days after infection. Used for the evaluation of the extent of the abnormalities.

Computed tomography

- Provides a good definition of cortical bone abnormalities, sequestra, involucra, intraosseous gas, periosteal reaction and blurring of fat planes.

Nuclear medicine

- Various modalities detect osteomyelitis 10–14 days before changes are visible on plain radiographs. These techniques are highly sensitive and depending on the clinical situation have a moderate-to-high specificity.

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