FDG uptake in 76% of 20 patients with proven temporal arthritis or polyarthritis. Thrombosis arteritis had a positive predictive value of 93% and a negative predictive value of 80%. Miller et al. compared FDG-PET with MRI in 13 patients with vasculitis and found that the radiologic study detected most sites of involvement than MRI and was more effective in the diagnosis and follow-up of patients with arthritis.

Endocarditis. The clinical value of the radiologic diagnosis of infective endocarditis has never been established. A recent pilot study suggests, however, that FDG-PET accurately postoperative changes, and aseptic loosening from infection of a prosthetic joint, it is likely that for FDG, optical sensitivity, and inflammation, perhaps even becoming the major role of FDG-PET in some of these conditions.

To complete this CME activity free of charge, please go to the accredited provider website www.mhgroup.com/study for post testing and Reader Evaluation.

L E A R N I N G  O B J E C T I V E S

1. Describe uptake mechanisms of FDG in infection and inflammation.
2. Name at least two indications for infection/inflammation imaging in which FDG may replace current agents.
3. Explain why it may be difficult, using FDG-PET, to distinguish the infected from the aseptically loosened joint replacement.
4. Describe the potential role of FDG-PET in this patient with vasculitis.

Nuclear medicine plays an important role in the evaluation of infection and inflammation. Fluorodeoxyglucose positron emission tomography (FDG-PET) is an imaging modality that for infection and inflammation has attracted considerable interest, perhaps even becoming the modality of choice in some of these conditions.

FDG-PET for differentiation of infection and aseptic loosening. (Reproduced with permission10)

Figure 1. Increased periprosthetic FDG activity at the bone-prosthesis interface along the lateral aspect of the femoral component of an infected left hip prosthesis (left). Similar uptake is present along the lateral margin of an aseptically loosened right hip prosthesis (right). Bone-prooactivity on FDG imaging, once thought to be specific for infection, is probably related to osteolysis, which is present in both infection and aseptic loosening. (Reproduced with permission).

One copy of this article provided by CME LLC may be printed by the individual participant in connection with acquiring CME credit. No other reproduction or distribution of the article without the written consent of CME LLC.

Imaging Infection and Inflammation with F-18 FDG-PET

Christopher J. Palestro, M.D.

©2005 CMP HEALTHCARE MEDIA • © 2006 CME LLC. ALL RIGHTS RESERVED. THIS ARTICLE MAY NOT BE REPRODUCED IN ANY MEDIA OR DISTRIBUTED WITHOUT THE WRITTEN CONSENT OF CME LLC.
**NODOSAL INFECTIOUS ARTHRITIS**

FDG-PET shows promise in several nosocomial conditions.  
- Acquired immunodeficiency syndrome (AIDS)  
- Patients with AIDS are subject to a variety of opportunistic infections and sarcoidosis, and gallium imaging is often performed to evaluate these patients. FDG-PET also appears to accurately localize foci of infection, as well as tumors, in this patient group. It is very important to recognize that, outside of the central nervous system, it is not possible to distinguish infection from tumor with FDG. In the CNS, however, FDG-PET is a useful tool in the management of cryptococcal meningitis.

**Aldrich et al** studied FDG-PET in 58 cases of FEO and found that FDG-PET was useful in 41% of patients. In a subgroup of 40 patients who also underwent gallium imaging, FDG-PET was helpful in 35% of the cases, while gallium was helpful in 25% of the cases. These investigations concluded that FDG-PET could replace scintigraphy as a test for the evaluation of patients with FEO. Meller et al** reported that FDG-PET was 84% sensitive and 80% specific for the detection of FEO and the FDG was superior to gallium imaging. Wreeker-Rover et al** evaluated 35 patients with FEO and found that combined FDG-PET studies were clinically helpful in 37% of the cases. The test was 93% sensitive and 90% specific and had a negative predictive value of 95%.

Only about half of all FUOs are caused by infection or tumor. Vasculitis, rheumatoid arthritis, sarcoidosis, and chronic granulomatous disease, all of which can be the source of an FUO, are associated with increased FDG uptake.

In the patient with FUO, FDG-PET identifies the organ or tissue likely to be the source of the fever, thereby guiding additional tests that may be needed. A negative FDG-PET makes it very unlikely that a malignant or metabolic condition is present.

