American College of Radiology
ACR Appropriateness Criteria®
Suspected Osteomyelitis of the Foot in Patients with Diabetes Mellitus

Variant 1: **Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
Radiography foot	Usually Appropriate	☢
US foot	Usually Not Appropriate	O
MRI foot without and with IV contrast	Usually Not Appropriate	O
MRI foot without IV contrast	Usually Not Appropriate	O
CT foot with IV contrast	Usually Not Appropriate	☢
CT foot without and with IV contrast	Usually Not Appropriate	☢
CT foot without IV contrast	Usually Not Appropriate	☢
3-phase bone scan foot	Usually Not Appropriate	☢☢☢
3-phase bone scan and WBC scan and sulfur colloid scan foot	Usually Not Appropriate	☢☢☢☢
3-phase bone scan and WBC scan foot	Usually Not Appropriate	☢☢☢☢
3-phase bone scan and WBC scan with SPECT or SPECT/CT foot	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT whole body	Usually Not Appropriate	☢☢☢☢
WBC scan and sulfur colloid scan foot	Usually Not Appropriate	☢☢☢☢
WBC scan foot	Usually Not Appropriate	☢☢☢☢

Variant 2: **Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus. Initial radiographs negative or indeterminate for osteomyelitis. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI foot without and with IV contrast	Usually Appropriate	O
MRI foot without IV contrast	Usually Appropriate	O
CT foot with IV contrast	May Be Appropriate	☢
CT foot without IV contrast	May Be Appropriate	☢
3-phase bone scan foot	May Be Appropriate (Disagreement)	☢☢☢
FDG-PET/CT whole body	May Be Appropriate	☢☢☢☢
US foot	Usually Not Appropriate	O
Image-guided biopsy foot	Usually Not Appropriate	Varies
CT foot without and with IV contrast	Usually Not Appropriate	☢
3-phase bone scan and WBC scan and sulfur colloid scan foot	Usually Not Appropriate	☢☢☢☢
3-phase bone scan and WBC scan foot	Usually Not Appropriate	☢☢☢☢
3-phase bone scan and WBC scan with SPECT or SPECT/CT foot	Usually Not Appropriate	☢☢☢☢
WBC scan and sulfur colloid scan foot	Usually Not Appropriate	☢☢☢☢
WBC scan foot	Usually Not Appropriate	☢☢☢☢

Variant 3: **Adult. Radiographs positive for osteomyelitis of the foot in patients with diabetes mellitus. Next imaging study for pretreatment planning.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI foot without and with IV contrast	Usually Appropriate	O
MRI foot without IV contrast	Usually Appropriate	O
Image-guided biopsy foot	May Be Appropriate	Varies
CT foot with IV contrast	May Be Appropriate	☢
CT foot without IV contrast	May Be Appropriate	☢
3-phase bone scan and WBC scan with SPECT or SPECT/CT foot	May Be Appropriate (Disagreement)	☢☢☢☢
WBC scan foot	May Be Appropriate	☢☢☢☢
US foot	Usually Not Appropriate	O
CT foot without and with IV contrast	Usually Not Appropriate	☢
3-phase bone scan foot	Usually Not Appropriate	☢☢☢
3-phase bone scan and WBC scan and sulfur colloid scan foot	Usually Not Appropriate	☢☢☢☢
3-phase bone scan and WBC scan foot	Usually Not Appropriate	☢☢☢☢
FDG-PET/CT whole body	Usually Not Appropriate	☢☢☢☢
WBC scan and sulfur colloid scan foot	Usually Not Appropriate	☢☢☢☢

Variant 4: **Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus and metal instrumentation in the foot. Initial radiographs negative or indeterminate for osteomyelitis. Next imaging study.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI foot without and with IV contrast	Usually Appropriate	O
MRI foot without IV contrast	Usually Appropriate	O
3-phase bone scan and WBC scan with SPECT or SPECT/CT foot	Usually Appropriate	☢☢☢☢
CT foot with IV contrast	May Be Appropriate	☢
CT foot without IV contrast	May Be Appropriate	☢
3-phase bone scan and WBC scan and sulfur colloid scan foot	May Be Appropriate	☢☢☢☢
3-phase bone scan and WBC scan foot	May Be Appropriate	☢☢☢☢
WBC scan and sulfur colloid scan foot	May Be Appropriate	☢☢☢☢
US foot	Usually Not Appropriate	O
Image-guided biopsy foot	Usually Not Appropriate	Varies
CT foot without and with IV contrast	Usually Not Appropriate	☢
3-phase bone scan foot	Usually Not Appropriate	☢☢☢
FDG-PET/CT whole body	Usually Not Appropriate	☢☢☢☢
WBC scan foot	Usually Not Appropriate	☢☢☢☢

Variant 5: **Adult. Radiographs positive for osteomyelitis of the foot in patients with diabetes mellitus and metal instrumentation in the foot. Next imaging study for pretreatment planning.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI foot without and with IV contrast	Usually Appropriate	O
MRI foot without IV contrast	Usually Appropriate	O
Image-guided biopsy foot	May Be Appropriate	Varies
CT foot with IV contrast	May Be Appropriate	☢
CT foot without IV contrast	May Be Appropriate	☢
3-phase bone scan and WBC scan and sulfur colloid scan foot	May Be Appropriate	☢☢☢☢
3-phase bone scan and WBC scan foot	May Be Appropriate	☢☢☢☢
3-phase bone scan and WBC scan with SPECT or SPECT/CT foot	May Be Appropriate	☢☢☢☢
WBC scan and sulfur colloid scan foot	May Be Appropriate	☢☢☢☢
US foot	Usually Not Appropriate	O
CT foot without and with IV contrast	Usually Not Appropriate	☢
3-phase bone scan foot	Usually Not Appropriate	☢☢☢
FDG-PET/CT whole body	Usually Not Appropriate	☢☢☢☢
WBC scan foot	Usually Not Appropriate	☢☢☢☢

SUSPECTED OSTEOMYELITIS OF THE FOOT IN PATIENTS WITH DIABETES MELLITUS

Expert Panel on Musculoskeletal Imaging: Jonathan C. Baker, MD[a]; Benjamin E. Northrup, MD[b]; Shivani Ahlawat, MD[c]; Hailey Allen, MD[d]; Geneve Allison, MD[e]; James Banks, MD[f]; Matthew P. Borloz, MD[g]; Murthy R. Chamarthy, MD[h]; Hillary W. Garner, MD[i]; Christopher Edward Gross, MD[j]; Jinel A. Scott, MD, MBA[k]; Timothy Switaj, MD[l]; Jennifer Zreloff, MD[m]; Daniel E. Wessell, MD, PhD.[n]

Summary of Literature Review

Introduction/Background

The Centers for Disease Control and Prevention National Diabetes Statistics Report of 2021 states that 38.1 million people aged 18 or older in the United States have diabetes mellitus (14.7% of all United States adults) [1]. Diabetes-related foot complications, such as soft tissue infection, osteomyelitis, and neuropathic osteoarthropathy, account for up to 20% of all diabetic-related North American hospital admissions, with as much as $1.5 billion spent annually in the United States on diabetic foot ulcer care [2].

In diabetic adults with suspected osteomyelitis of the foot, imaging findings alone should not guide patient management. Of patients with diabetic foot ulcers, 20% will develop osteomyelitis [3]. Clinical features that suggest osteomyelitis include an ulcer area >2 cm², an elevated erythrocyte sedimentation rate level of >70 mm/hour, a positive probe-to-bone test, a nonhealing ulcer present for 6 months, erythema, fever, and elevated white blood cell (WBC) count [2,4,5]. A negative probe-to-bone test may exclude the diagnosis of osteomyelitis with a high negative predictive value (NPV) [6]. The Infectious Diseases Society of America (International Working Group on the Diabetic Foot) recommends performing the probe-to-bone test, as well as C-reactive protein, erythrocyte sedimentation rate, or procalcitonin on any patient with diabetic foot infection and an open wound [7]. Although, some studies have found strong correlation between deep wound cultures and bone cultures for the identification of likely pathogens, the Infectious Diseases Society of America Practice Guidelines recommend obtaining bone rather than soft tissue specimens for culture [7,8].

For scenarios when clinical examination of a diabetic foot infection suggests the presence of crepitus, or where soft tissue gas associated with wet gangrene is suspected, the ACR Appropriateness Criteria® topic on Suspected Osteomyelitis, Septic Arthritis, or Soft Tissue Infection (Excluding Spine and Diabetic Foot) [9] offers appropriate guidance. If the primary clinical findings are related to chronic foot or ankle pain, please refer to the ACR Appropriateness Criteria® topics on Chronic Foot Pain [10] and Chronic Ankle Pain [11], respectively. If the patient's clinical findings are primarily related to trauma, please refer to the ACR Appropriateness Criteria® topics on Acute Trauma to the Foot [12] or Acute Trauma to the Ankle [13].

