

Osteomyelitis and Arthritis

Katrin D.M. Stumpe, MD, and Klaus Strobel, MD

Infections of bone and the joints can represent major diagnostic and therapeutic challenges to all clinicians. Together with osteomyelitis and septic arthritis, soft-tissue infections like cellulites/fasciitis and abscess formation can occur, which have to be treated appropriately. Bone scintigraphy is a sensitive method that can be used to search for bone and joint infections. Labeled leukocytes often are used as the gold standard to identify infectious foci in the musculoskeletal system, but major drawbacks of this method are the imaging of chronic infections and imaging of the axial skeleton. Like ^{111}In -labeled leukocyte imaging, $^{99\text{m}}\text{Tc}$ -labeled antigranulocyte antibody scintigraphy has a role in the imaging of osteomyelitis of the peripheral skeleton. Magnetic resonance imaging is widely used to evaluate musculoskeletal infections and is excellent in identifying abscess formation, but the extent and spread of infection is sometimes difficult to delineate because hyperemia and infection are not congruent. *Semin Nucl Med* 39:27-35 © 2009 Elsevier Inc. All rights reserved.

Recent studies indicate that ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET) has considerable value in the diagnosis of inflammatory and infectious disease of the axial and peripheral skeleton. FDG-PET makes use of the fact that there is no physiological FDG accumulation in white cells that are not actively fighting an infection, which permits excellent imaging of the axial skeleton, especially in patients with infection of the spine. PET/computed tomograph (CT) appears to be more accurate for confirming or excluding low-grade infection and chronic osteomyelitis than $^{99\text{m}}\text{Tc}$ bone scintigraphy, $^{99\text{m}}\text{Tc}$ -labeled antigranulocyte antibody scintigraphy, and ^{111}In -labeled leukocyte scintigraphy. Although this usefulness extends to infections associated with metallic implants used for trauma surgery, PET may not be as useful in the diagnosis of infections associated with prosthetic joints. Compared with PET alone, PET/CT offers additional information because it provides precise anatomical information and characterization of the infectious lesion, which is important for surgical planning.

Osteomyelitis

Choosing the appropriate combination of imaging methods in the evaluation of infection may be challenging. A variety of methods is available for imaging inflammation and infection. The role of imaging is to confirm the clinical suspicion, char-

acterize the lesion and its extent, and detect complications such as abscess or fistula formation in infectious disease.

Standard radiography, magnetic resonance imaging (MRI), and CT commonly are used to detect inflammatory and infectious lesions in the bone. Radiographs always should be performed to provide an anatomic overview of the region of interest and to select subsequent imaging modalities. MRI has been used widely because of its excellent soft-tissue contrast and its sensitivity to tissue edema and hyperemia. MRI is valuable in the visualization of septic arthritis, spinal infection, and diabetic foot infections. However, these modalities are of limited value to detect early infection when morphological changes are absent. In addition, diagnostic difficulties always arise when chronic infection is suspected, particularly when there are preexisting alterations in the spine as the result of trauma, surgery, or infection. Artifacts caused by prosthetic joints or metallic implants in the spine or extremities can degrade images sufficiently to make diagnosis impossible in both CT and MRI. Therefore, nuclear medicine procedures are needed as a functional adjunct to complement morphologic imaging techniques.

The choice of the best nuclear medicine procedure depends on the grade of inflammation, duration of infection, availability, cost, and radiation exposure. Commonly used conventional nuclear medicine procedures include 3-phase bone scintigraphy, ^{67}Ga -citrate, ^{111}In - and $^{99\text{m}}\text{Tc}$ -HMPAO-labeled leukocytes, $^{99\text{m}}\text{Tc}$ -radiolabeled murine monoclonal antigranulocyte antibodies and $^{99\text{m}}\text{Tc}$ -radiolabeled nanocolloids and human immunoglobulins.

Three-phase bone scintigraphy is readily available and has a high negative predictive value in undamaged bone. However, it is nonspecific in patients with previously violated

Division of Nuclear Medicine, Department of Medical Radiology, University Hospital, Zurich, Switzerland.

Address reprint requests to Katrin D.M. Stumpe, MD, Division of Nuclear Medicine, Department of Medical Radiology, University Hospital, 8091 Zurich, Switzerland. E-mail: katrin.stumpe@usz.ch

bone, in patients with prosthetic joints, and in the neuropathic joint. Under these circumstances, sequential bone/gallium-67 (^{67}Ga) scintigraphy is used; however, specificities still vary between less than 50% and 100%.¹⁻⁴ The need to perform 2 imaging procedures and delayed imaging are major disadvantages. Gallium-67 imaging alone is useful as an adjunct to MRI in the diagnosis of spinal infection.

Labeled leukocytes and antigranulocyte antibodies are neither sensitive nor specific for infection in the axial skeleton.⁵⁻⁷ The latter imaging techniques have appropriate diagnostic accuracy in the peripheral skeleton; however, differentiation between soft tissue and bone infection is often impossible because of limited spatial resolution (Fig. 1).

Among the various conventional nuclear medicine procedures, the use of ^{111}In -labeled leukocytes is one of the most specific imaging techniques and is useful in acute infections, in osteomyelitis of the diabetic foot, and in the neuropathic joint. In addition, the use of labeled leukocytes, together with complementary bone marrow scintigraphy, is the radionuclide procedure of choice in the assessment of prosthetic joint infection. However, presentation of patients with prosthetic joints and the diabetic foot is complex and discussed in separate articles in this seminar on infectious disease.

The development of single-photon emission computed tomography (SPECT)/computed tomography (CT) cameras partly has overcome the lack of spatial resolution in conventional nuclear medicine by the use image coregistration.⁸

FDG-PET has shown some advantages in contrast to other imaging methods as a result of the so-called “respiratory burst,” which mononuclear cells and neutrophilic granulocytes undergo when activated and while fighting an infection.^{9,10} Infection can be acute or chronic, the former showing predominantly neutrophilic granulocytes infiltrates. In the latter, macrophages join the neutrophils.

In contrast to acute osteomyelitis, low-grade and chronic infections are more difficult to diagnose with the current imaging modalities. In this setting, PET is successfully performed because FDG is avidly taken up by activated macrophages in the chronic phases of infection. FDG-PET has the greatest diagnostic accuracy for confirming or excluding chronic osteomyelitis.¹¹ According to the literature,^{12,13} a negative FDG-PET scan can virtually rule out osteomyelitis.

