Suspected Osteomyelitis of the Foot in Patients with Diabetes Mellitus
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Ledermann HP, Morrison WB, Schweitzer ME. Pedal abscesses in patients suspected of having pedal osteomyelitis: analysis with MR imaging. *Radiology* 2002; 224(3):649-655.	Observational-Dx	161 total feet; 51 women, 107 men	To document the expected frequency, location, and size of pedal abscesses in patients with advanced foot infection.	Abscesses were significantly more frequent in patients with osteomyelitis (n=28, 97%) (P<.001) and in feet that had been treated surgically (n=16, 33%) (P<.002). MRI revealed abscesses, predominantly in the forefoot, in 18% of patients suspected of having pedal osteomyelitis. Abscesses are significantly more frequent in patients with osteomyelitis and in feet that have been treated surgically.	3
2. Schweitzer ME, Morrison WB. MR imaging of the diabetic foot. *Radiol Clin North Am* 2004; 42(1):61-71, vi.	Review/Other-Dx	N/A	To review MRI of vascular disease and diabetic pedal disease.	Emphasize T1 imaging and second advantages of gadolinium enhanced imaging. Recognition of these MRI patterns is important for formulation of an appropriate treatment plan.	4
3. Tomas MB, Patel M, Marwin SE, Palestro CJ. The diabetic foot. *Br J Radiol* 2000; 73(868):443-450.	Review/Other-Dx	N/A	To review nuclear medicine in the diabetic foot.	Labeled leucocyte scintigraphy is valuable for diagnosis as well as follow-up of pedal osteomyelitis. MRI offers exquisite anatomical detail, which is invaluable for guiding surgical management Uptake of labeled leucocytes in the absence of infection may occur and is owing, at least in part, to haematopoietically active marrow. Combined leucocyte/marrow scintigraphy holds considerable promise for identifying the infected Charcot joint.	4
4. Chatha DS, Cunningham PM, Schweitzer ME. MR imaging of the diabetic foot: diagnostic challenges. *Radiol Clin North Am* 2005; 43(4):747-759, ix.	Review/Other-Dx	N/A	To review MRI of diabetic foot infections.	Emphasized looking for abscesses and differentiating soft tissue changes from neuropathy from infection.	4
5. Ledermann HP, Morrison WB. Differential diagnosis of pedal osteomyelitis and diabetic neuroarthropathy: MR Imaging. *Semin Musculoskelet Radiol* 2005; 9(3):272-283.	Review/Other-Dx	N/A	To review diagnosis of osteomyelitis in patients with diabetic neuroarthropathy.	Differentiation between osteomyelitis and acute or subacute neuroarthropathy requires careful analysis of the location of bone signal alterations, their distribution, and pattern because qualitative changes are often identical. Presence of secondary signs such as adjacent ulcer, cellulitis, and sinus tract is indicative of osteomyelitis. Differentiation of noninfected neuroarthropathy from infected neuroarthropathy based on MR examinations is difficult. Presence of a sinus tract, disappearance of subchondral cysts, diffuse bone marrow abnormality, and bone erosions are in favor of infection.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
6. Familiari D, Glaudemans AW, Vitale V, et al. Can Sequential 18F-FDG PET/CT Replace WBC Imaging in the Diabetic Foot? *J Nucl Med* 2011; 52(7):1012-1019.	Observational-Dx	13 patients	To evaluate the role of sequential FDG-PET/CT in patients with a high suspicion of osteomyelitis compared with WBC scintigraphy.	At final biopsy, 7 patients had osteomyelitis, 2 had soft-tissue infection without osteomyelitis, and 4 had no infection. The best interpretation criterion for osteomyelitis with WBC scintigraphy was a target-to-background ratio greater than 2.0 at 20 hours and increasing with time. A target-to-background ratio greater than 2.0 at 20 hours but stable or decreasing with time was suggestive of soft-tissue infection. A target-to-background ratio of no more than 2.0 at 20 hours excluded an infection. Thus, sensitivity, specificity, PPV, NPV, and accuracy for osteomyelitis were 86%, 100%, 100%, 86%, and 92%, respectively. For FDG-PET/CT, the best interpretation criterion for osteomyelitis was a maximal SUVmax >2.0 at 1 and 2 hours and increasing with time. A SUVmax > 2.0 after 1 and 2 hours but stable or decreasing with time was suggestive of a soft-tissue infection. A SUVmax <2.0 excluded an infection. FDG-PET/CT at 10 minutes was not useful. Using these criteria, sensitivity, specificity, PPV, NPV, and accuracy for osteomyelitis were 43%, 67%, 60%, 50%, and 54%, respectively. Combining visual assessment of PET at 1 hour and CT was best for differentiating between osteomyelitis and soft-tissue infection, with a diagnostic accuracy of 62%. FDG-PET/CT, even with sequential imaging, has a low diagnostic accuracy for osteomyelitis and cannot replace WBC scintigraphy in patients with diabetic foot.