Special Imaging Considerations

The use of dual-energy CT (DECT) with virtual noncalcium images to quantitatively assess bone marrow edema has grown in the literature since the last iteration of this document. This technique has potential value for diagnosing osteomyelitis in patients with diabetic foot ulcers, with one study showing a sensitivity of 87% and a specificity of 73%, with a positive predictive value (PPV) of 69% and an NPV of 89% [14]. DECT also can be used to decrease metallic artifact and to create virtual noncontrast images. Further discussion of the use of CT for the diagnosis of osteomyelitis in the diabetic foot is presented in the variants below.

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Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

- There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

- There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus. Initial imaging.

In patients with diabetes in which osteomyelitis of the foot is suspected, the patient should first undergo clinical evaluation, including a targeted physical examination with particular attention for ulcers or wounds involving the foot [15]. The goal of initial imaging in this setting is to evaluate for the presence of osteomyelitis, determine whether additional studies are required, and assess for the presence of pertinent alternative diagnoses, such as neuropathic arthropathy.

3-Phase Bone Scan and WBC Scan and Sulfur Colloid Scan Foot

There is no relevant literature to support the use of the combination of a 3-phase bone scan and WBC scan and sulfur colloid scan in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

3-Phase Bone Scan and WBC Scan Foot

There is no relevant literature to support the use of the combination of a 3-phase bone scan and WBC scan in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

3-Phase Bone Scan and WBC Scan with SPECT or SPECT/CT Foot

There is no relevant literature to support the use of the combination of a 3-phase bone scan and WBC scan with single-photon emission CT (SPECT) or SPECT/CT in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

3-Phase Bone Scan Foot

There is no relevant literature to support the use of a 3-phase bone scan in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

CT Foot With IV Contrast

There is no relevant literature to support the use of CT with intravenous (IV) contrast in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

CT Foot Without and With IV Contrast

There is no relevant literature to support the use of CT without and with IV contrast in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

CT Foot Without IV Contrast

There is no relevant literature to support the use of CT without IV contrast in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

FDG-PET/CT Whole Body

There is no relevant literature to support the use of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

MRI Foot Without and With IV Contrast

There is no relevant literature to support the use of MRI without and with IV contrast in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

MRI Foot Without IV Contrast
There is no relevant literature to support the use of MRI without IV contrast in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

Radiography Foot
Foot radiographs are valuable in the setting of suspected osteomyelitis of the foot in their ability to evaluate anatomic detail, detect findings of previous surgeries, and evaluate for other reasons for the patient's presentation, including fracture, (radiopaque) foreign body, soft tissue gas, neuropathic arthropathy, osteoarthritis, or tumor. Radiographs combined with clinical assessment (eg, probe-to-bone test) have a high diagnostic accuracy and might be the only diagnostic imaging required in some patients [16,17]. Radiographs are insensitive in the detection of early stages of acute osteomyelitis [17]. Radiographic osseous changes might not be visible until 10 to 14 days or more in adults, and require that the infection extends at least 1 cm and compromises 30% to 50% of bone mineral content to produce noticeable changes. These early changes include periosteal reaction, lytic bone destruction, endosteal scalloping, osteopenia, loss of trabecular architecture, and new bone apposition [18,19].

US Foot
There is no relevant literature to support the use of ultrasound (US) in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

WBC Scan and Sulfur Colloid Scan Foot
There is no relevant literature to support the use of the combination of a WBC scan and sulfur colloid scan in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

WBC Scan Foot
There is no relevant literature to support the use of a WBC scan in the initial imaging evaluation of suspected osteomyelitis of the foot in adult patients with diabetes mellitus.

Variant 2: Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus. Initial radiographs negative or indeterminate for osteomyelitis. Next imaging study.

When osteomyelitis of the foot is suspected in the diabetic patient and initial radiographs are negative or indeterminate, particularly when a wound or ulceration is present, further imaging is often necessary. Radiographs are frequently negative or equivocal for osteomyelitis early in the course of disease (within the first 10 to 14 days) or when involvement is less extensive (<1 cm and compromising less than 30% to 50% of bone mineral content), characterized by the absence of periosteal reaction, lytic bone destruction, endosteal scalloping, osteopenia, loss of trabecular architecture, and new bone apposition [18,19]. Because of the importance of early diagnosis and treatment of osteomyelitis, advanced imaging and image-guided procedures can be valuable in this scenario, as many of these modalities facilitate earlier detection of osteomyelitis and fulfill the goal of detecting radiographically occult osteomyelitis.

3-Phase Bone Scan and WBC Scan and Sulfur Colloid Scan Foot
The diagnostic value of combined labeled leukocyte and sulfur colloid bone marrow imaging is greatest when increased labeled leukocyte activity is secondary to altered bone marrow distribution [20]. Positive bone scan and WBC uptake with no uptake on the bone marrow (sulfur colloid) scan is considered positive for infection [21]. This combination of studies is also useful for distinguishing osteomyelitis from neuropathic arthropathy. Although this technique boasts high sensitivity and specificity, the complexity and care coordination challenges presented by this combination of studies represent a significant disadvantage [22-24]. Furthermore, planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are most efficacious in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery.

3-Phase Bone Scan and WBC Scan Foot
The combination of bone scan and labeled leukocyte scan (In-111 or Tc-99m) markedly improves specificity in the nonmarrow-containing skeleton when there has been previous surgery, radiographs are abnormal or indeterminate, or when any other cause for bone remodeling is present [25]. It is most useful for distinguishing true WBC accumulation secondary to osteomyelitis from nonspecific WBC uptake that occurs with neuropathic arthropathy, a common confounding factor in the diabetic foot [25,26]. This combination of studies shows a sensitivity range of 78% to 100% and a specificity range of 80% to 97% [27-29]. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful

in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery.

3-Phase Bone Scan and WBC Scan with SPECT or SPECT/CT Foot

Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. SPECT/CT fused imaging improves the diagnostic accuracy primarily because of more accurate anatomic localization [30-33], allowing for better differentiation of bone infection from soft tissue infection. Some studies have shown accuracy comparable to MRI. Although sensitivities are similar (87%-94%), dual isotope SPECT/CT (94%) is more specific than bone scan SPECT/CT (47%) or WBC SPECT/CT (68%) alone [22].

3-Phase Bone Scan Foot

Three-phase Tc-99m-phosphate bone scintigraphy demonstrates moderate accuracy but poor discriminating ability in the diagnosis of osteomyelitis of the foot, with 81% sensitivity and 28% specificity [6]. Several older studies demonstrate higher sensitivity (93%-95%) and specificity (43%-95%) [34-36]. This relatively low specificity is due to bone scintigraphy's sensitivity to increased osteoblastic activity, which is present not only in osteomyelitis, but also neuropathic arthropathy, fracture, neoplasm, trauma, and prior surgery [37]. Furthermore, increased blood flow is a nonspecific feature that occurs in many foot disorders. Bone scintigraphy is an excellent option for secondary screening for osteomyelitis when radiographs are negative, but the clinical concern for osteomyelitis is high. Three-phase bone scintigraphy is most useful when negative, as some studies have supported that this excludes infection with a high degree of certainty [37], whereas others report more modest sensitivity values.

CT Foot With IV Contrast

CT can rapidly image targeted anatomic regions and can provide multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. However, CT is less sensitive than MRI and some nuclear medicine studies in the detection of early changes of acute osteomyelitis [38]. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT is able to delineate the anatomic extent of soft tissue infections. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections [41].

CT Foot Without and With IV Contrast

CT can rapidly image targeted anatomic regions and can provide multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. However, CT is less sensitive than MRI and some nuclear medicine studies in the detection of early changes of acute osteomyelitis [38]. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT is able to delineate the anatomic extent of soft tissue infections. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections [41].

CT Foot Without IV Contrast

CT rapidly images targeted anatomic regions and permits multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. However, CT is less sensitive than MRI and some nuclear medicine studies in the detection of early changes of acute osteomyelitis [38]. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40].

FDG-PET/CT Whole Body

FDG-PET/CT has a potentially important role in evaluating for osteomyelitis in the setting of the diabetic foot and boasts advantages of short acquisition time and high spatial and contrast resolution. The added anatomic resolution provided by CT images fused with PET data permits precise anatomic localization of sites of increased uptake as compared with other nuclear medicine modalities. This also facilitates the differentiation of osteomyelitis from soft tissue infection [42,43]. Several studies have demonstrated mixed results of FDG-PET for the diagnosis of bone infection in the diabetic foot, with a sensitivity of 74% to 96% and a specificity of 91% to 93% [29,44,45]. FDG accumulation, however, lacks specificity because it occurs in both infectious and other inflammatory conditions [46].

