

**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	○
MRI foot without and with IV contrast	Usually Not Appropriate	○
MRI foot without IV contrast	Usually Not Appropriate	○
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	○
MRI foot without IV contrast	Usually Appropriate	○
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	○
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	○

MRI foot without IV contrast	Usually Appropriate	○
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	○
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	○
MRI foot without IV contrast	Usually Appropriate	○
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	○
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	○
MRI foot without IV contrast	Usually Appropriate	○
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	○
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	☼☼☼☼

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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.

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 wherein 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.

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

Initial imaging.

A. 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.

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

Initial imaging.

B. 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.

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

Initial imaging.

C. 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.

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

Initial imaging.

D. 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.

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

Initial imaging.

E. 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.

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

Initial imaging.

F. 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.

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

Initial imaging.

G. 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.

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

Initial imaging.

H. 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.

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

Initial imaging.

I. 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.

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

Initial imaging.

J. 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.

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

Initial imaging.

K. 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].

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

Initial imaging.

L. 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.

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

Initial imaging.

M. 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.

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

Initial imaging.

N. 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.

Variant 2: Adult. Suspected osteomyelitis of the foot in patients with diabetes mellitus.

Initial radiographs negative or indeterminate for osteomyelitis. Next imaging study.

A. 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.

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

B. 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.

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

C. 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].

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

D. 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.

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

E. 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].

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

F. 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].

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

G. 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].

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

H. 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].

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

I. 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].

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

J. 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].

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

K. 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].

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

L. 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].

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

M. 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.

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

N. 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].

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

A. 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.

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

B. 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.

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

C. 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.

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

D. 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.

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

E. 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].

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

F. 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].

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

G. 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].

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

H. 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.

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

I. 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].

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

J. 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].

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

K. 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.

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

L. 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.

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

M. 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.

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

N. 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.

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.

A. 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.

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.

B. 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.

Variante 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.

C. 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.

Variante 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.

D. 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.

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.

E. 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.

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.

F. 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.

Variante 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.

G. 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.

Variante 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.

H. 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.

Variante 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.

I. 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.

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.

J. 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.

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.

K. 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].

Variante 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.

L. 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].

Variante 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.

M. 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.

Variation 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.

N. 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.

Variation 5: 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.

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

A. 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.

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

B. 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.

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

C. 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.

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

D. 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.

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

E. 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.

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

F. 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.

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

G. 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.

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

H. 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.

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

I. 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.

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

J. 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.

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

K. 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.

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

L. 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.

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

M. 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.

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

N. 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.

- **Variants 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, please go to the ACR website at <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates 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.

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.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate	Pediatric Effective Dose
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	Range	Estimate Range
0	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 (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

References

- Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services; 2021. Available at: https://www.cdc.gov/diabetes/php/data-research/?CDC_AAref_Val=https://www.cdc.gov/diabetes/data/statistics-report/index.html.
- Duryea D, Bernard S, Flemming D, Walker E, French C. Outcomes in diabetic foot ulcer patients with isolated T2 marrow signal abnormality in the underlying bone: should the diagnosis of "osteitis" be changed to "early osteomyelitis"? *Skeletal Radiol.* 46(10):1327-1333, 2017 Oct.
- Palestro C, Clark A, Grady E, et al. Appropriate Use Criteria for the Use of Nuclear Medicine in Musculoskeletal Infection Imaging. *Journal of Nuclear Medicine.* 2021 Sep 30.
- Butalia S, Palda VA, Sargeant RJ, Detsky AS, Mourad O. Does this patient with diabetes have osteomyelitis of the lower extremity? *JAMA.* 2008; 299(7):806-813.
- Markanday A.. Diagnosing diabetic foot osteomyelitis: narrative review and a suggested 2-step score-based diagnostic pathway for clinicians. [Review]. *Open forum infect. dis.* 1(2):ofu060, 2014 Sep.
- Dinh MT, Abad CL, Safdar N. Diagnostic accuracy of the physical examination and imaging tests for osteomyelitis underlying diabetic foot ulcers: meta-analysis. *Clin Infect Dis.* 2008; 47(4):519-527.
- Senneville E, Albalawi Z, van Asten SA, et al. IWGDF/IDSA guidelines on the diagnosis and treatment of diabetes-related foot infections (IWGDF/IDSA 2023). [Review]. *Diabetes/Metabolism Research Reviews.* e3687, 2023 Oct 01.
- Malone M, Bowling FL, Gannass A, Jude EB, Boulton AJ. Deep wound cultures correlate well with bone biopsy culture in diabetic foot osteomyelitis. *Diabetes Metab Res Rev.* 29(7):546-50, 2013 Oct.
- Pierce JL, Perry MT, Wessell DE, et al. ACR Appropriateness Criteria® Suspected Osteomyelitis, Septic Arthritis, or Soft Tissue Infection (Excluding Spine and Diabetic Foot): 2022 Update. *J Am Coll Radiol* 2022;19:S473-S87.
- Tafur M, Bencardino JT, Roberts CC, et al. ACR Appropriateness Criteria® Chronic Foot Pain. *J Am Coll Radiol* 2020;17:S391-S402.
- Chang EY, Tadros AS, Amini B, et al. ACR Appropriateness Criteria® Chronic Ankle Pain. *J*