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. Basu S, Chryssikos T, Houseni M, et al. Potential role of FDG PET in the setting of diabetic neuro-osteoarthropathy: can it differentiate uncomplicated Charcot's neuroarthropathy from osteomyelitis and soft-tissue infection? Nucl Med Commun 2007; 28(6):465-472.	Observational-Dx	63 total patients	To evaluate the use of PET in the detection of infection and differentiation from acute neuropathic osteoarthropathy in the setting of a complicated diabetic foot.	Overall sensitivity and accuracy of FDG-PET in the diagnosis of Charcot's foot was 100% and 93.8%, respectively; and for MRI were 76.9% and 75%, respectively. FDG-PET showed foci of abnormally enhanced uptake in the soft-tissue which was suggestive of inflammation in 7 cases (43.75%) which were proven pathologically to be secondary to infection. In only two of these cases the features of soft tissue infection were noted on the MRI. The results support a valuable role of FDG-PET in the setting of Charcot's neuroarthropathy by reliably differentiating it from osteomyelitis both in general and when foot ulcer is present.	2
8. 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.	Observational-Dx	20 diabetic patients with foot ulcers; 7+ for osteomyelitis by biopsy	To assess the prevalence of clinically unsuspected osteomyelitis and to compare the value of MRI, FDG-PET and 99mTc-labelled monoclonal antigranulocyte antibody scintigraphy.	Clinically unsuspected osteomyelitis is frequent in persisting foot ulcers and is a high risk factor for adverse outcome. MRI appears superior to FDG-PET and 99mTc-labelled monoclonal antigranulocyte antibody scintigraphy in detecting foot ulcer-associated osteomyelitis. MRI was positive in 6/7 patients with proven osteomyelitis, whereas FDG-PET and 99mTc-labelled monoclonal antigranulocyte antibody scintigraphy were positive only in (the same) two patients. Clinically unsuspected osteomyelitis is frequent in persisting foot ulcers and is a high risk factor for adverse outcome. MRI appears superior to FDG-PET and 99mTc-labelled monoclonal antigranulocyte antibody scintigraphy in detecting foot ulcer-associated osteomyelitis and might be the preferred imaging modality in patients with nonhealing diabetic foot ulcers.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Strobel K, Stumpe KD. PET/CT in musculoskeletal infection. *Semin Musculoskelet Radiol* 2007; 11(4):353-364.	Review/Other-Dx	N/A	To illustrate the use of PET and PET/CT in musculoskeletal infection.	FDG-PET has shown promising results for diagnosing both acute and chronic infection of the axial and appendicular skeletons. PET imaging will have increased importance in patients with metallic implants because FDG uptake, in contrast to MRI and CT, is not hampered by metallic artifacts. PET/CT with the combination of PET and a low-dose or full-dose diagnostic CT provides exact anatomical correlation of bone and joint lesions and increases the accuracy of the test compared with PET alone.	4
10. 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* 2004; 25(12):890-895.	Observational-Dx	16 patients with type II diabetes	To investigate the value of two types of PET in the preoperative evaluation of diabetic patients with Charcot foot deformities.	Of 39 Charcot lesions confirmed at surgery, 37 were detected by ring PET, 30 by hybrid PET, and 31 by MRI. PET (ring or hybrid) can be used in the evaluation of patients with metal implants that would compromise the accuracy of MRI. Another advantage of PET is its ability to distinguish between inflammatory and infectious soft-tissue lesions, and between osteomyelitis and Charcot neuroarthropathy. The differentiation between Charcot neuroarthropathy and florid osteomyelitis provides the surgeon with important additional information that often is unavailable from MRI. Because it provides important additional data, ring PET may be preferable to radiography and MRI in the preoperative evaluation of patients with Charcot neuroarthropathy of the foot. Hybrid PET, because of its poorer resolution compared to ring PET, appears less suitable for routine clinical application.	2