FDG-PET is superior to labeled leukocyte imaging for the detection of chronic osteomyelitis in the axial skeleton because physiologic FDG uptake in the hematopoietic marrow is relatively low.¹¹ According to a recent meta-analysis by Termaat and coworkers¹¹ FDG-PET is not only the most sensitive examination for the detection of chronic osteomyelitis but also more specific than labeled leukocytes, bone scintigraphy, or MRI in this setting. Because of the high physiological uptake in the hematopoietic bone marrow in labeled leukocyte imaging, sensitivities are as low as 21% to detect chronic osteomyelitis in the axial skeleton.¹¹

Increased FDG accumulation in PET is also associated with inflammatory arthritis, fractures, normally healing bone, and degenerative changes.¹⁴⁻¹⁶ However, in contrast to bone scintigraphy, FDG-PET rapidly normalizes after traumatic or surgical fractures^{14,16} as fibroblasts predominate in normally

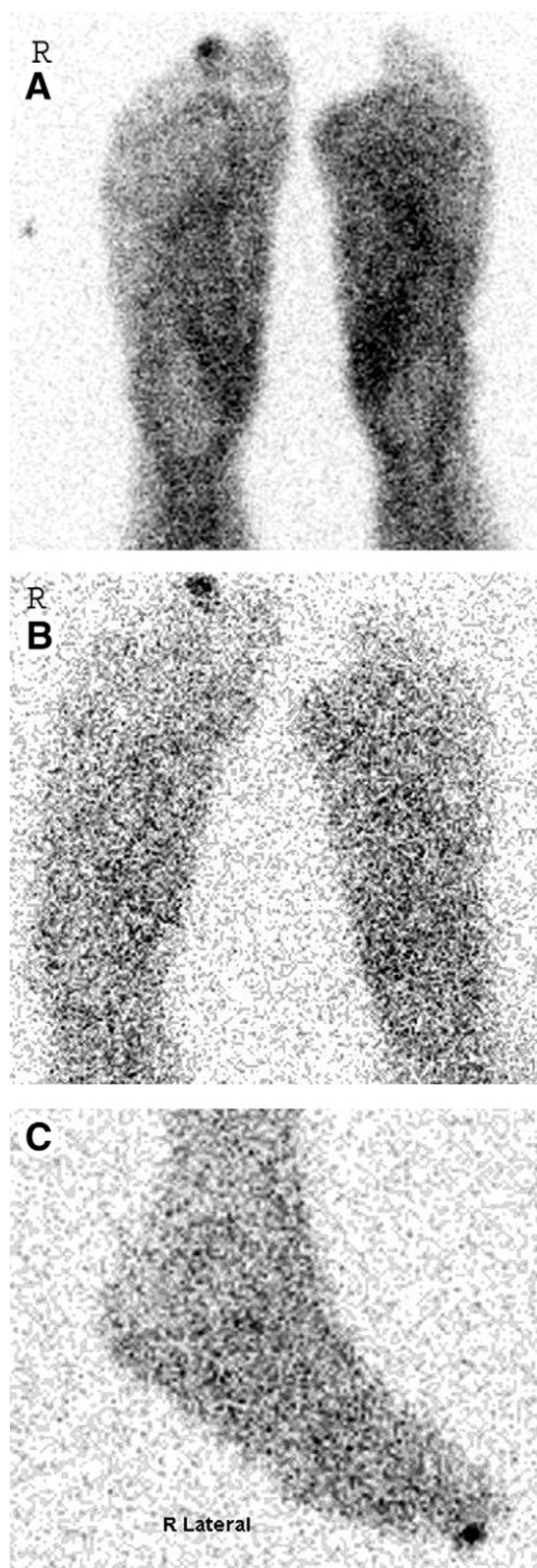


Figure 1 A 72-year old man with peripheral arterial occlusive disease after amputation of the first toe of the foot and with suspicion for osteomyelitis of the second toe of the right foot. $^{99\text{m}}\text{Tc}$ -labeled anti-granulocyte antibody scintigraphy shows focally increased radionuclide uptake of the distal tip of the second toe after 5 hours (A) and 24 hours (B, ventral view; C, right lateral view). Differentiation between soft tissue and bone infection was not possible. After partial amputation of the second toe of the right foot, histopathology confirmed osteomyelitis.

healing bone, and FDG uptake quickly subsides 4 months after surgery.¹⁷ The healing process shows most of the cells that are present in inflammation.¹⁸ Therefore, specificity increases if recently (less than 4 months) traumatized or operated bone is excluded.

Our group reported on FDG-PET in 18 patients with suspected acute and subacute osteomyelitis in the axial and peripheral skeleton and found sensitivities of 100% and specificities in the range of 83% to 99%, respectively.¹⁹ de Winter and coworkers¹³ prospectively studied FDG-PET in 60 patients with chronic osteomyelitis and found sensitivity, specificity, and accuracy of 100%, 86%, and 93%, respectively. In a retrospective study, Källicke and coworkers²⁰ reported on 15 true positive findings in 15 patients with histologically confirmed acute ($n = 7$) and chronic osteomyelitis ($n = 8$).

FDG-PET was superior to ^{99m}Tc-labeled antiglycylglycyl antibody scintigraphy in the evaluation of chronic osteomyelitis involving in the axial skeleton ($n = 15$ of 51).¹² ^{99m}Tc-labeled antiglycylglycyl antibody scintigraphy frequently cannot differentiate between active and inactive processes as the result of nonspecific areas of decreased radionuclide uptake. FDG-PET provides sufficient anatomical information and spatial resolution to distinguish soft tissue from bone infection, despite the presence of metallic implants. In another study by Guhlmann and coworkers,²¹ overall sensitivity and specificity were 100% and 92%, respectively, in the assessment of chronic osteomyelitis in the peripheral ($n = 21$) and axial skeleton ($n = 10$). In the latter study, the use of FDG-PET showed particularly promising results in the detection of chronic osteomyelitis in the axial skeleton, an area in which labeled white cell scanning is of limited value, with an accuracy in the range between 53% and 76%.²²

In a study performed by Zhuang and coworkers,²³ sensitivity, specificity, and accuracy were 100%, 87.5%, and 90.9%, respectively, for FDG-PET in 22 patients with suspected chronic osteomyelitis. Chacko and coworkers²⁴ reviewed the results of 167 FDG-PET scans in patients with the suspicion of various infections. Fifty-six of these 167 patients were suspected of having chronic osteomyelitis, with an accuracy of 91%. In addition, the available data show that the use of FDG-PET is superior to conventional nuclear medicine methods to distinguish between soft tissue and bone infection (Fig. 2).

FDG-PET and FDG-PET/CT have many advantages over conventional nuclear medicine imaging techniques: completion within 1 hour, high sensitivity, high target-to-background contrast, and high-resolution tomographic images. PET/CT with the combination of PET and a low-dose or full-dose diagnostic CT helps in this setting because it provides exact anatomic localization of FDG uptake and increases the specificity compared with PET alone. The logistics of the PET technique make its use easier in chronic than in acute inflammation.