Image-Guided Biopsy Foot

Percutaneous image-guided bone biopsy plays an important role in the diagnosis and management of diabetic foot infection. However, there is no relevant literature to support the use of bone biopsy as the next study after negative or indeterminate radiographs. Bone biopsy is generally performed after further evaluation with advanced imaging modalities. Bone biopsy is not required in every case of diabetic foot infection, but it has shown the ability, in a number of studies, to identify pathogenic organisms and guide accurate antibiotic treatment. Bone biopsy provides more accurate microbiological information than superficial soft tissue samples in patients with diabetic pedal osteomyelitis [47,48]. However, there are conflicting data on the usefulness of bone biopsy to influence clinical management. One small study showed that percutaneous bone biopsies can have a low rate of culture positivity, and even when positive, frequently do not have an impact on antibiotic choice [49]. A large meta-analysis demonstrated a high rate of culture positivity but also showed limited evidence of impact on clinical outcomes or antibiotic management [50]. When performing bone biopsy, it is vital to send specimens for both surgical pathology and cultures, as histology provides more accurate diagnosis of osteomyelitis than microbiology, especially in patients with chronic osteomyelitis [51].

MRI Foot Without and With IV Contrast

MRI performed without and with IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. The likelihood of osteomyelitis of the foot without an associated wound or ulceration is low, and ulcer depth can be predictive of progression to osteomyelitis [54]. MRI without or with IV contrast can identify other potential sources of pain, including soft tissue infection, tumor, abscess, neuropathic arthropathy, and fracture. In patients with foot radiographs that are negative or indeterminate for osteomyelitis, MRI offers superior accuracy, with prior meta-analyses reporting a pooled sensitivity of 90% and specificities ranging from 79% to 82.5% [6,55]. Normal bone marrow signal intensity reliably excludes osteomyelitis, with a sensitivity of 90% and a specificity of 71% [56]. Positive cases of osteomyelitis of the foot demonstrate decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences in 100% of surgically proven cases of osteomyelitis in one study [57]. MRI demonstrated a sensitivity of 95%, specificity of 91%, NPV of 98%, and PPV of 79% in other studies [57-60]. When increased T2-weighted bone marrow signal corresponds to normal T1-weighted bone marrow signal, but is adjacent to an ulcer, abscess, sinus tract or other findings of infection, this represents a site of high likelihood of osteomyelitis [2,58,60]. MRI is often the modality of choice in this variant because of its high sensitivity for osteomyelitis [55,61,62]. The addition of IV gadolinium contrast is useful in assessing for the presence of fluid collection/abscess, sinus tracts, and regions of devitalized bone and/or soft tissue. These findings are useful for surgical planning [63]. Notably, false-negative results on MRI can occur in dry gangrene, which is characterized by devitalized (often exposed) bone that does not show marrow edema or enhancement. However, this is frequently infected and IV antibiotics are unlikely to reach nonenhancing portions of the bone [58].

MRI Foot Without IV Contrast

MRI performed without IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. The likelihood of osteomyelitis of the foot without an associated wound or ulceration is low, and ulcer depth can be predictive of progression to osteomyelitis [54]. MRI without or with IV contrast can identify other potential sources of pain, including soft tissue infection, tumor, abscess, neuropathic arthropathy, and fracture. In patients with foot radiographs that are negative or indeterminate for osteomyelitis, MRI offers superior accuracy. Prior meta-analyses report a pooled sensitivity of 90% and specificities ranging from 79% to 82.5% [6,55]. Normal bone marrow signal intensity on MRI reliably excludes osteomyelitis, with a sensitivity of 90% and a specificity of 71% [56]. Positive cases of osteomyelitis of the foot demonstrate decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences in 100% of surgically proven cases of osteomyelitis in one study [57]. MRI demonstrated a sensitivity of 95%, specificity of 91%, NPV of 98%, and PPV of 79% in other studies [57-60]. When increased

T2-weighted bone marrow signal corresponds to normal T1-weighted bone marrow signal, but is adjacent to an ulcer, abscess, sinus tract, or other findings of infection, this represents a site of high likelihood of osteomyelitis [2,58,60]. MRI is often the modality of choice in this variant because of its high sensitivity for osteomyelitis [55,61,62]. An important recent development is abbreviated foot MRI for suspected osteomyelitis, which consists of coronal T1 and sagittal T2-weighted images, can be performed in an average total time of 8 minutes, and has been shown to be noninferior to standard protocols in the diagnosis of acute pedal osteomyelitis [64].

US Foot

Although the role of US in the assessment of osseous abnormalities has become more prominent in recent years, the role of this modality in the detection of direct findings of osteomyelitis is limited and is supported by scant evidence. US can accurately detect findings of soft tissue infection as well as secondary findings of osteomyelitis, including cortical disruption, increased blood flow, foreign body, subperiosteal abscess, and sometimes periosteal reaction. One small study demonstrated excellent sensitivity and specificity of cortical disruption and increased flow on power Doppler in the detection of diabetic foot osteomyelitis [65].

WBC Scan and Sulfur Colloid Scan Foot

The combination of labeled leukocyte and sulfur colloid bone marrow imaging is most useful when increased labeled leukocyte activity is secondary to altered bone marrow distribution [20]. Labeled leukocytes and sulfur colloid normally accumulate in bone marrow; discordant labeled leukocyte activity without corresponding sulfur colloid uptake indicates infection [66]. This makes this combination of studies particularly useful for distinguishing osteomyelitis from neuropathic arthropathy. The sulfur colloid image becomes photopenic within approximately 1 week after the onset of infection, so the study should be interpreted cautiously in the acute setting [21]. The addition of the sulfur colloid scan improves sensitivity (100%), specificity (94%), and accuracy (90%-96%) [23,24]. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery.

WBC Scan Foot

Labeled leukocyte scintigraphy is most useful for assessing for acute infection in patients with intact chemotaxis. Because the majority of labeled cells are neutrophils, this modality is most useful for identifying neutrophil-mediated inflammatory processes, including bacterial infections [67,68]. A meta-analysis demonstrated 92% sensitivity and 75% specificity of In-111-oxine–labeled WBC scintigraphy and 91% sensitivity and 92% specificity of Tc-99m-hexamethylpropyleneamine oxime (HMPAO)–labeled WBC scintigraphy in the diagnosis of bone infection in the diabetic foot [44]. However, some older studies demonstrate lower sensitivity (79%-87%) and specificity (12%-78%) for In-111-oxine–labeled WBC scintigraphy [24,34]. Chronic infection or inflammation can lead to inconsistent results, and neuropathic arthropathy can yield false-positive results. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery.

Variant 3: Adult. Radiographs positive for osteomyelitis of the foot in patients with diabetes mellitus. Next imaging study for pretreatment planning.

When osteomyelitis of the foot is suspected in the diabetic patient and initial radiographs are positive, further imaging workup is often necessary in order to fulfill the primary goal of advancing to the next step in management and treatment planning. Clinical diagnosis and treatment approaches that can be affected by the results of advanced imaging modalities include biopsy planning, antibiotic selection, and the choice between nonoperative therapy and surgical management [16,44].

3-Phase Bone Scan and WBC Scan and Sulfur Colloid Scan Foot

The diagnostic value of combined labeled leukocyte and sulfur colloid bone marrow imaging is greatest when increased labeled leukocyte activity is secondary to altered bone marrow distribution [20]. Positive bone scan and WBC uptake with no uptake on the bone marrow (sulfur colloid) scan is considered positive for infection [21]. This combination of studies is also useful for distinguishing osteomyelitis from neuropathic arthropathy. Although this technique boasts high sensitivity and specificity, the complexity and care coordination challenges presented by this combination of studies represent a significant disadvantage [22-24]. Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are most efficacious in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. In the setting of abnormal radiographs, this combination of studies is most valuable in its ability to detect multifocal infection and assess the extent of disease. This can aid in biopsy targeting and alter surgical decision-making. Furthermore, evidence as to the effect of the combination of 3-phase bone scintigraphy, labeled leukocyte, and sulfur colloid bone marrow imaging on treatment outcomes in this setting is lacking.

3-Phase Bone Scan and WBC Scan Foot

The combination of bone scan and labeled leukocyte scan (In-111 or Tc-99m) markedly improves specificity in the nonmarrow-containing skeleton when there has been previous surgery, when radiographs are abnormal or indeterminate, or when any other cause for bone remodeling is present [25]. It is most useful for distinguishing true WBC accumulation secondary to osteomyelitis from nonspecific WBC uptake that occurs with neuropathic arthropathy, a common confounding factor in the diabetic foot [25,26]. This combination of studies shows a sensitivity range of 78% to 100% and a specificity range of 80% to 97% [27-29]. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. In the setting of abnormal radiographs, this combination of studies can be valuable in its ability to detect multifocal infection and assess extent of disease. This can aid in biopsy targeting and alter surgical decision-making. However, this combination of studies introduces complexity and care coordination challenges for this variant.

3-Phase Bone Scan and WBC Scan with SPECT or SPECT/CT Foot

Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. SPECT/CT fused imaging improves the diagnostic accuracy primarily due to accurate anatomic localization [30-33], allowing for better differentiation of bone infection from soft tissue infection. Some studies have shown accuracy comparable to MRI. Although sensitivities are similar (87%-94%), dual isotope SPECT/CT (94%) is more specific than bone scan SPECT/CT (47%) or WBC SPECT/CT (68%) alone [22]. A recent study demonstrated that quantitative Tc-99m-HMPAO–labeled WBC SPECT/CT is an excellent predictor of lower extremity amputation in the setting of diabetic foot infection [69]. In the presence of abnormal radiographs, these studies are most valuable in their ability to detect multifocal infection and assess extent of disease. This can aid in biopsy targeting and alter surgical decision-making.