11. 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.	Observational-Dx	34 bone scans	To retrospectively evaluate the utility of bone scans in determining the treatment of diabetic patients with foot ulcers.	There was no significant difference in the amputation rate for patients with confirmatory, indeterminate, or nonconfirmatory bone scans for osteomyelitis (36%, 37%, and 50%, respectively) ($P>0.5$). Therefore, it is concluded that the ultimate treatment should be based on clinical indicators of the presence of uncontrolled infection or gangrene rather than on bone scan findings.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Melkun ET, Lewis VL, Jr. Evaluation of (111) indium-labeled autologous leukocyte scintigraphy for the diagnosis of chronic osteomyelitis in patients with grade IV pressure ulcers, as compared with a standard diagnostic protocol. *Ann Plast Surg* 2005; 54(6):633-636.	Observational-Dx	11 patients	To evaluate the efficacy of indium scanning in the diagnosis of chronic osteomyelitis in spinal-cord-injury patients with grade IV pressure ulcers.	The sensitivity and specificity were 100% and 50%, respectively. Indium scanning appears to be more sensitive than specific. These data suggest that the value of indium scanning may primarily be to rule out osteomyelitis and not as a primary diagnostic modality.	3
13. 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.	Observational-Dx	24 patients	To evaluate combined bone scan, labeled white cells, and MRI.	Evidence of osteomyelitis was based on the presence of at least one of the following criteria: 1) Clinical bone involvement, 2) Radiological bone involvement, 3) Both positive combined radionuclide imaging and MRI, and 4) Evidence of clinical bone involvement during the follow-up period. 13 patients had osteomyelitis. 7 patients had clinical bone involvement (sensitivity, 54%), 5 patients had radiological bone involvement (sensitivity, 38%), and 10 had positive combined radionuclide imaging for osteomyelitis (sensitivity, 77%). MRI demonstrated a higher sensitivity (100%). The specificity for combined radionuclide imaging and MRI was 82%. These results lead to a new diagnostic strategy for the early detection of minimal or localized osteomyelitis to avoid amputations. MRI is most appropriate following a negative radiograph in determining whether to treat osteomyelitis, since a negative MRI result rules out osteomyelitis. Antibiotic therapy should be used in the case of a positive MRI result, but Charcot joint disease can lead to false-positive MRI results. In this case, combined radionuclide imaging should be performed.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
14. Ahmadi ME, Morrison WB, Carrino JA, Schweitzer ME, Raikin SM, Ledermann HP. Neuropathic arthropathy of the foot with and without superimposed osteomyelitis: MR imaging characteristics. *Radiology* 2006; 238(2):622-631.	Observational-Dx	128 neuropathic joints; 43 with super-imposed osteomyelitis	To determine retrospectively the MRI findings associated with pedal neuropathic arthropathy with and without superimposed osteomyelitis and to identify any useful discriminating features.	Effusion was common in all neuropathic joints, but thin rim enhancement was more common in noninfected joints (62% vs 21%, P<.001) and diffuse joint fluid enhancement was more common with infection (47% vs 26%, P=.052). Subluxation, bone proliferation, fragmentation, and erosion were seen in both groups, but intra-articular bodies were more common in noninfected joints (53% vs 12%, P<.001). In the periarticular soft tissues, edema, enhancement, and ulceration were common in both groups. Fluid collections in the soft tissues were more commonly associated with infected joints (95% vs 48%, P<.001) and, when present next to an infected joint, were larger than those next to noninfected neuropathic joints. Soft-tissue fat replacement (68% vs 36%, P=002) and sinus tracts (84% vs 0%, P<.001) were also more common with infection. In the marrow, periarticular signal intensity abnormality was common in both groups, but the extent was greater with infection. Subchondral cysts were seen almost exclusively in noninfected joints (76% vs 2%, P<.001). Sinus tract, replacement of soft-tissue fat, fluid collection, and extensive marrow abnormality are MRI features indicating superimposed infection. Thin rim enhancement of effusion, presence of subchondral cysts, or intra-articular bodies indicates absence of infection.	4