Am Coll Radiol 2018;15:S26-S38.

12. Gorbachova T, Chang EY, Ha AS, et al. ACR Appropriateness Criteria® Acute Trauma to the Foot. *J Am Coll Radiol* 2020;17:S2-S11.
13. Smith SE, Chang EY, Ha AS, et al. ACR Appropriateness Criteria® Acute Trauma to the Ankle. *J Am Coll Radiol* 2020;17:S355-S66.
14. Mens MA, de Geus A, Wellenberg RHH, et al. Preliminary evaluation of dual-energy CT to quantitatively assess bone marrow edema in patients with diabetic foot ulcers and suspected osteomyelitis. *Eur Radiol*. 33(8):5645-5652, 2023 Aug.
15. Heidari N, Oh I, Li Y, et al. What Is the Best Method to Differentiate Acute Charcot Foot From Acute Infection?. *Foot & Ankle International*. 40(1_suppl):39S-42S, 2019 Jul.
16. Llewellyn A, Kraft J, Holton C, Harden M, Simmonds M. Imaging for detection of osteomyelitis in people with diabetic foot ulcers: A systematic review and meta-analysis. *European Journal of Radiology*. 131:109215, 2020 Oct.
17. Simpfendorfer CS.. Radiologic Approach to Musculoskeletal Infections. [Review]. *Infect Dis Clin North Am*. 31(2):299-324, 2017 06.
18. Harmer JL, Pickard J, Stinchcombe SJ. The role of diagnostic imaging in the evaluation of suspected osteomyelitis in the foot: a critical review. [Review]. *FOOT*. 21(3):149-53, 2011 Sep.
19. Pineda C, Espinosa R, Pena A. Radiographic imaging in osteomyelitis: the role of plain radiography, computed tomography, ultrasonography, magnetic resonance imaging, and scintigraphy. *Seminars in plastic surgery* 2009;23:80-9.
20. Palestro CJ, Mehta HH, Patel M, et al. Marrow versus infection in the Charcot joint: indium-111 leukocyte and technetium-99m sulfur colloid scintigraphy. *Journal of Nuclear Medicine*. 39(2):346-50, 1998 Feb.
21. Trevail C, Ravindranath-Reddy P, Sulkin T, Bartlett G. An evaluation of the role of nuclear medicine imaging in the diagnosis of periprosthetic infections of the hip. *Clin Radiol*. 71(3):211-9, 2016 Mar.
22. Heiba SI, Kolker D, Mocherla B, et al. The optimized evaluation of diabetic foot infection by dual isotope SPECT/CT imaging protocol. *J Foot Ankle Surg*. 49(6):529-36, 2010 Nov-Dec.
23. Palestro CJ.. Radionuclide Imaging of Musculoskeletal Infection: A Review. [Review]. *J Nucl Med*. 57(9):1406-12, 2016 09.
24. Palestro CJ, Roumanas P, Swyer AJ, Kim CK, Goldsmith SJ. Diagnosis of musculoskeletal infection using combined In-111 labeled leukocyte and Tc-99m SC marrow imaging. *Clin Nucl Med* 1992;17:269-73.
25. Schauwecker DS, Park HM, Burt RW, Mock BH, Wellman HN. Combined bone scintigraphy and indium-111 leukocyte scans in neuropathic foot disease. *J Nucl Med*. 29(10):1651-5, 1988 Oct.
26. Seabold JE, Flickinger FW, Kao SC, et al. Indium-111-leukocyte/technetium-99m-MDP bone and magnetic resonance imaging: difficulty of diagnosing osteomyelitis in patients with neuropathic osteoarthropathy. *J Nucl Med*. 31(5):549-56, 1990 May.
27. Devillers A, Moisan A, Hennion F, Garin E, Poirier JY, Bourguet P. Contribution of