Disc Space Infection

The diagnosis of disc space infection has always been a challenge for the clinician. Conventional radiography is normal within the first 8 weeks before structural changes occur. The

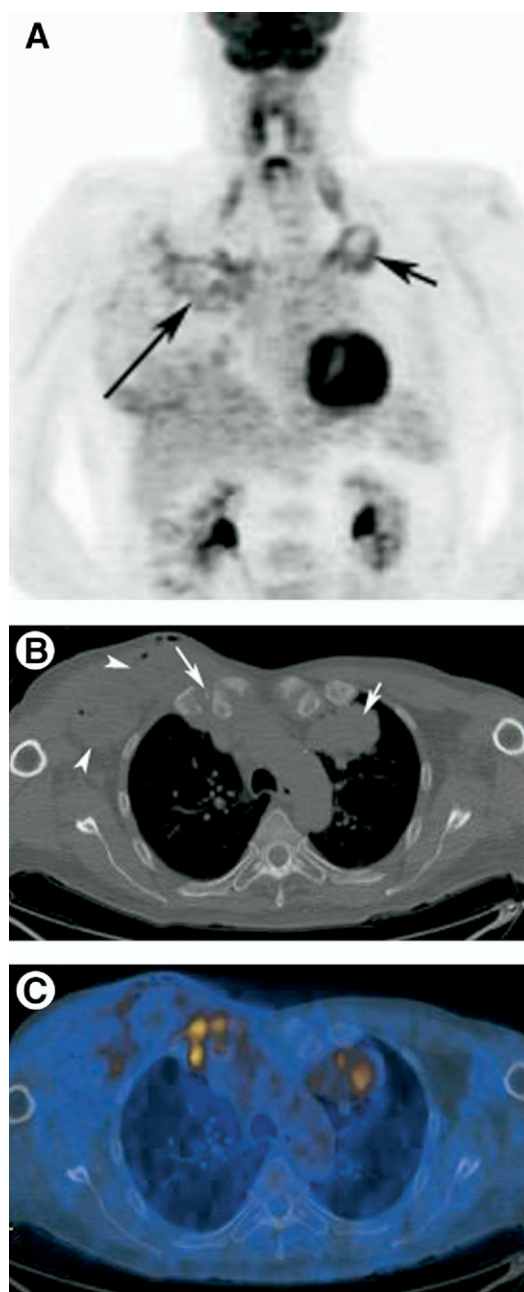


Figure 2 A 75-year-old man with adenocarcinoma of the left upper lobe. In addition, the patient presented with an abscess in the right thoracic wall. (A) Maximum intensity projection (MIP) demonstrates circular increased FDG uptake in the left upper lung (short arrow) as well as diffuse FDG uptake in the right upper hemithorax (long arrow). Physiological FDG uptake is seen in the scaleni muscles as well as in the larynx. (B) Axial CT scan demonstrates the lung tumor in the right upper lobe (short arrow) and a tumorous lesion subpectoral (arrowheads) in the right thoracic wall with air and involvement of the right sterno-clavicular joint (long arrow). (C) Axial PET/CT scan shows increased FDG uptake in the bronchial carcinoma in the left upper lobe. In addition, circular increased FDG uptake is found in the tumorous lesion in the right hemithorax representing the abscess as well as focally increased FDG uptake of the right sterno-clavicular joint and the adjacent bones with osseous destruction. In addition, the right sternocostal joint was involved. In contrast to PET or CT imaging alone, coregistered PET/CT helps to diagnose soft tissue infection and additional infectious involvement of the adjacent bones.

diagnostic imaging technique of choice is contrast-enhanced MRI with an accuracy of approximately 90%, which provides early diagnosis of disc space infection.^{25,26} In addition to bone marrow abnormalities, epidural, subdural, intramedullary, and paraspinal soft-tissue changes are signs for spinal infection that can be clearly delineated in contrast-enhanced MRI. However, differentiation between degenerative (so-called Modic abnormalities) and infectious disc disease can be difficult because of potentially similar abnormalities.

Three-phase bone scintigraphy is of limited value in the differentiation of degenerative from infectious end plate abnormalities. It showed an overall accuracy of only 67% and cannot be recommended in the clinical routine.²⁷ Modic and coworkers²⁵ described a sensitivity and specificity of 90% and 78% for bone scintigraphy and 96% and 92% for MRI, respectively. Bone scintigraphy, together with ⁶⁷Ga SPECT, is the radionuclide imaging method of choice so far for diagnosing spinal osteomyelitis. Love and coworkers⁴ reported that ⁶⁷Ga scintigraphy was more sensitive than bone scintigraphy and, when performed as SPECT, was comparable with sequential bone-gallium scintigraphy with sensitivities of 91% and specificities of 77%, respectively.

In contrast to bone scintigraphy, ⁶⁷Ga scintigraphy can more easily identify local extension of spinal infection (eg, soft-tissue infection). In addition, ⁶⁷Ga is more useful in monitoring treatment response as it reflects more accurately the

degree of activity of infective processes.²⁸ ¹¹¹In-labeled leukocytes have a limited value in the diagnosis of spinal infection because of photopenic defects, which are nonspecific as several noninfectious conditions (eg, tumors and infarction) tend to show photopenia.^{29,30} Although most of the published series are small, FDG-PET appears to be superior in the evaluation of spinal osteomyelitis with higher sensitivities and specificities compared with ⁶⁷Ga-citrate imaging.³¹⁻³³ In a study performed by Gratz and coworkers³³ in which they used a coincidence camera, they found that FDG-PET was superior to MRI and gallium imaging in patients with suspected disc space infection. Schmitz and coworkers³² reported that FDG-PET is sensitive in the detection of disc space infection and additional paravertebral soft-tissue involvement. Twelve of 16 patients had a histopathologically confirmed disc space infection.

According to our results, the use of FDG-PET appears to be useful for excluding disc space infection in equivocal MR cases. In the latter PET study, we included 30 symptomatic patients with substantial end-plate abnormalities of the lumbar spine in MRI.³¹ FDG-PET did not show uptake in the intervertebral spaces of any patient with degenerative disease, whereas infectious end plate abnormalities were always positive (Fig. 3). The sensitivity and specificity for MRI in detecting disc space infection were 50% and 96%, and for FDG-PET 100% and 100%, respectively.