15. Palestro CJ, Love C. Nuclear medicine and diabetic foot infections. *Seminars in nuclear medicine* 2009; 39(1):52-65.	Review/Other-Dx	N/A	To review role of bone scintigraphy and labeled leukocyte imaging in diabetic foot infections.	Labeled leukocyte imaging is the nuclear medicine procedure of choice for investigation of diabetic foot infections. The overall accuracy of the test is about 80%-85%, and either Tc-99m- or 111In-labeled leukocytes can be used.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
16. Palestro CJ, Mehta HH, Patel M, et al. Marrow versus infection in the Charcot joint: indium-111 leukocyte and technetium-99m sulfur colloid scintigraphy. *J Nucl Med* 1998; 39(2):346-350.	Observational-Dx	17 patients	To evaluate the role of combined leukocyte/marrow scintigraphy in the assessment of the neuropathic or Charcot joint.	Labeled leukocyte accumulation in the uninfected Charcot joint does occur and is related, at least in part, to hematopoietically active marrow. Leukocyte/marrow scintigraphy is a reliable way to differentiate between marrow and infection as the cause of labeled leukocyte accumulation in the neuropathic joint and, in this series, was superior to both three-phase bone scintigraphy and combined leukocyte/bone scintigraphy.	3
17. 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.	Observational-Dx	29 diabetic patients with suspected infection	To evaluate the capability of MRI to depict and characterize the changes seen in diabetic foot infections.	MRI showed osteomyelitis in 14 patients, abscess in 5, cellulitis in 26, tenosynovitis in 4 and neuropathic joint in 8. 3 cases were normal. Pathological confirmations were obtained in 19 patients. MRI and histological diagnosis were in concordance in 79% of osteomyelitis cases, 100% of neuropathy cases and 100% of cellulitis cases. The sensitivity and specificity of MRI in diagnosing osteomyelitis were 100% and 63% respectively. PPV and NPV, and accuracy were 79%, 100% and 84%, respectively. MRI is a sensitive and accurate imaging modality for the evaluation of foot infections in diabetic patients and for planning proper treatment.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
18. 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.	Review/Other-Dx	21articles reviewed	To determine the accuracy of historical features, physical examination, and laboratory and basic radiographic testing. We searched for systematic reviews of MRI in the diagnosis of lower extremity osteomyelitis in patients with diabetes to compare its performance with the reference standard.	The gold standard for diagnosis is bone biopsy. An ulcer area larger than 2 cm^2 (positive LR, 7.2; 95% CI, 1.1-49; negative LR, 0.48; 95% CI, 0.31-0.76) and a positive "probe-to-bone" test result (summary positive LR, 6.4; 95% CI, 3.6-11; negative LR, 0.39; 95% CI, 0.20-0.76) were the best clinical findings. An erythrocyte sedimentation rate of more than 70 mm/h increases the probability of a diagnosis of osteomyelitis (summary LR, 11; 95% CI, 1.6-79). An abnormal radiograph doubles the odds of osteomyelitis (summary LR, 2.3; 95% CI, 1.6-3.3). A positive MRI result increases the likelihood of osteomyelitis (summary LR, 3.8; 95% CI, 2.5-5.8). However, a normal MRI result makes osteomyelitis much less likely (summary LR, 0.14; 95% CI, 0.08-0.26). The overall accuracy (ie, the weighted average of the sensitivity and specificity) of the MRI is 89% (95% CI, 83.0%-94.5%). An ulcer area larger than 2 cm^2, a positive probe-to-bone test result, an erythrocyte sedimentation rate of more than 70 mm/h, and an abnormal radiograph result are helpful in diagnosing the presence of lower extremity osteomyelitis in patients with diabetes. A negative MRI result makes the diagnosis much less likely when all of these findings are absent. No single historical feature or physical examination reliably excludes osteomyelitis. The diagnostic utility of a combination of findings is unknown.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