- **Focal infection:** Patients with suspected focal infection often present with a discrete abnormality detected, but not characterized with morphologic tests. This population includes patients suspected of having a postoperative infection or those who have a history of recent surgery. The radiologist is used to help differentiate infection from postoperative changes that may be difficult to distinguish. Scans have found that in patients suspected of having focal infection, FDG-PET demonstrates sensitivity and specificity comparable to the morphologic tests. FDG-PET is particularly useful in differentiating infection from tumor that is obvious. Persistent uptake of FDG in uninfected surgical scars is usually associated with inflammation. Patients with FUO and no localizing signs demonstrate a hypermetabolic focus in mediastinum (arrow), corresponding to CT-identified lymphadenopathy. Biopsy confirmed mediastinal mycosis (Figure 1). The success of labeled leukocyte imaging is encouraging, extensive investigations focused on neurologic dysfunction are needed to define its role in musculoskeletal infection.

**MUSCULOSKELETAL INFECTION**

In otherwise normal bone, three-phase bone scintigraphy is both sensitive and specific for osteomyelitis. Bone scintigraphy is less useful in patients with previously traumatized bone and in the presence of orthopedic hardware or the neuropathic joint infection. Combined FDG-PET/MRI is effective in these patients. The use of multiple tracers and the need to image at multiple times increases the expense and complexity of the tests and increases additional burdens on patients, who are often elderly and debilitated. FDG has generated considerable interest as an alternative to technetium-99m, and recent reports suggest that it may be useful for diagnosing osteomyelitis. FDG uptake by normal cortical bone is quite low, whereas the bone marrow is variable.

In osteomyelitis, activated inflammatory cells, such as neutrophils, lymphocytes, and macrophages, are metastatic active cells with large amounts of glucose and, hence, FDG. Unfortunately, increased uptake of FDG is also associated with inflammatory arthritis, acute fractures, and normally healing bone. Since FDG accumulates in the bone marrow, increased marrow uptake may also be related to localized hypercellular marrow.

While reports about the value of FDG-PET for diagnosing osteomyelitis in general are encouraging, extensive investigations focused on specific indications are needed to define its role in musculoskeletal infection.

- **Prosthetic joint infection.** Nearly 500,000 lower extremity joint replacements are performed annually in the U.S. While many compilations of joint replacement surgery can be easily and accurately diagnosed and promptly remedied, differentiating infection from the most common cause of joint prosthesis failure—aseptic loosening—is a more challenging task. These entities are remarkably similar, both clinically and histopathologically. Aseptic loosening is often caused by an immune reaction to the prosthetic components. Histocytosis, granulomatous reaction of bone, and plasma cells accompany the inflammation. The secretion of proinflammatory cytokines and proinflammatory cytokines leads to inflammation. Enzymes are present in joint fluid. In the mid- and haptoglobin, the most commonly encountered components in aseptic loosening, are aseptically present in joint fluid. Differentiating infection from aseptic loosening is crucial because both procedures have a similar clinical appearance. Persistent leukocyte/gallium scintigraphy is the radionuclide procedure of choice for determining whether the joint infection is infected.

FDG imaging is helpful in circumventing some of the problems associated with bone scintigraphy, but it does require at least a small maligization focus in mediastinum, corresponding to CT-identified lymphadenopathy. Biopsy confirmed mediastinal mycosis (Figure 1). The success of labeled leukocyte imaging is encouraging, extensive investigations focused on neurologic dysfunction are needed to define its role in musculoskeletal infection.

- **Painful lower extremity joint prostheses has been investigated extensively. Although initial reports suggested that FDG-PET could accurately identify the infected joint, many recent studies are less encouraging. They suggest that the test cannot accurately differentiate aseptic loosening from true infection (Figure 3). To minimize FDG uptake in normal tissues, fluorodeoxyglucose (FDG) is often injected intravenously 30- to 60-minutes before tracer FDG injection reduces uptake in FDG-avid striated muscle and FDG, and it may also result in decreased uptake of FDG by the target cells, which is in the setting of infection would be activated leuko
cytos. Successful FDG imaging of infection in diabetic patients is likely to be more complicat
ted than in the general population. At the present time, scant, if any, data are available about the role of FDG-PET in the evaluation of foot complications in diabetes.