- technetium-99m hexamethylpropylene amine oxime labelled leucocyte scintigraphy to the diagnosis of diabetic foot infection. *Eur J Nucl Med*. 25(2):132-8, 1998 Feb.
28. Johnson JE, Kennedy EJ, Shereff MJ, Patel NC, Collier BD. Prospective study of bone, indium-111-labeled white blood cell, and gallium-67 scanning for the evaluation of osteomyelitis in the diabetic foot. *Foot Ankle Int* 1996;17:10-6.
 29. Termaat MF, Raijmakers PG, Scholten HJ, Bakker FC, Patka P, Haarman HJ. The accuracy of diagnostic imaging for the assessment of chronic osteomyelitis: a systematic review and meta-analysis. *J Bone Joint Surg Am*. 2005; 87(11):2464-2471.
 30. Filippi L, Schillaci O. Usefulness of hybrid SPECT/CT in 99mTc-HMPAO-labeled leukocyte scintigraphy for bone and joint infections. *J Nucl Med*. 2006;47(12):1908-1913.
 31. Horger M, Eschmann SM, Pfannenbergs C, et al. The value of SPET/CT in chronic osteomyelitis. *Eur J Nucl Med Mol Imaging*. 2003;30(12):1665-1673.
 32. Horger M, Eschmann SM, Pfannenbergs C, et al. Added value of SPECT/CT in patients suspected of having bone infection: preliminary results. *Arch Orthop Trauma Surg*. 2007;127(3):211-221.
 33. La Fontaine J, Bhavan K, Lam K, et al. Comparison Between Tc-99m WBC SPECT/CT and MRI for the Diagnosis of Biopsy-proven Diabetic Foot Osteomyelitis. *WOUNDS*. 28(8):271-8, 2016 Aug.
 34. Larcos G, Brown ML, Sutton RT. Diagnosis of osteomyelitis of the foot in diabetic patients: value of 111In-leukocyte scintigraphy. *AJR* 1991;157:527-31.
 35. Schauwecker DS. The scintigraphic diagnosis of osteomyelitis. *AJR* 1992;158:9-18.
 36. Yuh WT, Corson JD, Baraniewski HM, et al. Osteomyelitis of the foot in diabetic patients: evaluation with plain film, 99mTc-MDP bone scintigraphy, and MR imaging. *AJR* 1989;152:795-800.
 37. Jay PR, Michelson JD, Mizel MS, Magid D, Le T. Efficacy of three-phase bone scans in evaluating diabetic foot ulcers. *Foot Ankle Int*. 1999; 20(6):347-355.
 38. Mandell JC, Khurana B, Smith JT, Czuczman GJ, Ghazikhanian V, Smith SE. Osteomyelitis of the lower extremity: pathophysiology, imaging, and classification, with an emphasis on diabetic foot infection. [Review]. *EMERG. RADIOL.* 25(2):175-188, 2018 Apr.
 39. Chantelau EA, Grutzner G. Is the Eichenholtz classification still valid for the diabetic Charcot foot?. [Review]. *Swiss Med Wkly*. 144:w13948, 2014.
 40. Trieb K.. The Charcot foot: pathophysiology, diagnosis and classification. [Review]. *Bone Joint J*. 98-B(9):1155-9, 2016 Sep.
 41. Fayad LM, Carrino JA, Fishman EK. Musculoskeletal infection: role of CT in the emergency department. *Radiographics*. 2007;27(6):1723-1736.
 42. Kagna O, Srour S, Melamed E, Militianu D, Keidar Z. FDG PET/CT imaging in the diagnosis of osteomyelitis in the diabetic foot. *Eur J Nucl Med Mol Imaging*. 39(10):1545-50, 2012 Oct.
 43. Keidar Z, Militianu D, Melamed E, Bar-Shalom R, Israel O. The diabetic foot: initial experience with 18F-FDG PET/CT. *J Nucl Med*. 46(3):444-9, 2005 Mar.
 44. Lauri C, Tamminga M, Glaudemans AWJM, et al. Detection of Osteomyelitis in the Diabetic Foot by Imaging Techniques: A Systematic Review and Meta-analysis Comparing MRI, White