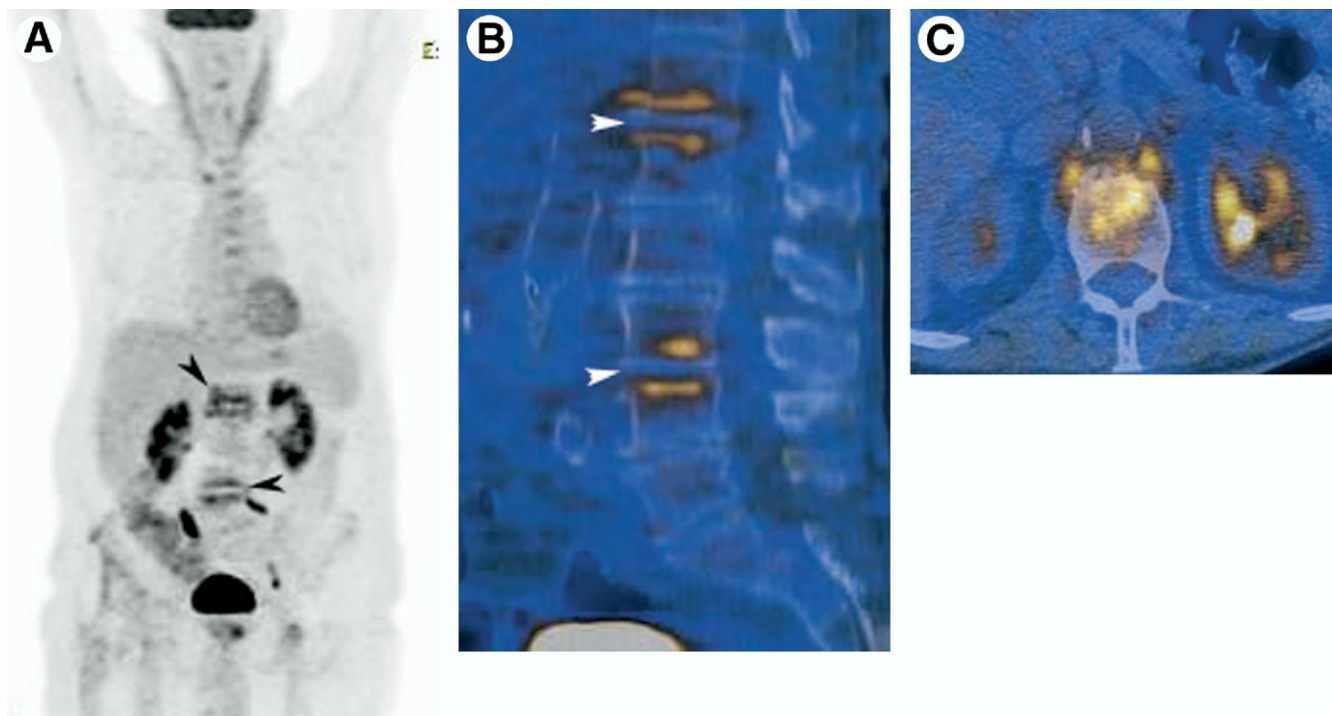


Figure 3 A 72-year-old man with fever of unknown origin. (A) MIP shows linear increased FDG uptake in the upper and lower lumbar spine (black arrowheads). (B) Sagittal PET/CT image shows FDG uptake in the endplates of the vertebral bodies L1-L2 and L4-L5 (white arrowheads). (C) On axial PET/CT scan, additional increased FDG accumulation in the soft tissues ventrally to L1-L2 is seen. Disc space infection at L1-L2 and L4-L5 intervertebral disc level was confirmed.