3-Phase Bone Scan Foot

Three-phase Tc-99m-phosphate bone scintigraphy demonstrates moderate accuracy but poor discriminating ability in the diagnosis of osteomyelitis of the foot, with 81% sensitivity and 28% specificity [6]. Several older studies demonstrate higher sensitivities (93%-95%) and specificities (43%-95%) [34-36]. This relatively low specificity is due to bone scintigraphy’s sensitivity to increased osteoblastic activity, which is present not only in osteomyelitis, but also neuropathic arthropathy, fracture, neoplasm, trauma, and prior surgery [37]. Furthermore, increased blood flow is a nonspecific feature that occurs in many foot disorders. Three-phase bone scintigraphy is likely to be positive in the setting of radiographs that are positive for osteomyelitis, limiting the usefulness of this study. However, the detection of multifocal infection or greater-than-expected extent of disease can alter treatment planning. Compromised vascular perfusion can render findings of osteomyelitis reduced or absent. Recognition of this on flow phase images can influence treatment planning.

CT Foot With IV Contrast

CT can rapidly image targeted anatomic regions and can provide multiplanar reconstructions. Expected CT findings in this variant demonstrating osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. However, CT is less sensitive than MRI and some nuclear medicine studies in the detection of early changes of acute osteomyelitis, an important consideration when evaluating the extent of disease or planning biopsy or surgery [38]. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT delineates the anatomic location and extent of soft tissue infection, facilitating the planning of fluid aspiration, percutaneous bone biopsy, and surgical debridement. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections, an important consideration in treatment planning [41].

CT Foot Without and With IV Contrast

CT can rapidly image targeted anatomic regions and can provide multiplanar reconstructions. Expected CT findings of osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. However, CT is less sensitive than MRI and some nuclear medicine studies in the detection of early changes of acute osteomyelitis, an important consideration when evaluating extent of disease or planning biopsy or surgery [38]. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT delineates the anatomic location and extent of soft tissue infection, facilitating the planning of fluid aspiration, percutaneous bone biopsy, and surgical debridement. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections, an important consideration in treatment planning [41]. DECT (discussed in the Special Imaging Considerations section) with virtual noncalcium images can quantitatively assess for the presence of bone marrow edema and could alter treatment planning if these images demonstrate a greater extent of disease than expected [14].

CT Foot Without IV Contrast

CT can rapidly image targeted anatomic regions and can provide multiplanar reconstructions. Expected CT findings of osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. However, CT is less sensitive than MRI and some nuclear medicine studies in the detection of early changes of acute osteomyelitis, an important consideration when evaluating extent of disease or planning biopsy or surgery [38]. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. DECT (discussed in the Special Imaging Considerations section) with virtual noncalcium images can quantitatively assess for the presence of bone marrow edema and could alter treatment planning if these images demonstrate a greater extent of disease than expected [14].

FDG-PET/CT Whole Body

FDG-PET/CT has a potential role in further evaluation of known osteomyelitis in the setting of the diabetic foot and boasts advantages of a short acquisition time and relatively high resolution. FDG accumulation, however, lacks specificity as it occurs in both infectious and other inflammatory conditions [46]. The added anatomic resolution provided by CT images fused with PET data permits precise anatomic localization of sites of increased uptake as compared with other nuclear medicine modalities. This also facilitates the differentiation of osteomyelitis from soft tissue infection [42,43]. Several studies have demonstrated mixed results of FDG-PET for the diagnosis of bone infection in the diabetic foot, with a sensitivity of 74% to 96% and a specificity of 91% to 93% [29,44,45]. FDG-PET/CT is most useful in the setting of known pedal osteomyelitis when assessment for multifocal disease and extent of disease is necessary for treatment planning.

Image-Guided Biopsy Foot

Percutaneous image-guided bone biopsy plays an important role in the diagnosis and management of diabetic foot infection. Specifically, bone biopsy may be performed to direct antibiotic coverage when radiographs or advanced imaging is positive, or when advanced imaging is indeterminate or equivocal for osteomyelitis. Although not required in every case of diabetic foot infection, bone biopsy has shown the ability, in a number of studies, to identify pathogenic organisms and guide accurate antibiotic treatment. Bone biopsy provides more accurate microbiological information than superficial soft tissue samples in patients with diabetic pedal osteomyelitis [47,48]. However, there are conflicting data on the usefulness of bone biopsy to influence clinical management. One small study showed that percutaneous bone biopsies can have a low rate of culture positivity, and even when positive, frequently do not have an impact on antibiotic choice [49]. A large meta-analysis demonstrated a high rate of culture positivity but also showed limited evidence of impact on clinical outcomes or antibiotic management [50]. When performing bone biopsy, it is vital to send specimens for both surgical pathology and cultures, as histology provides more accurate diagnosis of osteomyelitis than microbiology, especially in patients with chronic osteomyelitis [51].

MRI Foot Without and With IV Contrast

MRI performed without and with IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. The likelihood of acute osteomyelitis of the foot without an associated wound or ulceration is low, and ulcer depth can be predictive of progression to osteomyelitis [54]. MRI without or with IV contrast can identify other potential sources of pain, including soft tissue infection, tumor, abscess, neuropathic arthropathy, and fracture. MRI offers superior accuracy, with prior meta-analyses reporting pooled sensitivity of 90%, and specificities ranging from 79% to 82.5% [6,55]. Normal bone marrow signal intensity reliably excludes osteomyelitis, with a sensitivity of 90% and a specificity of 71% [56]. Positive cases of osteomyelitis of the foot demonstrate decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences in 100% of surgically proven cases of osteomyelitis in one study [57]. MRI demonstrated a sensitivity of 95%, specificity of 91%, NPV of 98%, and PPV of 79% in other studies [57-60]. Therefore, findings on T1-weighted images are valuable for biopsy targeting and surgical planning. When increased T2-weighted bone marrow signal corresponds to normal T1-weighted bone marrow signal, but is adjacent to an ulcer, abscess, sinus tract, or other findings of infection, this represents a site of high likelihood of osteomyelitis [2,58,60]. MRI is often the modality of choice in this variant because of its high sensitivity for osteomyelitis [55,61,62]. MRI adds value in guiding surgical management, even in the setting of positive radiographs, due to detection of additional segments of disease [70].

The addition of IV gadolinium contrast increases sensitivity in assessing for the presence of fluid collection/abscess, sinus tracts, and regions of devitalized bone and/or soft tissue. These findings are useful for surgical planning [63]. MRI is the modality of choice for the evaluation of devitalized soft tissue and bone [71], as this is frequently infected and IV antibiotics are unlikely to reach nonenhancing portions of the bone and MRI findings are key for appropriate surgical planning [58].

MRI Foot Without IV Contrast

MRI performed without IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. The likelihood of acute osteomyelitis of the foot without an associated wound or ulceration is low, and ulcer depth can be predictive of progression to osteomyelitis [54]. MRI can identify other potential sources of pain, including soft tissue infection, tumor, abscess, neuropathic arthropathy, and fracture. MRI offers superior accuracy, with prior meta-analyses reporting pooled sensitivity of 90%, and specificities ranging from 79% to 82.5% [6,55]. Normal bone marrow signal intensity reliably excludes osteomyelitis, with a sensitivity of 90% and a specificity of 71% [56]. Positive cases of osteomyelitis of the foot demonstrate decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences in 100% of surgically proven cases of osteomyelitis in one study [57]. MRI demonstrated a sensitivity of 95%, specificity of 91%, NPV of 98%, and PPV of 79% in other studies [57-60]. Therefore, findings on T1-weighted images are valuable for biopsy targeting and surgical planning. When increased T2-weighted bone marrow signal corresponds to normal T1-weighted bone marrow signal, but is adjacent to an ulcer, abscess, sinus tract, or other findings of infection, this represents a site of high likelihood of osteomyelitis [2,58,60]. MRI is often the modality of choice in this variant because of its high sensitivity for osteomyelitis [55,61,62]. MRI adds value in guiding surgical management, even in the setting of positive radiographs, due to the detection of additional segments of disease [70]. Furthermore, noncontrast findings suggestive of cellulitis, fluid collection/abscess, or sinus tract are also useful for treatment planning.

US Foot

Although the role of US in the assessment of osseous abnormalities has become more prominent in recent years, the role of this modality in the detection of direct findings of osteomyelitis is limited and is supported by scant evidence. US can accurately detect findings of soft tissue infection as well as secondary findings of osteomyelitis, including cortical disruption, increased blood flow, foreign body, subperiosteal abscess, and sometimes periosteal reaction. One small study demonstrated excellent sensitivity and specificity of cortical disruption and increased flow on power Doppler in the detection of diabetic foot osteomyelitis [65]. However, because US is less reliable in assessing the extent of osteomyelitis, findings of cellulitis, fluid collection/abscess, or sinus tract are most important in guiding treatment. In particular, US can be useful in facilitating surgical or image-guided abscess drainage.