19. 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.	Review/Other-Dx	68 total studies; 9 studies from literature search including 59 additional studies found from references	To critically evaluate the diagnostic accuracy of clinical examination, radiographs, bone scan, WBC scan and MRI for diagnosis of osteomyelitis in diabetic patients with foot ulcers.	Exposed bone or probe-to-bone test had a sensitivity of 0.60 and a specificity of 0.91. Radiography had a sensitivity of 0.54 and a specificity of 0.68. MRI had a sensitivity of 0.90 and a specificity of 0.79. Bone scan was found to have a sensitivity of 0.81 and a specificity of 0.28. Leukocyte scan was found to have a sensitivity of 0.74 and a specificity of 0.68. The diagnostic odds ratios for clinical examination, radiography, MRI, bone scan, and leukocyte scan were 49.45, 2.84, 24.36, 2.10, and 10.07, respectively. Radiography: 54% sensitive, 68% specific. MRI: 90% sensitive, 79% specific. Tc-MDP: 81% sensitive, 28% specific. In-WBC: 74% sensitive, 68% specific. The presence of exposed bone or a positive probe-to-bone test result is moderately predictive of osteomyelitis. MRI is the most accurate imaging test for diagnosis of osteomyelitis.	4
20. 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* 2002; 178(1):215-222.	Observational-Dx	110 foot exams in 102 patients	To study the frequency, location, extent, and signal characteristics of nonenhancing tissue in pedal infections and correlated those areas with surgical and histologic findings.	Signal characteristics on T1-weighted images were isointense to muscle (n=21, 77.8%), hypointense to muscle (n=3, 11.1%), heterogeneous (n=2, 7.4%), and isointense to fat (n=1, 3.7%). On T2-weighted images, the signal was hyperintense to muscle (n=12, 44.4%), heterogeneous to muscle (n=9, 33.3%), equal to fluid (n=3, 11.1%), and hypointense to muscle (n=3, 11.1%). The mean signal increase after contrast administration was 3.57% for observer 1 and 2.68% for observer 2. Necrotic tissue was surgically confirmed in the nonenhancing areas in 26 feet (96.3%). Nonenhancing areas are seen in one fourth of pedal infections, occur almost exclusively in diabetic patients, and represent necrotic tissue. Only contrast-enhanced images allow reliable recognition of these regions. Lack of enhancement in these areas can mask the presence of abscess and osteomyelitis.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
21. 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* 2009; 114(1):121-132.	Observational-Dx	16 patients with infected ulcers	To evaluate MRI in infected diabetic foot ulcers.	The final diagnosis, based on clinical imaging, microbiological and histological findings, was osteomyelitis in 13/16 cases. Foot MRI allowed a correct diagnosis in 15/16 patients, with one false positive result demonstrated by CT-guided bone biopsy. MRI has high sensitivity for the detection of osteomyelitis in the diabetic foot but lower specificity related to Charcot neuropathic osteoarthropathy.	3
22. Lavery LA, Armstrong DG, Peters EJ, Lipsky BA. Probe-to-bone test for diagnosing diabetic foot osteomyelitis: reliable or relic? *Diabetes Care* 2007; 30(2):270-274.	Observational-Dx	1,666 consecutive diabetic individuals	To assess the accuracy of the probe-to-bone test in diagnosing foot osteomyelitis in a cohort of diabetic patients with bone culture proven disease.	Over a mean of 27.2 months of follow-up 247 patients developed a foot wound and 151 developed 199 foot infections. Osteomyelitis was found in 30 patients: 12% of those with a foot wound and 20% in those with a foot infection. When all wounds were considered, the probe-to-bone test was highly sensitive (0.87) and specific (0.91); the PPV was only 0.57, but the NPV was 0.98. The probe-to-bone test, when used in a population of diabetic patients with a foot wound among whom the prevalence of osteomyelitis was 12%, had a relatively low PPV, but a negative test may exclude the diagnosis.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