- Blood Cell Scintigraphy, and FDG-PET. [Review]. *Diabetes Care*. 40(8):1111-1120, 2017 08.
45. Treglia G, Sadeghi R, Annunziata S, et al. Diagnostic performance of Fluorine-18-Fluorodeoxyglucose positron emission tomography for the diagnosis of osteomyelitis related to diabetic foot: a systematic review and a meta-analysis. [Review]. *FOOT*. 23(4):140-8, 2013 Dec.
 46. Lauri C, Glaudemans AWJM, Campagna G, et al. Comparison of White Blood Cell Scintigraphy, FDG PET/CT and MRI in Suspected Diabetic Foot Infection: Results of a Large Retrospective Multicenter Study. *Journal of Clinical Medicine*. 9(6), 2020 May 30.
 47. Al-Balas H, Metwalli ZA, Nagaraj A, Sada DM. Is fluoroscopy-guided percutaneous bone biopsy of diabetic foot with suspected osteomyelitis worthwhile? A retrospective study. *Journal Of Diabetes*. 15(4):332-337, 2023 Apr.
 48. Heidari N, Kwok I, Vris A, Charalambous A. Should Treatment of Diabetic Foot Osteomyelitis Be Based on Bone Biopsies?. *Foot & Ankle International*. 40(1_suppl):73S-74S, 2019 Jul.
 49. Said N, Chalian M, Fox MG, Nacey NC. Percutaneous image-guided bone biopsy of osteomyelitis in the foot and pelvis has a low impact on guiding antibiotics management: a retrospective analysis of 60 bone biopsies. *Skeletal Radiology*. 48(9):1385-1391, 2019 Sep.
 50. Schechter MC, Ali MK, Risk BB, et al. Percutaneous Bone Biopsy for Diabetic Foot Osteomyelitis: A Systematic Review and Meta-Analysis. *Open Forum Infectious Diseases*. 7(10):ofaa393, 2020 Oct.
 51. Tardaguila-Garcia A, Sanz-Corbalan I, Garcia-Morales E, Garcia-Alvarez Y, Molines-Barroso RJ, Lazaro-Martinez JL. Diagnostic Accuracy of Bone Culture Versus Biopsy in Diabetic Foot Osteomyelitis. *Advances in Skin & Wound Care*. 34(4):204-208, 2021 Apr 01.
 52. Al-Khawari HA, Al-Saeed OM, Jumaa TH, Chishti F. Evaluating diabetic foot infection with magnetic resonance imaging: Kuwait experience. *Med Princ Pract*. 2005; 14(3):165-172.
 53. Rozzanigo U, Tagliani A, Vittorini E, Pacchioni R, Brivio LR, Caudana R. Role of magnetic resonance imaging in the evaluation of diabetic foot with suspected osteomyelitis. *Radiol Med (Torino)*. 114(1):121-32, 2009 Feb.
 54. Sax AJ, Halpern EJ, Zoga AC, Roedl JB, Belair JA, Morrison WB. Predicting osteomyelitis in patients whose initial MRI demonstrated bone marrow edema without corresponding T1 signal marrow replacement. *Skeletal Radiology*. 49(8):1239-1247, 2020 Aug.
 55. Kapoor A, Page S, Lavalley M, Gale DR, Felson DT. Magnetic resonance imaging for diagnosing foot osteomyelitis: a meta-analysis. [Review] [38 refs]. *Arch Intern Med*. 167(2):125-32, 2007 Jan 22.
 56. Craig JG, Amin MB, Wu K, et al. Osteomyelitis of the diabetic foot: MR imaging-pathologic correlation. *Radiology*. 203(3):849-55, 1997 Jun.
 57. Collins MS, Schaar MM, Wenger DE, Mandrekar JN. T1-weighted MRI characteristics of pedal osteomyelitis. *AJR Am J Roentgenol*. 185(2):386-93, 2005 Aug.
 58. Alaia EF, Chhabra A, Simpfendorfer CS, et al. MRI nomenclature for musculoskeletal infection. [Review]. *Skeletal Radiology*. 50(12):2319-2347, 2021 Dec. *Skeletal Radiol*. 50(12):2319-2347, 2021 Dec.
 59. Johnson PW, Collins MS, Wenger DE. Diagnostic utility of T1-weighted MRI characteristics in evaluation of osteomyelitis of the foot. *AJR Am J Roentgenol*. 192(1):96-100, 2009 Jan.