WBC Scan and Sulfur Colloid Scan Foot

The combination of labeled leukocyte and sulfur colloid bone marrow imaging is most useful when increased labeled leukocyte activity is secondary to altered bone marrow distribution [20]. Labeled leukocytes and sulfur colloid normally accumulate in bone marrow; discordant labeled leukocyte activity without corresponding sulfur colloid uptake indicates infection [66]. This makes this combination of studies particularly useful for distinguishing osteomyelitis from neuropathic arthropathy. The sulfur colloid image becomes photopenic within approximately 1 week after the onset of infection, so the study should be interpreted cautiously in the acute setting [21]. The addition of the sulfur colloid scan improves sensitivity (100%), specificity (94%), and accuracy (90%-96%) [23,24]. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. In the setting of abnormal radiographs, this combination of studies is most valuable in its ability to detect multifocal infection and assess extent of disease. This can aid in biopsy targeting and alter surgical decision-making. However, the complexity and care coordination challenges presented by this combination of studies represent a significant disadvantage.

WBC Scan Foot

Labeled leukocyte scintigraphy is most useful for assessing for acute infection in patients with intact chemotaxis. Because the majority of labeled cells are neutrophils, this modality is best for identifying neutrophil-mediated inflammatory processes, including bacterial infections [67,68]. A meta-analysis demonstrated 92% sensitivity and 75% specificity of In-111-oxine–labeled WBC scintigraphy and 91% sensitivity and 92% specificity of Tc-99m-HMPAO–labeled WBC scintigraphy in the diagnosis of bone infection in the diabetic foot [44]. However, some older studies demonstrate lower sensitivities (79%-87%) and specificities (12%-78%) for In-111-oxine–labeled WBC scintigraphy [24,34]. Chronic infection or inflammation can lead to inconsistent results, and neuropathic arthropathy can yield false-positive results. This can limit the usefulness of this study in treatment planning, given the high risk of false-positive sites when the evaluation of extent of disease and multifocal infection is desired. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery.

Variant 4: Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus and metal instrumentation in the foot. Initial radiographs negative or indeterminate for osteomyelitis. Next imaging study.

When osteomyelitis is suspected in the patient with diabetes in the setting of metal instrumentation in the foot and initial radiographs are negative or indeterminate, particularly when a wound or ulceration is present, further imaging is often necessary. Selection of an appropriate imaging modality or image-guided procedure that minimizes artifact due to metal is necessary to fulfill the goal of detecting radiographically occult osteomyelitis in this clinical scenario.

3-Phase Bone Scan and WBC Scan and Sulfur Colloid Scan Foot

Combined labeled leukocyte and sulfur colloid bone marrow imaging is most useful when increased labeled leukocyte activity is secondary to altered bone marrow distribution, common around prosthetic joints and metal instrumentation [20]. In evaluating arthroplasties and sites of metal instrumentation, positive bone scan and WBC uptake with no uptake on the bone marrow (sulfur colloid) scan is considered positive for infection [21]. This study combination is most helpful when significant metal instrumentation is present that would impair MRI or CT imaging. Although this technique boasts high sensitivity and specificity, the complexity and care coordination challenges presented by this combination of studies represent a significant disadvantage [22-24]. Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful in cases in which infection is multifocal or when the infection is associated with orthopedic hardware or chronic bone alterations from trauma or surgery. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, the combination of bone scan, labeled leukocyte scan, and sulfur colloid scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

3-Phase Bone Scan and WBC Scan Foot

The combination of bone scan and labeled leukocyte scan (In-111 or Tc-99m) markedly improves specificity in the nonmarrow-containing skeleton when there has been previous surgery, radiographs are abnormal or indeterminate, or when any other cause for bone remodeling is present [25]. It is most useful for distinguishing true WBC accumulation secondary to osteomyelitis from nonspecific WBC uptake that occurs with neuropathic arthropathy, a common confounding factor in the diabetic foot [25,26]. This combination of studies shows a sensitivity range of 78% to 100% and a specificity range of 80% to 97% [27-29]. This modality can be helpful when significant metal instrumentation is present that would impair MRI or CT imaging, although without a concurrent sulfur colloid scan, specificity is low. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, the combination of bone scan and labeled leukocyte scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

3-Phase Bone Scan and WBC Scan With SPECT or SPECT/CT Foot
The combination of bone scan and labeled leukocyte scan (In-111 or Tc-99m) markedly improves specificity in the nonmarrow-containing skeleton when there has been previous surgery, radiographs are abnormal or indeterminate, or when any other cause for bone remodeling, including metal instrumentation, is present [25]. It is most useful for distinguishing true WBC accumulation secondary to osteomyelitis from nonspecific WBC uptake that is seen in the setting of neuropathic arthropathy, a common confounding factor in the diabetic foot [25,26]. This modality can be helpful when significant metal instrumentation is present that would impair MRI or CT imaging, although without a concurrent sulfur colloid scan, specificity is low. Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. SPECT/CT fused imaging improves the diagnostic accuracy primarily because of more accurate anatomic localization [30-33], allowing for better differentiation of bone infection from soft tissue infection. Some studies have shown accuracy comparable to MRI. Although sensitivities are similar (87%-94%), dual isotope SPECT/CT (94%) is more specific than bone scan SPECT/CT (47%) or WBC SPECT/CT (68%) alone [22]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, the combination of bone scan and labeled leukocyte scan with SPECT/CT scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

3-Phase Bone Scan Foot
Three-phase Tc-99m-phosphate bone scintigraphy demonstrates moderate accuracy but poor discriminating ability in the diagnosis of osteomyelitis of the foot, with 81% sensitivity and 28% specificity [6]. Several older studies demonstrate higher sensitivity (93%-95%) and specificity (43%-95%) [34-36]. This relatively low specificity is due to bone scintigraphy's sensitivity to increased osteoblastic activity, which is present not only in osteomyelitis but also in neuropathic arthropathy, fracture, neoplasm, trauma, and prior surgery [37]. Furthermore, increased blood flow is a nonspecific feature that occurs in many foot disorders. Bone scintigraphy is an option for secondary screening for osteomyelitis when radiographs are negative, but the clinical concern for osteomyelitis is high. Three-phase bone scintigraphy can be useful when negative, as some studies have supported that this excludes infection with a high degree of certainty [37], whereas others report more modest sensitivity values. This modality can also be helpful when significant metal instrumentation is present that would impair MRI or CT imaging, although evidence as to its efficacy in this setting is lacking.

CT Foot With IV Contrast
CT rapidly images targeted anatomic regions and permits multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. Although CT is less sensitive than MRI in the detection of early changes of acute osteomyelitis [38], metal artifact on CT is often less limiting. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT is able to delineate the anatomic extent of soft tissue infections. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections [41]. When metal is present near the site of potential infection, some techniques result in significant loss of image quality due to beam-hardening artifact [19]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, CT with iterative metal artifact reduction or DECT may be helpful to assess for findings of osteomyelitis [14]. However, there are no published data comparing the 2 techniques in this specific situation.

CT Foot Without and With IV Contrast
CT rapidly images targeted anatomic regions and permits multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. Although CT is

less sensitive than MRI in the detection of early changes of acute osteomyelitis [38], metal artifact on CT is often less limiting. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT is able to delineate the anatomic extent of soft tissue infections. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections [41]. When metal is present near the site of potential infection, some techniques result in significant loss of image quality due to beam-hardening artifact [19]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, CT with iterative metal artifact reduction or DECT may be helpful to assess for findings of osteomyelitis [14]. However, there are no published data comparing the 2 techniques in this specific situation. Furthermore, outside of the aforementioned specific indications, MRI remains the preferred modality for the evaluation for osteomyelitis after initial radiographs are negative or indeterminate.

CT Foot Without IV Contrast

CT can rapidly image targeted anatomic regions and can provide multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These are visible without or with IV contrast and are often seen to better advantage as compared with radiographs. Although CT is less sensitive than MRI in the detection of early changes of acute osteomyelitis [38], metal artifact on CT is often less limiting. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. When metal is present near the site of potential infection, some techniques result in significant loss of image quality due to beam-hardening artifact [19]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, CT with iterative metal artifact reduction or DECT may be helpful to assess for findings of osteomyelitis [14]. However, there are no published data comparing the 2 techniques in this specific situation.