23. Shone A, Burnside J, Chipchase S, Game F, Jeffcoate W. Probing the validity of the probe-to-bone test in the diagnosis of osteomyelitis of the foot in diabetes. *Diabetes Care* 2006; 29(4):945.	Observational-Dx	81 patients (104 foot ulcers)	To determine the validity of the probe-to-bone test in a consecutive series of outpatients.	A total of 14 patients had osteomyelitis complicating a single ulcer. A total of 21 ulcers (20.2% of 104) were associated with osteomyelitis. The probe-to-bone test was positive in 8 of these 21 ulcers and in 7 of 83 without associated bone infection (sensitivity 38%, specificity 91%). While the NPV was 85%, the PPV (the probability that a patient with a positive test would have osteomyelitis) was only 53%. The data emphasize that the predictive value of a positive probe-to bone test in the original report was influenced by the high prevalence of osteomyelitis in the population studied. The prevalence of osteomyelitis in the present population was still high at 23.5% patients (20.2% ulcers) but was only approximately one-third of that in the earlier study, and the PPV was correspondingly lower. It is likely that the PPV would be lower still in patients managed in a less-specialized service.	2
24. Grayson ML, Gibbons GW, Balogh K, Levin E, Karchmer AW. Probing to bone in infected pedal ulcers. A clinical sign of underlying osteomyelitis in diabetic patients. *JAMA* 1995; 273(9):721-723.	Observational-Dx	75 patients (76 infected foot ulcers)	To prospectively assess infected pedal ulcers for detectable bone by probing with a sterile, blunt, stainless steel probe. The relationship between detection of bone and the presence or absence of osteomyelitis that was defined histopathologically and/or clinically was examined.	Osteomyelitis was diagnosed in 50 instances (66%) and was excluded in 26 instances. Bone was detected by probing in 33/50 ulcers with contiguous osteomyelitis; in contrast, bone was probed in 4/26 ulcers without contiguous osteomyelitis (P<.001). Bone detected on probing was visible in only 3 instances. Palpating bone on probing the pedal ulcer had a sensitivity of 66% for osteomyelitis, a specificity of 85%, a PPV of 89%, and NPV of 56%. Palpation of bone in the depths of infected pedal ulcers in patients with diabetes is strongly correlated with the presence of underlying osteomyelitis. If bone is palpated on probing, specialized roentgenographic and radionuclide tests to diagnose osteomyelitis are unnecessary. Probing for bone should be included in the initial assessment of all diabetic patients with infected pedal ulcers.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
25. Keidar Z, Militianu D, Melamed E, Bar-Shalom R, Israel O. The diabetic foot: initial experience with 18F-FDG PET/CT. *J Nucl Med* 2005; 46(3):444-449.	Observational-Dx	14 diabetic patients	To assess the role of PET/CT using FDG for the diagnosis of diabetic foot osteomyelitis.	PET detected 14 foci of increased FDG uptake suspected as infection in 10 patients. PET/CT correctly localized 8 foci in 4 patients to bone, indicating osteomyelitis. PET/CT correctly excluded osteomyelitis in 5 foci in 5 patients, with the abnormal FDG uptake limited to infected soft tissues only. One site of mildly increased focal FDG uptake was localized by PET/CT to diabetic osteoarthropathy changes demonstrated on CT. Four patients showed no abnormally increased FDG uptake and no further evidence of an infectious process on clinical and imaging follow-up. FDG-PET can be used for diagnosis of diabetes-related infection. The precise anatomic localization of increased FDG uptake provided by PET/CT enables accurate differentiation between osteomyelitis and soft-tissue infection.	3