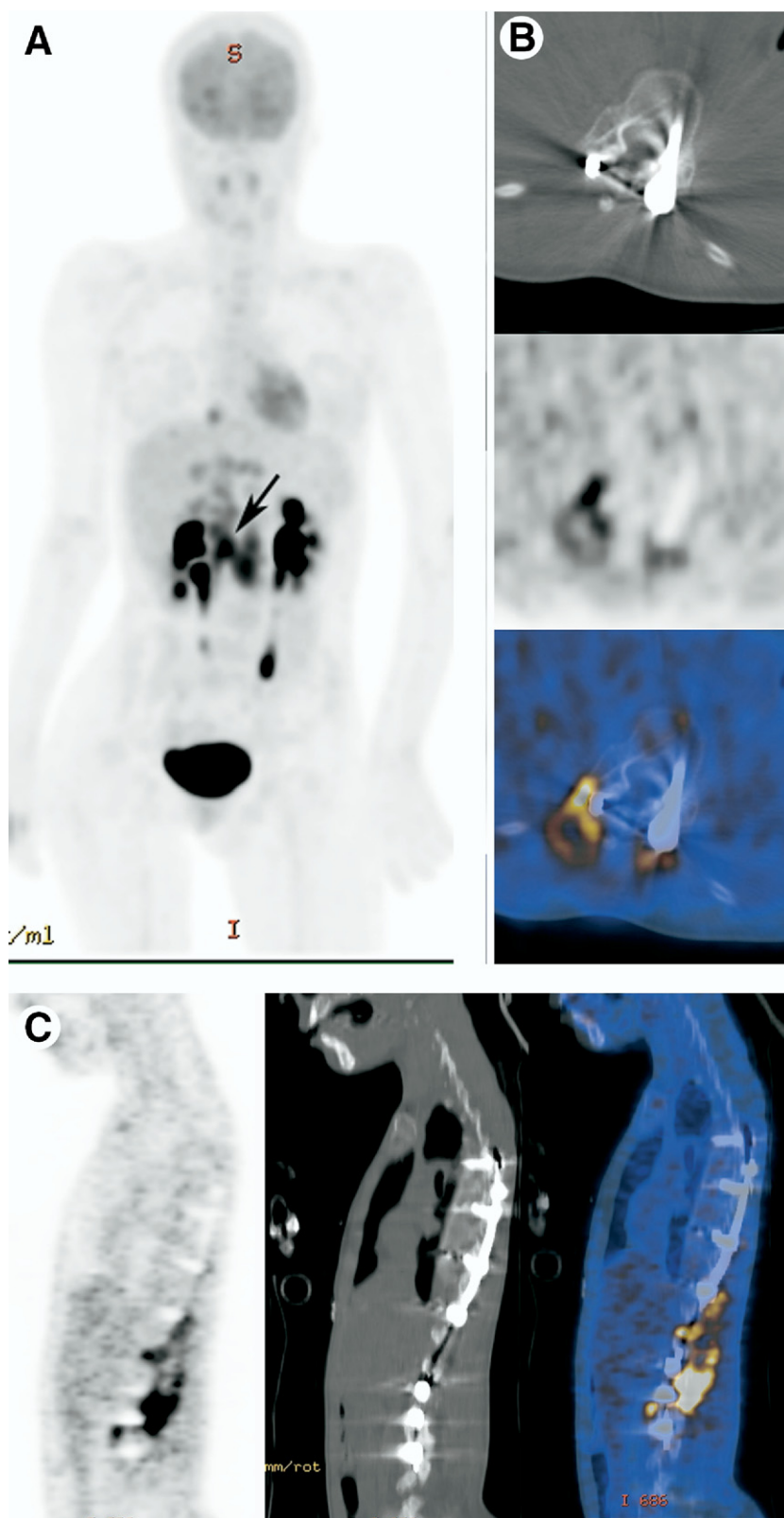


Figure 4 A 19-year-old woman with pain and increased inflammatory blood parameters 18 months after lumbar spine stabilization surgery because of severe scoliosis. (A) MIP shows increased FDG accumulation in the lower thoracic and upper lumbar spine (black arrow). Axial (B) and sagittal (C) FDG-PET/CT show increased FDG uptake around the screws and the adjacent muscles of the spine. Infection of the soft tissues and metallic device was confirmed intraoperatively and the metallic device was removed.

Metallic Implant-Associated Infections in Trauma Patients (Except Prosthetic Joints)

Standard radiography in trauma patients may demonstrate nonunion, sequestered bone, intraosseous abscess formation, and bone resorption at implant–bone interfaces in in-

fection. Standard radiography is not useful, however, for the diagnosis of early or low-grade infection. The use of MRI demonstrates abnormalities of bone marrow and soft tissue if not hampered by artifacts caused by metallic implants. However, healing and infected tissue may be impossible to differ-

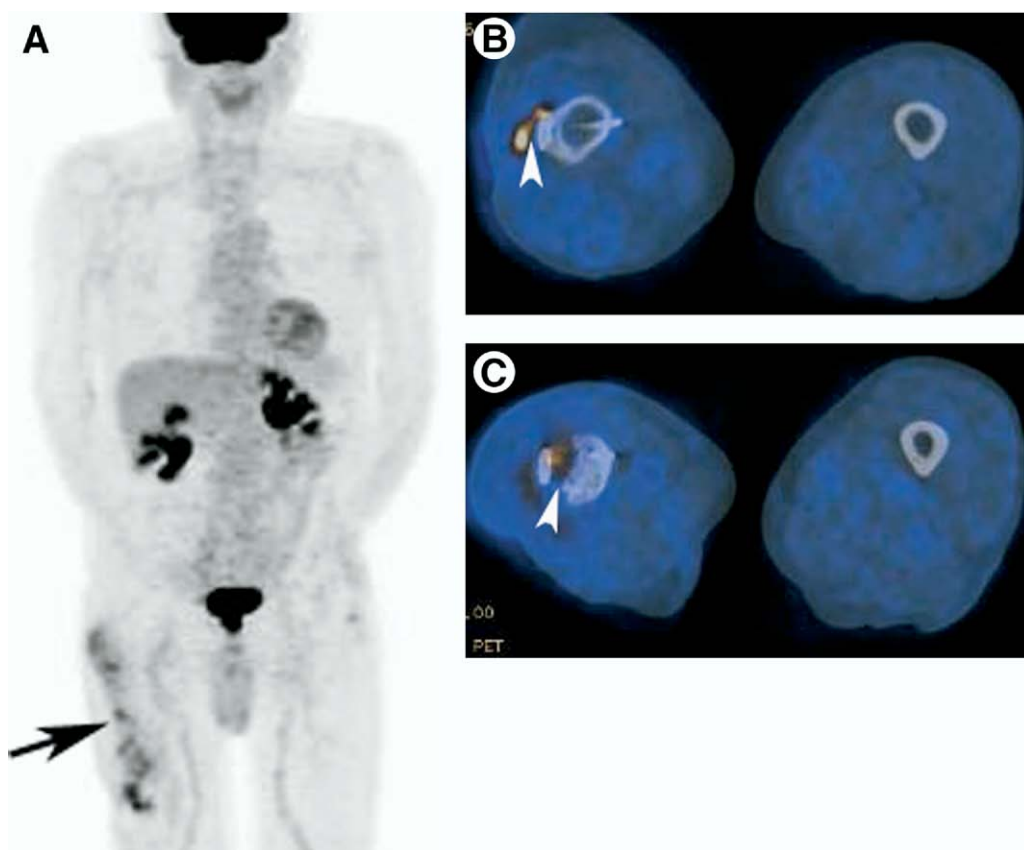


Figure 5 A 72-year-old man with suspicion for metallic implant associated infection of the right femur is shown. The patient had a history of chronic osteomyelitis in the past as the result of undergoing surgery for liposarcoma of the right thigh. (A) MIP shows increased FDG uptake around the metallic implant in the right lateral femur (black arrow). Axial PET/CT demonstrates focally increased FDG along the metallic material and the adjacent femur (B and C, white arrows). Diagnosis of an infected metallic implant with osteomyelitis was established.

entiate. This is also true for ultrasound, the use of which is also limited to bone surfaces and soft tissue. CT more precisely demonstrates fragments and sequestration than standard radiography but is inferior to MRI in soft tissue and bone marrow assessment. In conventional nuclear medicine, 3-phase bone scintigraphy is used for the initial evaluation for osteomyelitis, but the findings are affected by previous surgery and trauma and often are not specific. The limitations of spatial resolution are a relevant problem. Specificity increases if combined bone and gallium scanning is used.

In the last decade, the use of ^{111}In -labeled leukocytes combined with $^{99\text{m}}\text{Tc}$ bone marrow scintigraphy has been shown to be highly accurate for the diagnosis of various musculoskeletal infections, which could alter distribution of bone marrow with sensitivities and specificities of 100% and 94%, respectively.³⁴

Labeled leukocyte scintigraphy combined with bone marrow scintigraphy is the conventional radionuclide procedure of choice for diagnosing complicating osteomyelitis like in trauma patients with metallic implants. FDG-PET represents a promising imaging technique in the diagnosis of implant-associated infections the imaging of in trauma patients and has shown to be both sensitive and specific.^{13,35} Conventional radionuclide methods are often first-line imaging procedures in the diagnosis of implant-associated infections in patients with trauma. However, nonspecific tissue uptake of imaging agents and imaging over several days restrict their usefulness. Unlike MRI and CT, FDG-PET images are not substantially affected by metallic implants inserted for fixing fractures, in

contradistinction to PET imaging in prosthetic joint devices. This is most likely attributable to the more slender materials (eg, titanium) and methods (eg, external fixation) used in trauma patients (Figs. 4 and 5). Patients with prosthetic joint devices show artifacts because of the relatively high photon absorption of the prosthesis.^{35,36}

FDG-PET demonstrates a sensitivity of nearly 100% and a specificity in the range of 88-93% in the diagnosis of chronic musculoskeletal infections, including patients with and without metallic implants or prosthetic replacements.^{13,21,35} de Winter and coworkers¹³ evaluated the use of FDG-PET in the diagnosis of chronic musculoskeletal infections in 34 patients with metallic implants. Seventeen patients demonstrated infections around metallic implants used in trauma surgery. Infectious lesions in the peripheral, as well as in the axial skeleton, were correctly identified with the use of FDG-PET, in contrast to the results of 17 patients with suspected periprosthetic infections.