FDG-PET/CT Whole Body

FDG-PET/CT has a potentially important role in evaluating for osteomyelitis in the setting of the diabetic foot and boasts advantages of a short acquisition time and high resolution. The added anatomic resolution provided by CT images fused with PET data permits precise anatomic localization of sites of increased uptake as compared with other nuclear medicine modalities. This also facilitates the differentiation of osteomyelitis from soft tissue infection [42,43]. Several studies have demonstrated mixed results of FDG-PET for the diagnosis of bone infection in the diabetic foot with a sensitivity of 74% to 96% and a specificity of 91% to 93% [29,44,45]. FDG-PET/CT can be used in the evaluation of patients with metal implants that would compromise the accuracy of MRI or CT [72]. Prior studies have demonstrated high accuracy in the detection of osteomyelitis in cases complicated by prior surgery, trauma, and the presence of orthopedic instrumentation [73-75]. However, metallic artifact can impair PET attenuation correction, sometimes leading to spurious areas of increased uptake and the overestimation of standard uptake values. Furthermore, FDG accumulation lacks specificity, as it occurs in both infectious and other inflammatory conditions [46], limiting the usefulness of FDG-PET/CT for this variant. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, FDG-PET/CT may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

Image-Guided Biopsy Foot

Percutaneous image-guided bone biopsy plays an important role in the diagnosis and management of diabetic foot infection. However, there is no relevant literature to support the use of bone biopsy as the next study after negative or indeterminate radiographs. Bone biopsy is generally performed after further evaluation with advanced imaging modalities. Bone biopsy is not required in every case of diabetic foot infection, but it has shown the ability, in a number of studies, to identify pathogenic organisms and guide accurate antibiotic treatment. Bone biopsy provides more accurate microbiological information than superficial soft tissue samples in patients with diabetic pedal osteomyelitis [47,48]. However, there are conflicting data on the usefulness of bone biopsy to influence clinical management. One small study showed that percutaneous bone biopsies can have a low rate of culture positivity, and even when positive, frequently do not have an impact on antibiotic choice [49]. A large meta-analysis demonstrated a high rate of culture positivity but also showed limited evidence of impact on clinical outcomes or antibiotic management [50]. When performing bone biopsy, it is vital to send specimens for both surgical pathology and cultures, as histology provides more accurate diagnosis of osteomyelitis than microbiology, especially in patients with chronic osteomyelitis [51]. Image-guided biopsy is most commonly performed with CT or fluoroscopy, and the presence of metal generally does not significantly limit the ability of the operator to target the site of concern.

MRI Foot Without and With IV Contrast

MRI performed without and with IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. However, this soft tissue contrast and sensitivity is reduced in the presence of susceptibility artifact. The use of newer metal artifact-reduction sequences, such as slice encoding for metal artifact correction and multi-acquisition with variable-resonance image combination have allowed for more effective use of MRI in the evaluation of infections associated with metal instrumentation. Recently, surgical implants made of less ferromagnetic materials have gained popularity and can produce less artifact [76]. Metal artifact reduction sequences can mitigate the susceptibility artifact associated with metallic instrumentation, but the sensitivity (38%-55%) and specificity (81%-93%) of medullary, confluent T1 hypointensity for the diagnosis of osteomyelitis is decreased [77] as compared with that which is observed in the absence of metal (sensitivity of 95%, specificity of 91%) [59]. In this setting, reliance on secondary MRI findings in areas free of artifact is key. The presence of a wound or ulcer increases the likelihood of osteomyelitis, and ulcer depth can be predictive of progression to osteomyelitis [54]. Adjacent sinus tract, abscess, or cellulitis also increases the likelihood of osteomyelitis, and these findings are better assessed on postcontrast images. Positive cases of osteomyelitis of the foot demonstrate decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences (short tau inversion recovery [STIR] is most commonly used in the setting of metal) [57-60]. MRI without and with IV gadolinium contrast is also useful in assessing for the presence of devitalized bone and soft tissue [63]. However, the presence of metal limits the use of fat-suppressed sequences, making the identification of devitalized bone and soft tissue much more difficult as compared with areas without metal.

MRI Foot Without IV Contrast

MRI performed without IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. However, this soft tissue contrast and sensitivity is reduced in the presence of susceptibility artifact. The use of newer metal artifact-reduction sequences, such as slice encoding for metal artifact correction and multi-acquisition with variable-resonance image combination have allowed for more effective use of MRI in the evaluation of infections associated with metal instrumentation. Recently, surgical implants made of less ferromagnetic materials have gained popularity and can produce less artifact [76]. Metal artifact reduction sequences can mitigate the susceptibility artifact associated with metallic instrumentation, but the sensitivity (38%-55%) and specificity (81%-93%) of medullary, confluent T1 hypointensity for the diagnosis of osteomyelitis is decreased [77] as compared with that which is observed in the absence of metal (sensitivity of 95%, specificity of 91%) [59]. In this setting, reliance on secondary MRI findings in areas free of artifact is key. The presence of a wound or ulcer increases the likelihood of osteomyelitis, and ulcer depth can be predictive of progression to osteomyelitis [54]. Adjacent sinus tract, abscess, or cellulitis also increases the likelihood of osteomyelitis. Positive cases of osteomyelitis of the foot demonstrate decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences (STIR is most commonly used in the setting of metal) [57-60].

US Foot

Although the role of US in the assessment of osseous abnormalities has become more prominent in recent years, the role of this modality in the detection of direct findings of osteomyelitis is limited and is supported by scant evidence. US can accurately detect findings of soft tissue infection as well as secondary findings of osteomyelitis, including cortical disruption, increased blood flow, foreign body, subperiosteal abscess, and sometimes periosteal reaction. One small study demonstrated excellent sensitivity and specificity of cortical disruption and increased flow on power Doppler in the detection of diabetic foot osteomyelitis [65].

WBC Scan and Sulfur Colloid Scan Foot

The combination of labeled leukocyte and sulfur colloid bone marrow imaging is most useful when increased labeled leukocyte activity is secondary to altered bone marrow distribution, such as in the setting of a metallic implant [20]. Labeled leukocytes and sulfur colloid normally accumulate in bone marrow; discordant labeled leukocyte activity without corresponding sulfur colloid uptake indicates infection [66]. This makes this combination of studies particularly useful for distinguishing osteomyelitis from neuropathic arthropathy. The sulfur colloid image becomes photopenic within approximately 1 week after the onset of infection, so the study should be interpreted cautiously in the acute setting [21]. The addition of the sulfur colloid scan improves sensitivity (100%), specificity (94%), and accuracy (90%-96%) [23,24]. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, the combination of labeled leukocyte scan and sulfur colloid scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

WBC Scan Foot

Labeled leukocyte scintigraphy is most useful for assessing for acute infection in patients with intact chemotaxis. Because the majority of labeled cells are neutrophils, this modality is most useful for identifying neutrophil-mediated inflammatory processes, including bacterial infections [67,68]. A meta-analysis demonstrated 92% sensitivity and 75% specificity of In-111-oxine–labeled WBC scintigraphy and 91% sensitivity and 92% specificity of Tc-99m-HMPAO–labeled WBC scintigraphy in the diagnosis of bone infection in the diabetic foot [44]. However, some older studies demonstrate lower sensitivity (79%-87%) and specificity (12%-78%) for In-111-oxine–labeled WBC scintigraphy [24,34]. Chronic infection or inflammation can lead to inconsistent results, and neuropathic arthropathy can result in false-positives. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities such as WBC scan are useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. However, specific evidence of efficacy in detecting osteomyelitis in the diabetic foot with metal instrumentation is lacking. Furthermore, when MRI is nondiagnostic due to metal artifact at the suspected site of infection, labeled leukocyte scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

Variant 5: Adult. Radiographs positive for osteomyelitis of the foot in patients with diabetes mellitus and metal instrumentation in the foot. Next imaging study for pretreatment planning.

When osteomyelitis of the foot is suspected in the patient with diabetes with metal instrumentation and initial radiographs are positive, further imaging workup is often necessary to fulfill the primary goal of the next step in management and treatment planning. Clinical diagnosis and treatment approaches that can be affected by the results of advanced imaging modalities include biopsy planning, antibiotic selection, and the choice between nonoperative therapy and surgical management [16,44]. However, procedure choices can be limited in this clinical scenario, as reducing metallic artifact while maintaining adequate sensitivity and specificity for the detection of osteomyelitis is paramount.

3-Phase Bone Scan and WBC Scan and Sulfur Colloid Scan Foot

Combined labeled leukocyte and sulfur colloid bone marrow imaging is most useful when increased labeled leukocyte activity is secondary to altered bone marrow distribution, common around prosthetic joints and metal instrumentation [20]. In evaluating arthroplasties and sites of metal instrumentation, positive bone scan and WBC uptake with no uptake on the bone marrow (sulfur colloid) scan is considered positive for infection [21]. This combination of studies is most helpful in treatment planning in the setting of significant metal instrumentation when there is a question of extent of infection or multifocal infection that cannot be adequately answered by MRI or CT imaging due to artifact. Although this technique boasts high sensitivity and specificity, the complexity and care coordination challenges presented by this combination of studies represent a significant disadvantage [22-24]. Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, the combination of bone scan, labeled leukocyte scan, and sulfur colloid scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation. Furthermore, evidence as to the effect of the combination of 3-phase bone scintigraphy, labeled leukocyte, and sulfur colloid bone marrow imaging on treatment outcomes in this setting is lacking.