26. Becker W. Imaging osteomyelitis and the diabetic foot. *Q J Nucl Med* 1999; 43(1):9-20.	Review/Other-Dx	N/A	To discuss the possible results of conventional radiography and tomography, CT and MRI as radiological methods and on bone scan, autologous WBC scintigraphy with 111In-oxin or 99mTc-HMPAO, antigranulocyte antibodies, 99mTc-/111In-human immunoglobulin, 67Ga-citrate and 99mTc-nanocolloid.	If osteomyelitis is suspected, radiography should be the first, 3-phase bone scintigraphy the second and infection specific radiopharmaceuticals the third step of examination. Only in negative images with high clinical suspicion CT or MRI should be the final imaging procedure. In the diabetic foot imaging cascade should also start with radiography, followed by 3-phase bone scintigraphy or MRI. If clinically neuropathy is present specific nuclear medicine imaging should be performed.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
27. Kapoor A, Page S, Lavalley M, Gale DR, Felson DT. Magnetic resonance imaging for diagnosing foot osteomyelitis: a meta-analysis. *Arch Intern Med* 2007; 167(2):125-132.	Review/Other-Dx	16 studies	To determine the diagnostic test performance of MRI for osteomyelitis of the foot and compared this performance with that of Tc-99m bone scanning, radiography, and WBC studies.	In all studies combined, the diagnostic odds ratio for MRI was 42.1 (95% CI, 14.8-119.9), and the specificity at a 90% sensitivity cut point was 82.5%. The diagnostic odds ratio did not vary greatly among subsets of studies. In studies in which a direct comparison could be made with other technologies, the diagnostic odds ratio for MRI was consistently better than that for bone scanning (7 studies; 149.9 vs 3.6), radiography (9 studies; 81.5 vs 3.3), and WBC studies (3 studies; 120.3 vs 3.4). MRI performs well in the diagnosis of osteomyelitis of the foot and ankle and can be used to rule in or rule out the diagnosis. MRI performance was markedly superior to that of Tc-99m bone scanning, radiography, and WBC studies.	4
28. 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.	Review/Other-Dx	23 clinical studies	To identify clinical studies on chronic osteomyelitis that evaluated diagnostic imaging modalities.	Pooled sensitivity demonstrated that FDG-PET was the most sensitive technique, with a sensitivity of 96% (95% CI, 88%-99%) Pooled specificity demonstrated that bone scintigraphy had the lowest specificity, with a specificity of 25% (95% CI, 16%-36%) FDG-PET has the highest diagnostic accuracy for confirming or excluding the diagnosis of chronic osteomyelitis. Leukocyte scintigraphy has an appropriate diagnostic accuracy in the peripheral skeleton, but FDG-PET is superior for detecting chronic osteomyelitis in the axial skeleton.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
29. Capriotti G, Chianelli M, Signore A. Nuclear medicine imaging of diabetic foot infection: results of meta-analysis. *Nucl Med Commun* 2006; 27(10):757-764.	Review/Other-Dx	57 papers; 50 original and 7 reviews examining 2,889 lesions	The aim of this study was to develop a practical guideline to describe the radiopharmaceuticals to be used for different clinical conditions and different aims in diabetic foot infection.	Bone scan: a positive test is not diagnostic for osteomyelitis; a negative image excludes infection with a high grade of certainty (good NPV of bone scan). Most nuclear physicians consider the bone scan to be a useful screening test to exclude bone infection. Scintigraphy with radiolabeled WBC plays a key role in the diagnosis of bone infection in the diabetic foot. The mean values of sensitivity, specificity and accuracy in the detection of osteomyelitis of 99mTc- and 111In-WBC scintigraphy reveals that the specificity and diagnostic accuracy of 99mTc-WBC scintigraphy are higher than those of 111In-WBC scintigraphy. Radiolabeled WBC imaging is probably the most accurate test for determining the presence of infection in the mid foot. Although a negative result strongly indicates the absence of osteomyelitis, it is important to note that a positive result requires a complementary study with a marrow agent for confirmation.	4