Similar results were found by Guhlmann and coworkers,²¹ who examined 6 patients with suspected metallic implant-associated infection in a group of 31 patients with suspected chronic osteomyelitis. The only false-positive finding was a patient with a soft-tissue infection, which in PET was localized to bone because of missing anatomic landmarks. In a study performed by Kälücke and coworkers,²⁰ FDG-PET was true positive in all cases. FDG-PET was not affected by metal-like implants used for fixation of fractures. Moreover, Kälücke and coworkers²⁰ demonstrated that FDG uptake at the sites

of fractures and nonunions is significantly lower than it is at the sites of infections, thereby facilitating differentiation.

The results of our own data showed a sensitivity of 100%, a specificity of 93%, and an accuracy of 97% when FDG-PET is used in the diagnosis of metallic implant-associated chronic infections in 22 patients (29 scans) with a previous history of trauma.³⁵ One false-positive finding was detected in the soft tissue of a patient six weeks after surgery and no false-negative findings were observed. In addition, the surgeons assessed the influence of FDG-PET on their treatment decisions. FDG-PET influenced the clinical decision-making process in almost two-thirds of the patients. FDG-PET could accurately differentiate between bone and soft-tissue infection.

One of the largest studies was prospectively performed by de Winter and coworkers.³⁷ The latter group investigated FDG-PET in 57 patients (n = 27 with metallic implants) with suspected infection after previous spinal surgery. The median interval between surgery and FDG-PET examination was 10 months (range 1.25-288 months). Infection was detected in 10 of 27 patients with and in 5 of 30 patients without metallic implants in the spine. Sensitivity, specificity, and accuracy were 100%, 81%, and 86%, respectively. In approximately 60% of patients, infection could be ruled out with FDG-PET. Although specificity of FDG-PET was not greater than 81%, comparable results are not obtained with bone scintigraphy, labeled leukocytes, or MRI in the postoperative spine.³⁸

In a recent study performed by our own group, we evaluated the diagnostic value of FDG-PET/CT in trauma patients with suspected chronic osteomyelitis and found promising results (Fig. 6).³⁹ Among 33 PET/CT scans, 17 were true positive, 13 true negative, 2 false positive, and 1 false negative. Sensitivity, specificity, and accuracy for FDG-PET/CT was 94%, 87%, and 91% for the whole group; 88%, 100%, and 90% for the axial skeleton; and 100%, 85%, and 91% for the peripheral skeleton, respectively. Our data showed 2 false-positive (both in the peripheral skeleton) and one false-negative finding (in the axial skeleton). Summarizing the results of these studies, FDG-PET is superior for detecting chronic osteomyelitis in the axial skeleton in contrast to labeled leukocyte imaging.¹¹ PET/CT allowed precise localization of the infectious focus and demonstrated the extent of chronic osteomyelitis with a high degree of accuracy.

Septic Arthritis

Bacterial arthritis may be caused by penetrating trauma or through ulcers such as those occurring in diabetes. Direct implantation of infectious agents also may occur after injections or surgery. Hematogenous routes of infection occur, especially in immunocompromised patients. Although bone scintigraphy is used widely in imaging non-infectious arthritis in rheumatologic patients, radionuclide imaging has a limited role in the management of septic arthritis because ultrasound and joint fluid aspiration with microbiologic workup are easy to perform and available everywhere. Radionuclide imaging can be useful in the differentiation of septic arthritis from osteomyelitis

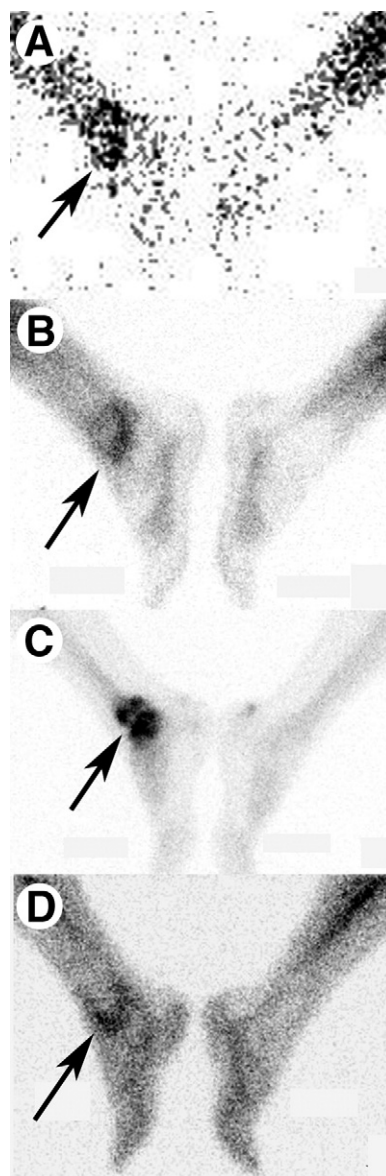


Figure 6 A 57-year-old man a year after implantation of a prosthetic ankle joint on the right side is shown. Perfusion (A), blood pool (B), and osseous phase (C) of bone scintigraphy show markedly increased activity around the right ankle joint. Additionally ^{99m}Tc -labeled antigranulocyte antibody scintigraphy (D) was performed, again showing increased uptake in the right ankle joint. Diagnosis of septic arthritis of the right prosthetic ankle joint was confirmed intraoperatively.

and soft tissue infection as well as in the detection of multifocal joint infections.