3-Phase Bone Scan and WBC Scan Foot

The combination of bone scan and labeled leukocyte scan (In-111 or Tc-99m) markedly improves specificity in the nonmarrow-containing skeleton when there has been previous surgery, radiographs are abnormal or indeterminate, or when any other cause for bone remodeling is present [25]. It is most useful for distinguishing true WBC accumulation secondary to osteomyelitis from nonspecific WBC uptake that occurs with neuropathic arthropathy, a common confounding factor in the diabetic foot [25,26]. This combination of studies shows a sensitivity range of 78% to 100% and a specificity range of 80% to 97% [27-29]. This study combination can be helpful when significant metal instrumentation is present that would impair MRI or CT imaging, although without a concurrent sulfur colloid scan, specificity is low. In particular, this combination of studies is useful when the evaluation of extent of infection could alter treatment planning, and this cannot be assessed with MRI or CT due to metallic artifact. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Nuclear medicine modalities are also useful in cases in which infection is multifocal or when the infection is associated with orthopedic instrumentation or chronic bone alterations from trauma or surgery. Additionally, compromised vascular perfusion can render findings of osteomyelitis reduced or absent on these studies. Recognition of this on flow phase images can influence treatment planning.

3-Phase Bone Scan and WBC Scan With SPECT or SPECT/CT Foot

Planar scintigraphic imaging modalities have low spatial resolution, and anatomic localization is often challenging. SPECT/CT fused imaging improves the diagnostic accuracy primarily due to accurate anatomic localization [30-33], allowing for better differentiation of bone infection from soft tissue infection. Some studies have shown accuracy comparable to MRI. Although sensitivities are similar (87%-94%), dual isotope SPECT/CT (94%) is more specific than bone scan SPECT/CT (47%) or WBC SPECT/CT (68%) alone [22]. A recent study demonstrated that quantitative Tc-99m-HMPAO–labeled WBC SPECT/CT is an excellent predictor of lower extremity amputation in the setting of diabetic foot infection [69]. In the presence of abnormal radiographs, these studies are most valuable in their ability to detect multifocal infection and assess extent of disease. Additionally, this combination of studies is useful when evaluation of extent of infection could alter treatment planning (and this cannot be assessed with MRI or CT due to metallic artifact) and planar imaging is inadequate for biopsy or surgical planning.

3-Phase Bone Scan Foot

Three-phase Tc-99m-phosphate bone scintigraphy demonstrates moderate accuracy but poor discriminating ability in the diagnosis of osteomyelitis of the foot, with 81% sensitivity and 28% specificity [6]. Several older studies demonstrate higher sensitivity (93%-95%) and specificity (43%-95%) [34-36]. This relatively low specificity is due to bone scintigraphy's sensitivity to increased osteoblastic activity, which is present not only in osteomyelitis, but also neuropathic arthropathy, fracture, neoplasm, trauma, and prior surgery [37]. Furthermore, increased blood flow is a nonspecific feature that occurs in many foot disorders. Three-phase bone scintigraphy is most useful in treatment planning in the setting of significant metal instrumentation when there is a question of extent of infection or multifocal infection that cannot be adequately answered by MRI or CT imaging due to artifact. Compromised vascular perfusion can render findings of osteomyelitis reduced or absent. Recognition of this on flow phase images can influence treatment planning. However, specific evidence that 3-phase bone scintigraphy affects treatment planning in the diabetic foot in the setting of metal instrumentation is lacking.

CT Foot With IV Contrast

CT rapidly images targeted anatomic regions and permits multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These findings are often seen to better advantage as compared with radiographs. Although CT is less sensitive than MRI in the detection of early changes of acute osteomyelitis [38], metal artifact on CT is often less limiting. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast and are better delineated with CT as compared with radiographs. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT is able to delineate the anatomic extent of soft tissue infections. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections [41]. When metal is present near the site of potential infection, some techniques result in significant loss of image quality due to beam-hardening artifact [19]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, CT with iterative metal artifact reduction or DECT may be helpful to assess for findings of osteomyelitis [14]. However, there are no published data comparing the 2 techniques in this specific situation. CT is a viable option to facilitate treatment planning in this variant due to its ability to rapidly image sites of concern, reduce metallic artifact, and evaluate for associated soft tissue abnormalities.

CT Foot Without and With IV Contrast

CT rapidly images targeted anatomic regions and permits multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These findings are often seen to better advantage as compared with radiographs. Although CT is less sensitive than MRI in the detection of early changes of acute osteomyelitis [38], metal artifact on CT is often less limiting. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast and are better delineated with CT as compared with radiographs. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. With high-resolution multiplanar imaging, CT is able to delineate the anatomic extent of soft tissue infections. Contrast is preferred for the evaluation of soft tissue infection and assessment of fluid collections [41]. When metal is present near the site of potential infection, some techniques result in significant loss of image quality due to beam-hardening artifact [19]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, CT with iterative metal artifact reduction or DECT may be helpful to assess for findings of osteomyelitis [14]. However, there are no published data comparing the 2 techniques in this specific situation. Although CT demonstrates some strengths for evaluating infection, such as its ability to rapidly image sites of concern, reduce metallic artifact, and evaluate for associated soft tissue abnormalities, it is rarely a viable option to facilitate treatment planning in this variant, given limitations in assessing for sites of active osteomyelitis.

CT Foot Without IV Contrast

CT rapidly images targeted anatomic regions and permits multiplanar reconstructions. Characteristic CT findings of acute osteomyelitis include periosteal reaction, endosteal scalloping, and osseous destruction. These findings are often seen to better advantage as compared with radiographs. Although CT is less sensitive than MRI in the detection of early changes of acute osteomyelitis [38], metal artifact on CT is often less limiting. Features of chronic osteomyelitis, including sequestrum, involucrum, cloaca, and sinus tracts, are visible without or with IV contrast and are better delineated with CT as compared with radiographs. Some studies have shown that CT is superior to MRI for the detection of sequestra and foreign bodies and might facilitate earlier detection of changes of neuropathic arthropathy [39,40]. When metal is present near the site of potential infection, some techniques result in significant loss of image quality due to beam-hardening artifact [19]. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, CT with iterative metal artifact reduction or DECT may be helpful to assess for findings of osteomyelitis [14]. However, there are no published data comparing the 2 techniques in this specific situation. Although CT demonstrates some strengths for evaluating infection, such as its ability to rapidly image sites of concern, reduce metallic artifact, and evaluate for associated soft tissue abnormalities, it is rarely a viable option to facilitate treatment planning in this variant, given limitations in assessing for sites of active osteomyelitis.

FDG-PET/CT Whole Body

FDG-PET/CT has a potential role in further evaluation of known osteomyelitis in the setting of the diabetic foot and boasts advantages of a short acquisition time and relatively high resolution. The added anatomic resolution provided by CT images fused with PET data permits precise anatomic localization of sites of increased uptake as compared with other nuclear medicine modalities. This also facilitates the differentiation of osteomyelitis from soft tissue infection [42,43]. Several studies have demonstrated mixed results of FDG-PET for the diagnosis of bone infection in the diabetic foot with a sensitivity of 74% to 96% and a specificity of 91% to 93% [29,44,45]. FDG-PET/CT can be used in the evaluation of patients with metal implants that would compromise the accuracy of MRI or CT [72]. Prior studies have demonstrated high accuracy in the detection of osteomyelitis in cases complicated by prior surgery, trauma, and the presence of orthopedic instrumentation [73-75]. However, metallic artifact can impair PET attenuation correction, sometimes leading to spurious areas of increased uptake and the overestimation of standard uptake values. Furthermore, FDG accumulation lacks specificity, as it occurs in both infectious and other inflammatory conditions [46], limiting the usefulness of FDG-PET/CT for this variant. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, FDG-PET/CT may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation. Furthermore, specific evidence that FDG-PET/CT affects treatment planning in the diabetic foot in the setting of metal instrumentation is lacking.

Image-Guided Biopsy Foot

Percutaneous image-guided bone biopsy plays an important role in the diagnosis and management of diabetic foot infection. Specifically, bone biopsy may be performed to direct antibiotic coverage when radiographs or advanced imaging is positive, or when advanced imaging is indeterminate or equivocal for osteomyelitis. Although not required in every case of diabetic foot infection, bone biopsy has shown the ability, in a number of studies, to identify pathogenic organisms and guide accurate antibiotic treatment. Bone biopsy provides more accurate microbiological information than superficial soft tissue samples in patients with diabetic pedal osteomyelitis

[47,48]. However, there are conflicting data on the usefulness of bone biopsy to influence clinical management. One small study showed that percutaneous bone biopsies can have a low rate of culture positivity, and even when positive, frequently do not have an impact on antibiotic choice [49]. A large meta-analysis demonstrated a high rate of culture positivity but also showed limited evidence of impact on clinical outcomes or antibiotic management [50]. When performing bone biopsy, it is vital to send specimens for both surgical pathology and cultures, as histology provides more accurate diagnosis of osteomyelitis than microbiology, especially in patients with chronic osteomyelitis [51]. In the setting of known radiographic findings of osteomyelitis, image-guided biopsy is performed with fluoroscopy or CT, and the presence of metal generally does not significantly limit the ability of the operator to target the site of concern.