30. Ertugrul MB, Baktiroglu S, Salman S, et al. The diagnosis of osteomyelitis of the foot in diabetes: microbiological examination vs. magnetic resonance imaging and labelled leucocyte scanning. *Diabet Med* 2006; 23(6):649-653.	Observational-Dx	31 total patients: 28 MRI, 26 Tc-99m WBC+Tc-MDP	To compare the diagnostic values of Tc-labeled leucocyte, MRI and microbiological examination of bone tissue specimens with histopathology, the definitive diagnostic procedure.	Microbiology had a sensitivity of 92% and specificity of 60%. Labeled leucocyte scanning had a sensitivity of 91%, specificity of 67%. MRI a sensitivity of 78%, specificity of 60%. Microbiological: 92% sensitivity, 60% specificity, PPV 92%, NPV 60%. MRI: 78% sensitivity, 60% sensitivity, PPV 90%, NPV 37.5%. Tc-WBC: 91% sensitivity, 67% sensitivity, PPV 95%, NPV 50%. Microbiological examination may be as useful as and less costly than other diagnostic procedures and is the only method which can guide the choice of antibiotic therapy.	3

Suspected Osteomyelitis of the Foot in Patients with Diabetes Mellitus
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
31. Durham JR, Lukens ML, Campanini DS, Wright JG, Smead WL. Impact of magnetic resonance imaging on the management of diabetic foot infections. *Am J Surg* 1991; 162(2):150-153; discussion 153-154.	Review/Other-Dx	18 diabetic patients	Combined retrospective/prospective study to evaluate the value of MRI in diabetic patients with foot infections.	MRI provides a rapid and reliable means of "viewing" the diabetic foot. Unsuspected or poorly localized abscess cavities can be pinpointed for thorough drainage with minimal exploration. An abscess can be differentiated from cellulitis or osteomyelitis. Moreover, persistent fever following drainage of a foot abscess can be reliably evaluated via MRI, obviating the need for empiric surgical reexploration. This exciting noninvasive imaging technique leads to the most accurate surgical drainage of foot abscesses and, at the same time, can prevent unnecessary surgical exploration of the tenuous diabetic foot.	4
32. 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.	Observational-Dx	41 diabetic patients	Prospective study to evaluate the ability of MRI to manage acute diabetic foot infections.	Based on clinical outcome during the acute hospitalization period, operative findings, and/or pathologic confirmation, the PPV of MRI in defining infectious pathology in the foot was 100% in this series of 20 positive scans. The NPV of MRI was 96%. MRI is a diagnostic modality particularly well suited to evaluate acute diabetic foot infections and reliably aids in the management of acute infection to avoid exploration and debridement of uninvolved tissue.	3

Suspected Osteomyelitis of the Foot in Patients with Diabetes Mellitus
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Ledermann HP, Morrison WB, Schweitzer ME, Raikin SM. Tendon involvement in pedal infection: MR analysis of frequency, distribution, and spread of infection. *AJR* 2002; 179(4):939-947.	Observational-Dx	156 consecutive patients; 159 infected feet	To evaluate the frequency, distribution, and extent of tendon involvement in patients with pedal infections.	Of the 129 MRI examinations showing an infection in the forefoot, MRI evidence of tendon involvement in the infection was observed in 56 MRI examinations (43%). Of the 32 MRI examinations showing infection in the hindfoot, 14 examinations (44%) showed evidence of tendon involvement, most frequently of the distal Achilles tendon. MRI evidence of the spread of infection along a tendon was seen in 12 examinations, always with proximal spread of infection; and infection led to the development of an abscess in the central plantar compartment in 3 patients. Intraoperative evidence of a tendon infection was documented in 11 patients. The surgical procedure was altered because of the tendon infection in 6 patients. MRI evidence of tendon infection is present in approximately half the patients who require surgery for pedal infection. Evidence of spread of the infection along tendons is seen infrequently on MRI. Detection of a tendon infection could influence surgical therapy.	3
34. American College of Radiology. *Manual on Contrast Media*. Available at: http://www.acr.org/~/link.aspx?_id=29C40D1FE0EC4E5EAB6861BD213793E5&_z=z	Review/Other-Dx	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

CI = Confidence interval

CT = Computed Tomography

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

LR = Likelihood ratios

MDP = Methylene diophosphate

MRI = Magnetic resonance imaging

NPV = Negative predictive value

PET = Positron emission tomography

PPV = Positive predictive value

SUV = Standardized uptake value

WBC = White blood cell