The appearance of septic arthritis in 3-phase bone scintigraphy with ^{99m}Tc -diphosphonates is characteristic: because of hyperemia in synovial vessels, all 3 phases (the perfusion, blood pool, and osseous phase) show increased radionuclide uptake.⁴⁰⁻⁴² Normal or even decreased radiotracer uptake can occur in cases of arthritis if the blood flow is compromised by high intracapsular pressure. Majd and Frankel⁴³ found increased uptake in 6 of 7 children and decreased uptake in 1 of 7 children with proven septic arthritis. Bone scintigraphy is

more sensitive than standard radiography in the diagnosis of arthritis because radionuclide uptake precedes morphological bone changes.^{41,44} If the bone scan is negative but the clinical impression is still suspicious for septic arthritis, the specificity of bone scans can be improved by the additional performance of ⁶⁷Ga, labeled leukocytes, or monoclonal antibody studies (Fig. 6). However, the need to use multiple radionuclide tracers and to perform imaging at multiple times adds complexity, delays the start of treatment, and causes inconvenience to the patients. SPECT and SPECT/CT are useful supplements to planar scintigraphy, especially in equivocal cases and in the differentiation of soft tissue and bone infection as demonstrated in a patient with osteomyelitis.^{8,45} SPECT/CT also should be considered in patients with arthritis in complex body regions like the spine.^{46,47}

MRI with intravenous contrast administration reliably demonstrates the abnormalities associated with septic arthritis, including joint effusion, synovial hyperemia, and proliferation. In addition, reactive bone marrow and soft-tissue edema, secondary osteomyelitis, tendon abnormalities, and soft-tissue abscesses are found.⁴⁸ Although MRI might be superior in monoarticular infections, the advantage of bone scintigraphy over MRI is that a bone scan is a whole-body imaging technique and covers all involved joints in one investigation. Thus, in infections involving multiple joints, radionuclide studies should be performed.

The role of FDG-PET/CT in the workup of septic arthritis has not been defined yet. According to our experience, FDG-PET/CT is particularly useful in clinically difficult cases in which the advantage of PET as a relatively fast, whole-body imaging modality plays an important role, as demonstrated in Fig. 7. Compared with bone scintigraphy, FDG-PET/CT also can be used to discover infectious foci outside the bone in the lung or other organs. Dumarey and coworkers showed promising initial results using ¹⁸F-FDG-labeled leukocytes for infection imaging and reported 1 case of septic knee arthritis among the 23 patients included.⁴⁹ Cost effectiveness of advanced and expensive imaging modalities like SPECT/CT or PET/CT have not been investigated, and further studies are needed to define the role of nuclear medicine in septic arthritis compared with morphologic imaging like ultrasound and MRI.

Conclusion

Bone scintigraphy, ⁶⁷Ga, and labeled leukocytes are the conventional nuclear medicine imaging techniques of choice for imaging musculoskeletal infection. At the present time, FDG-PET has an incremental value over other imaging modalities and appears to be more sensitive and specific in the detection of various infectious diseases. In the diagnosis of osseous infection, FDG-PET has a major impact in patients with chronic osteomyelitis. Particularly in the axial skeleton, FDG-PET is an important imaging technique in the diagnosis and exclusion of chronic osteomyelitis, showing superior accuracy to other radionuclide imaging modalities. Moreover, FDG-PET plays an



Figure 7 A 48-year-old woman with bacteremia and septic polyarthritis. *Staphylococcus aureus* was found in the left ankle joint. FDG-PET/CT was performed for screening of the involved joints. MIP shows multiple joints (left shoulder, right sternoclavicular joint, left wrist, both knees and ankles, arrows) with increased FDG uptake.

important role in the differentiation between disc space infection and erosive degenerative disc disease, where both MRI and bone scan may be falsely positive. FDG-PET may replace other imaging modalities in the assessment of metallic implant-associated infection in trauma patients (excluding prosthetic joints). Differentiation between osteomyelitis and soft-tissue infection may be better obtained with the use of FDG-PET than with CT or MRI, because of better lesion-to-background contrast and the scarcity of artifacts arising from metallic implants used in trauma surgery compared with CT and MRI. FDG-PET/CT permits more precise delineation and characterization of the infectious focus and helps to improve the management of patients with various infectious diseases.