60. Tiegs-Heiden CA, Anderson TC, Collins MS, Johnson MP, Osmon DR, Wenger DE. Outcomes in patients with clinically suspected pedal osteomyelitis based on bone marrow signal pattern on MRI. *Journal Of Bone And Joint Infection*. 8(2):99-107, 2023.
61. Schwegler B, Stumpe KD, Weishaupt D, et al. Unsuspected osteomyelitis is frequent in persistent diabetic foot ulcer and better diagnosed by MRI than by 18F-FDG PET or 99mTc-MOAB. *J Intern Med*. 2008; 263(1):99-106.
62. Vesco L, Boulahdour H, Hamissa S, et al. The value of combined radionuclide and magnetic resonance imaging in the diagnosis and conservative management of minimal or localized osteomyelitis of the foot in diabetic patients. *Metabolism*. 1999; 48(7):922-927.
63. Horowitz JD, Durham JR, Nease DB, Lukens ML, Wright JG, Smead WL. Prospective evaluation of magnetic resonance imaging in the management of acute diabetic foot infections. *Ann Vasc Surg*. 1993; 7(1):44-50.
64. Kotecha HM, Lo HS, Vedantham S, Shin H, Cerniglia CA. Abbreviated MRI of the foot in patients with suspected osteomyelitis. *Emergency Radiology*. 27(1):9-16, 2020 Feb.
65. Lopez-Moral M, Garcia-Madrid M, Molines-Barroso RJ, Garcia-Alvarez Y, Alvaro-Afonso FJ, Lazaro-Martinez JL. Diagnostic Performance of Ultrasonography for Diabetic Foot Osteomyelitis. *Advances in Wound Care*. 2023 Dec 20.
66. Palestro CJ, Love C, Miller TT. Infection and musculoskeletal conditions: Imaging of musculoskeletal infections. [Review] [95 refs]. *Baillieres Best Pract Res Clin Rheumatol*. 20(6):1197-218, 2006 Dec.
67. Al-Sheikh W, Sfakianakis GN, Mnaymneh W, et al. Subacute and chronic bone infections: diagnosis using In-111, Ga-67 and Tc-99m MDP bone scintigraphy, and radiography. *Radiology* 1985;155:501-6.
68. Palestro CJ, Love C, Tronco GG, Tomas MB, Rini JN. Combined labeled leukocyte and technetium 99m sulfur colloid bone marrow imaging for diagnosing musculoskeletal infection. *Radiographics*. 2006;26:859-70.
69. Park SB, Lim CH, Chun DI, Kim YJ, Kim TH, Park JM. The usefulness of quantitative (99m)Tc-HMPAO WBC SPECT/CT for predicting lower extremity amputation in diabetic foot infection. *Sci Rep* 2024;14:9260.
70. Cohen M, Cerniglia B, Gorbachova T, Horrow J. Added value of MRI to X-ray in guiding the extent of surgical resection in diabetic forefoot osteomyelitis: a review of pathologically proven, surgically treated cases. *Skeletal Radiology*. 48(3):405-411, 2019 Mar.
71. Ledermann HP, Schweitzer ME, Morrison WB. Nonenhancing tissue on MR imaging of pedal infection: characterization of necrotic tissue and associated limitations for diagnosis of osteomyelitis and abscess. *AJR Am J Roentgenol*. 2002 Jan;178(1):215-22.
72. Hopfner S, Krolak C, Kessler S, et al. Preoperative imaging of Charcot neuroarthropathy in diabetic patients: comparison of ring PET, hybrid PET, and magnetic resonance imaging. *Foot Ankle Int*. 25(12):890-5, 2004 Dec.
73. Chacko TK, Zhuang H, Nakhoda KZ, Moussavian B, Alavi A. Applications of fluorodeoxyglucose positron emission tomography in the diagnosis of infection. *Nucl Med Commun*. 2003;24(6):615-624.
74. Crymes WB, Jr., Demos H, Gordon L. Detection of musculoskeletal infection with 18F-FDG

PET: review of the current literature. *J Nucl Med Technol.* 2004;32(1):12-15.

75. Wang GL, Zhao K, Liu ZF, Dong MJ, Yang SY. A meta-analysis of fluorodeoxyglucose-positron emission tomography versus scintigraphy in the evaluation of suspected osteomyelitis. *Nucl Med Commun.* 32(12):1134-42, 2011 Dec.
76. Porrino J, Wang A, Moats A, Mulcahy H, Kani K. Prosthetic joint infections: diagnosis, management, and complications of the two-stage replacement arthroplasty. *Skeletal radiology* 2020;49:847-59.
77. Park BN, Hong SJ, Yoon MA, Oh JK. MRI Diagnosis for Post-Traumatic Osteomyelitis of Extremities Using Conventional Metal-Artifact Reducing Protocols: Revisited. *Acad Radiol.* 26(11):e317-e323, 2019 11.
78. Measuring Sex, Gender Identity, and Sexual Orientation.
79. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: <https://edge.sitecorecloud.io/americancoldf5f-acrorgf92a-productioncb02-3650/media/ACR/Files/Clinical/Appropriateness-Criteria/ACR-Appropriateness-Criteria-Radiation-Dose-Assessment-Introduction.pdf>.

Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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