MRI Foot Without and With IV Contrast

MRI performed without and with IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. However, this soft tissue contrast and sensitivity is reduced in the presence of susceptibility artifact. The use of newer metal artifact-reduction sequences, such as slice encoding for metal artifact correction and multi-acquisition with variable-resonance image combination have allowed for more effective use of MRI in the evaluation of infections associated with metal instrumentation. Recently, surgical implants made of less ferromagnetic materials have gained popularity and can produce less artifact [76]. Metal artifact reduction sequences can mitigate the susceptibility artifact associated with metallic instrumentation, but the sensitivity (38%-55%) and specificity (81%-93%) of medullary, confluent T1 hypointensity for the diagnosis of osteomyelitis is decreased [77] as compared with that which is observed in the absence of metal (sensitivity of 95%, specificity of 91%) [59]. In this setting, reliance on secondary MRI findings in areas free of artifact is key. The presence of a wound or ulcer increases the likelihood of osteomyelitis, and ulcer depth can be predictive of progression to osteomyelitis [54]. Adjacent sinus tract, abscess, or cellulitis also increases the likelihood of osteomyelitis, and these findings are better assessed on postcontrast images. Positive cases of osteomyelitis of the foot can be confirmed on MRI by observing decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences (STIR is most commonly used in the setting of metal) [57-60]. MRI without and with IV gadolinium contrast can facilitate treatment planning by assessing for the presence of devitalized bone and soft tissue [63]. However, the presence of metal limits the use of fat-suppressed sequences, making identification of devitalized bone and soft tissue much more difficult as compared with areas without metal. In cases in which metal has limited evaluation of primary findings of osteomyelitis, MRI still adds value, as findings of cellulitis, fluid collection/abscess, or sinus tract are well seen on postcontrast images and are important findings for treatment planning.

MRI Foot Without IV Contrast

MRI performed without IV contrast demonstrates excellent soft tissue contrast and sensitivity to marrow abnormalities with relatively high resolution in multiple anatomic planes [52,53]. However, this soft tissue contrast and sensitivity is reduced in the presence of susceptibility artifact. The use of newer metal artifact-reduction sequences, such as slice encoding for metal artifact correction and multi-acquisition with variable-resonance image combination have allowed for more effective use of MRI in the evaluation of infections associated with metal instrumentation. Recently, surgical implants made of less ferromagnetic materials have gained popularity and can produce less artifact [76]. Metal artifact reduction sequences can mitigate the susceptibility artifact associated with metallic instrumentation, but the sensitivity (38%-55%) and specificity (81%-93%) of medullary, confluent T1 hypointensity for the diagnosis of osteomyelitis is decreased [77] as compared with that which is observed in the absence of metal (sensitivity 95%, specificity 91%) [59]. In this setting, reliance on secondary MRI findings in areas free of artifact is key. The presence of a wound or ulcer increases the likelihood of osteomyelitis, and ulcer depth can be predictive of progression to osteomyelitis [54]. Adjacent sinus tract, abscess, or cellulitis also increases the likelihood of osteomyelitis. Positive cases of osteomyelitis of the foot can be confirmed on MRI by observing decreased T1-weighted bone marrow signal (hypointense or isointense to skeletal muscle) in a confluent pattern (contiguous and complete replacement of marrow signal) and a medullary distribution (signal hypointensity involving a geographic portion of the medullary canal), with corresponding matching high signal on fluid-sensitive sequences (STIR is most commonly used in the setting of metal) [57-60]. In cases in which metal has limited the evaluation of primary findings of osteomyelitis, noncontrast MRI still adds value, as findings of cellulitis, fluid collection/abscess, or sinus tract are also useful for treatment planning.

US Foot

Although the role of US in the assessment of osseous abnormalities has become more prominent in recent years, the role of this modality in the detection of direct findings of osteomyelitis is limited and is supported by scant evidence. US can accurately detect findings of soft tissue infection as well as secondary findings of osteomyelitis, including cortical disruption, increased blood flow, foreign body, subperiosteal abscess, and sometimes periosteal reaction. One small study demonstrated excellent sensitivity and specificity of cortical disruption and increased flow on power Doppler in the detection of diabetic foot osteomyelitis [65]. However, because US is less reliable in assessing the extent of osteomyelitis, particularly in the setting of metal instrumentation, findings of cellulitis, fluid collection/abscess, or sinus tract are most important in guiding treatment. In particular, US can be useful in facilitating surgical or image-guided abscess drainage.

WBC Scan and Sulfur Colloid Scan Foot

The combination of labeled leukocyte and sulfur colloid bone marrow imaging is most useful when increased labeled leukocyte activity is secondary to altered bone marrow distribution [20]. Labeled leukocytes and sulfur colloid normally accumulate in bone marrow; discordant labeled leukocyte activity without corresponding sulfur colloid uptake indicates infection [66]. This makes this combination of studies particularly useful for distinguishing osteomyelitis from neuropathic arthropathy. The sulfur colloid image becomes photopenic within approximately 1 week after the onset of infection, so the study should be interpreted cautiously in the acute setting [21]. The addition of the sulfur colloid scan improves sensitivity (100%), specificity (94%), and accuracy (90%-96%) [23,24]. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. In the setting of abnormal radiographs and metal instrumentation, this combination of studies is most valuable in its ability to detect multifocal infection and assess the extent of disease, particularly in areas where MRI or CT could be limited by metallic artifact. This can aid in biopsy targeting and alter surgical decision-making. When MRI is nondiagnostic due to metal artifact at the suspected site of infection, the combination of labeled leukocyte scan and sulfur colloid scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

WBC Scan Foot

Labeled leukocyte scintigraphy is most useful for assessing for acute infection in patients with intact chemotaxis. Because the majority of labeled cells are neutrophils, this modality is most useful for identifying neutrophil-mediated inflammatory processes, including bacterial infections [67,68]. A meta-analysis demonstrated 92% sensitivity and 75% specificity of In-111-oxine–labeled WBC scintigraphy and 91% sensitivity and 92% specificity of Tc-99m-HMPAO–labeled WBC scintigraphy in the diagnosis of bone infection in the diabetic foot [44]. However, some older studies demonstrate lower sensitivity (79%-87%) and specificity (12%-78%) for In-111-oxine–labeled WBC scintigraphy [24,34]. Chronic infection or inflammation can lead to inconsistent results, and neuropathic arthropathy can result in false positives. This study is most helpful in treatment planning in the setting of significant metal instrumentation when there is a question of extent of infection or multifocal infection that cannot be adequately answered by MRI or CT imaging due to artifact. Planar scintigraphic imaging modalities alone have low spatial resolution, and anatomic localization is often challenging. Specific evidence that labeled leukocyte scintigraphy affects treatment planning in the diabetic foot in the setting of metal instrumentation is lacking. Furthermore, when MRI is nondiagnostic due to metal artifact at the suspected site of infection, labeled leukocyte scan may be helpful to assess for findings of osteomyelitis. However, there are no published data comparing the 2 techniques in this specific situation.

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- **Variant 1**: Radiography is recommended as the initial imaging evaluation for suspected pedal osteomyelitis in an adult with diabetes mellitus, in order to detect osteomyelitis, screen for an alternative diagnosis such as neuropathic arthropathy, and determine whether additional imaging will be needed.
- **Variants 2 and 3**: When initial radiographs are negative or indeterminate for suspected diabetic pedal osteomyelitis, MRI of the foot—either without, or without and with IV contrast—is recommended because of its ability to detect early osteomyelitis before radiography. MRI of the foot is also appropriate after a diagnosis of osteomyelitis on radiographs, when treatment planning decisions require additional information offered by MRI, such as the extent of bone infection and the presence and location of devitalized bone or abscess. Three-

phase bone scintigraphy of the foot may be an appropriate alternative to MRI when radiographs are negative or indeterminate for osteomyelitis, and 3-phase bone scintigraphy or WBC scan with SPECT or SPECT/CT of the foot may be an appropriate alternative to MRI for treatment planning when foot radiographs are positive for osteomyelitis. However, there was panel disagreement on the role of these scintigraphic studies based on the strength of evidence and local practice variations.

- **Variants 4 and 5**: For adults with suspected diabetic pedal osteomyelitis and metal instrumentation in the foot, MRI of the foot—either without, or without and with IV contrast—is recommended as the next imaging study both for the detection of osteomyelitis when radiographs are negative or indeterminate, and for treatment planning when initial radiographs are positive. Three-phase bone scintigraphy and WBC scan with SPECT or SPECT/CT of the foot are appropriate alternatives in both scenarios and may be particularly helpful when MRI images are limited by metal artifact from instrumentation adjacent to the area of interest.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, click here.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that pre-dates the use of the current understanding of language inclusive of diversity in sex, intersex, gender and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health [78].

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [79].

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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