References

- Rosenthal L, Lisbona R, Hernandez M, et al: 99mTc-PP and 67Ga imaging following insertion of orthopedic devices. *Radiology* 133:717-721, 1979
- Schauwecker DS, Park HM, Mock BH, et al: Evaluation of complicating osteomyelitis with Tc-99m MDP, In-111 granulocytes, and Ga-67 citrate. *J Nucl Med* 25:849-853, 1984
- Schauwecker DS: The scintigraphic diagnosis of osteomyelitis. *AJR Am J Roentgenol* 158:9-18, 1992
- Palestro CJ, Torres MA: Radionuclide imaging in orthopedic infections. *Semin Nucl Med* 27:334-345, 1997
- Chung JK, Yeo J, Lee DS, et al: Bone marrow scintigraphy using technetium-99m-antigranulocyte antibody in hematologic disorders. *J Nucl Med* 37:978-982, 1996
- Jacobson AF, Gilles CP, Cerqueira MD: Photopenic defects in marrow-containing skeleton on indium-111 leucocyte scintigraphy: Prevalence at sites suspected of osteomyelitis and as an incidental finding. *Eur J Nucl Med* 19:858-864, 1992
- Gratz S, Braun HG, Behr TM, et al: Photopenia in chronic vertebral osteomyelitis with technetium-99m-antigranulocyte antibody (BW 250/183). *J Nucl Med* 38:211-216, 1997
- Horger M, Eschmann SM, Pfannenber C, et al: The value of SPET/CT in chronic osteomyelitis. *Eur J Nucl Med Mol Imaging* 30:1665-1673, 2003
- Babior BM: The respiratory burst of phagocytes. *J Clin Invest* 73:599-601, 1984
- Kaim AH, Weber B, Kurrer MO, et al: Autoradiographic quantification of 18F-FDG uptake in experimental soft-tissue abscesses in rats. *Radiology* 223:446-451, 2002
- Termaat MF, Raijmakers PG, Scholten HJ, et al: The accuracy of diagnostic imaging for the assessment of chronic osteomyelitis: a systematic review and meta-analysis. *J Bone Joint Surg Am* 87:2464-2471, 2005
- Guhlmann A, Brecht-Krauss D, Suger G, et al: Fluorine-18-FDG PET and technetium-99m antigranulocyte antibody scintigraphy in chronic osteomyelitis. *J Nucl Med* 39:2145-2152, 1998
- de Winter F, van de Wiele C, Vogelaers D, et al: Fluorine-18 fluorodeoxyglucose-positron emission tomography: A highly accurate imaging modality for the diagnosis of chronic musculoskeletal infections. *J Bone Joint Surg Am* 83-A:651-660, 2001
- Meyer M, Gast T, Raja S, et al: Increased F-18 FDG accumulation in an acute fracture. *Clin Nucl Med* 19:13-14, 1994
- von Schulthess GK, Meier N, Stumpe KD: Joint accumulations of FDG in whole body PET scans. *Nuklearmedizin* 40:193-197, 2001
- Zhuang H, Sam JW, Chacko TK, et al: Rapid normalization of osseous FDG uptake following traumatic or surgical fractures. *Eur J Nucl Med Mol Imaging* 30:1096-1103, 2003
- Kaim AH, Gross T, von Schulthess GK: Imaging of chronic posttraumatic osteomyelitis. *Eur Radiol* 12:1193-1202, 2002
- Henry G, Garner WL: Inflammatory mediators in wound healing. *Surg Clin North Am* 83:483-507, 2003
- Stumpe KD, Dazzi H, Schaffner A, et al: Infection imaging using whole-body FDG-PET. *Eur J Nucl Med* 27:822-832, 2000
- Kálicke T, Schmitz A, Risse JH, et al: Fluorine-18 fluorodeoxyglucose PET in infectious bone diseases: Results of histologically confirmed cases. *Eur J Nucl Med* 27:524-528, 2000
- Guhlmann A, Brecht-Krauss D, Suger G, et al: Chronic osteomyelitis: Detection with FDG PET and correlation with histopathologic findings. *Radiology* 206:749-754, 1998
- Palestro CJ, Kim CK, Swyer AJ, et al: Radionuclide diagnosis of vertebral osteomyelitis: Indium-111-leukocyte and technetium-99m-methylene diphosphonate bone scintigraphy. *J Nucl Med* 32:1861-1865, 1991
- Zhuang H, Duarte PS, Pourdehand M, et al: Exclusion of chronic osteomyelitis with F-18 fluorodeoxyglucose positron emission tomographic imaging. *Clin Nucl Med* 25:281-284, 2000
- Chacko TK, Zhuang H, Nakhoda KZ, et al: Applications of fluorodeoxyglucose positron emission tomography in the diagnosis of infection. *Nucl Med Commun* 24:615-624, 2003
- Modic MT, Feiglin DH, Piraino DW, et al: Vertebral osteomyelitis: Assessment using MR. *Radiology* 157:157-166, 1985
- Meyers SP, Wiener SN: Diagnosis of hematogenous pyogenic vertebral osteomyelitis by magnetic resonance imaging. *Arch Intern Med* 151:683-687, 1991
- Love C, Patel M, Lonner BS, et al: Diagnosing spinal osteomyelitis: a comparison of bone and Ga-67 scintigraphy and magnetic resonance imaging. *Clin Nucl Med* 25:963-977, 2000
- Tyrrell PN, Cassar-Pullicino VN, McCall IW: Spinal infection. *Eur Radiol* 9:1066-1077, 1999
- Gemmel F, Dumarey N, Palestro CJ: Radionuclide imaging of spinal infections. *Eur J Nucl Med Mol Imaging* 33:1226-1237, 2006
- Whalen JL, Brown ML, McLeod R, et al: Limitations of indium leukocyte imaging for the diagnosis of spine infections. *Spine* 16:193-197, 1991
- Stumpe KD, Zanetti M, Weishaupt D, et al: FDG positron emission tomography for differentiation of degenerative and infectious endplate abnormalities in the lumbar spine detected on MR imaging. *AJR Am J Roentgenol* 179:1151-1157, 2002
- Schmitz A, Risse JH, Grunwald F, et al: Fluorine-18 fluorodeoxyglucose positron emission tomography findings in spondylodiscitis: preliminary results. *Eur Spine J* 10:534-539, 2001
- Gratz S, Dorner J, Fischer U, et al: 18F-FDG hybrid PET in patients with suspected spondylitis. *Eur J Nucl Med Mol Imaging* 29:516-524, 2002
- Palestro CJ, Roumanas P, Swyer AJ, et al: Diagnosis of musculoskeletal infection using combined In-111 labeled leukocyte and Tc-99m SC marrow imaging. *Clin Nucl Med* 17:269-273, 1992
- Schiesser M, Stumpe KD, Trentz O, et al: Detection of metallic implant-associated infections with FDG PET in patients with trauma: correlation with microbiologic results. *Radiology* 226:391-398, 2003
- Stumpe KD, Notzli HP, Zanetti M, et al: FDG PET for differentiation of infection and aseptic loosening in total hip replacements: Comparison with conventional radiography and three-phase bone scintigraphy. *Radiology* 231:333-341, 2004
- De Winter F, Gemmel F, Van De Wiele C, et al: 18-Fluorine fluorodeoxyglucose positron emission tomography for the diagnosis of infection in the postoperative spine. *Spine* 28:1314-1319, 2003
- Rothman SL: The diagnosis of infections of the spine by modern imaging techniques. *Orthop Clin North Am* 27:15-31, 1996
- Hartmann A, Eid K, Dora C, et al: Diagnostic value of (18)F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis. *Eur J Nucl Med Mol Imaging* 2006.
- Rosenthal L, Kloiber R, Damte B, et al: Sequential use of radiophosphate and radiogallium imaging in the differential diagnosis of bone, joint and soft tissue infection: quantitative analysis. *Diagn Imaging* 51:249-258, 1982
- Gilday DL, Paul DJ, Paterson J: Diagnosis of osteomyelitis in children by combined blood pool and bone imaging. *Radiology* 117:331-335, 1975
- Maurer AH, Chen DC, Camargo EE, et al: Utility of three-phase skeletal scintigraphy in suspected osteomyelitis: Concise communication. *J Nucl Med* 22:941-949, 1981
- Majd M, Frankel RS: Radionuclide imaging in skeletal inflammatory and ischemic disease in children. *AJR Am J Roentgenol* 126:832-841, 1976
- Gilday DL: Problems in the scintigraphic detection of osteomyelitis. *Radiology* 135:791, 1980
- Filippi L, Schillaci O: Usefulness of hybrid SPECT/CT in 99mTc-HMPAO-labeled leukocyte scintigraphy for bone and joint infections. *J Nucl Med* 47:1908-1913, 2006
- Michel-Batot C, Dintinger H, Blum A, et al: A particular form of septic arthritis: Septic arthritis of facet joint. *Joint Bone Spine* 75:78-83, 2008
- Swayne LC, Dorsky S, Caruana V, et al: Septic arthritis of a lumbar facet joint: Detection with bone SPECT imaging. *J Nucl Med* 30:1408-1411, 1989
- Learch TJ, Farooki S: Magnetic resonance imaging of septic arthritis. *Clin Imaging* 24:236-242, 2000
- Dumarey N, Egrise D, Blocklet D, et al: Imaging infection with 18F-FDG-labeled leukocyte PET/CT: Initial experience in 21 patients. *J Nucl Med* 47:625-632, 2006