- **Sternal osteomyelitis.** MR is the imaging modality of choice for diagnosing sternal osteomyelitis. It is sensitive to motion degra
dation, however, and patients with movement dis
turbances may not be suitable candidates for imag
ing. Certain metallic implants are contraindica
tions to the study, and MRI cannot always dis
tinguish osteomyelitis from severe degenerative arthropathy. Nuclear medicine provides important information in these patients. The radionuclide study of choice for diagnosing sternal osteo
yelitis is gallium imaging, with or without bone scintigraphy. Regardless of whether galli
um imaging is used alone or in combination with bone scintigraphy, the imaging quality is less
than desirable, the study is time-consuming, and the patient must make multiple visits to the nuclear medicine department. Almost all of the cases reported to date are small, FDG-PET appears to be useful for diagnosing sternal osteomyelitis, with accuracy comparable to that of gallium imaging (Figure 2).
Imaging infection and inflammation with F-18 FDG-PET.

**FREE CATEGORY 1 CME CREDIT** • TEST CODE #419 / Imaging Infection and Inflammation with F-18 FDG-PET

used in these situations. The use of multiple tracers and the need to image at multiple times automatically be attributed to infection or tumor.

In otherwise normal bone, three-phase bone scintigraphy is both sensitive and specific for infection likely reflects increased glucose utilization by the body’s immune system. Increased splenic activity in infection is also associated with inflammatory arthritis, fevers, and no localizing signs. Chest x-ray was reported as showing an abscess. (Reproduced with permission)

FDG uptake by normal cortical bone is quite low, and patients often have large quantities of glucose and hence, FDG. Unfortunately, increased uptake of FDG is also associated with inflammatory arthritis, acute fractures, and normally healing bone.

Since FDG accumulates in the bone marrow, increased marrow uptake also may be related to localized hyperemia.

While reports about the value of FDG-PET for diagnosing osteomyelitis in general are encouraging, extensive investigations focused on specific indications are needed to define its role in managing patients with orthopedic hardware. Nearly 500,000 lower extremity joint replacements for its use must be developed.

In otherwise normal bone, three-phase bone scintigraphy is both sensitive and specific for diagnosing osteomyelitis, with accuracy comparable to that of In-111-labeled leukocytes. The radionuclide study of the central nervous system, it is not possible to distinguish infection from tumor with FDG. In the CNS, however, FDG-PET is very sensitive early in the course of an illness, while toxoplasmosis is not.

The standardized uptake values of toplasmosis are significantly lower than those of lymphoma, with virtually no overlap of the uptake values between these two groups.

The radionuclide study of the radionuclide study of choice for diagnosing spinal osteomyelitis. It is sensitive to motion degrada-
tion, however, and patients with movement disorders may not be suitable candidates for imaging.

FDG images are acquired by circulating glucose and insulin levels, as FDG and glucose compete for transporters. Elevated glucose lev-

FDG-PET reliably differentiates osteomyelitis from other inflammatory conditions, including patients suspected of having a postoperative infection or those who have a history of prosthetic joint infection.

FDG-PET was helpful in 35% of a subgroup of 40 patients who also underwent gallium imaging. FDG-PET was helpful in 35% of the cases, while gallium was helpful in 25%.

These investigations concluded that FDG-PET could replace scintigraphy as a test for the evaluation of patients with FUO. Miller et al. reported that FDG-PET was 84% sensitive and 86% specific for diagnosing osteomyelitis, and the FDG-PET was superior to gallium imaging.

Keefer et al. reviewed 35 patients with FUO and found that FDG-PET studies were clinically helpful in 37% of the cases. The test was 93% sensitive and 95% specific and had a negative predictive value of 95%.

Only about half of all FUOs are caused by infection or tumor. Vasculitis, rheumatoid arthritis, cancer, and chronic granulomatous disease, all of which can be the source of an FUO, are associated with increased uptake of FDG.

In the patient with FUO, FDG-PET identifies the organ or tissue likely to be the source of the fever, thereby guiding additional tests. The negative predictive value is equally important. A negative FDG-PET makes it very unlikely that a specific organ or tissue will be found.

The radionuclide study of choice for diagnosing spinal osteomyelitis is the radionuclide study of choice for diagnosing spinal osteomyelitis. It is sensitive to motion degrada-
tion, however, and patients with movement disorders may not be suitable candidates for imaging.

FDG imaging is used to guide bone marrow aspiration and autologous leukocytes, but it is considerably less specific. False-positive results were associated with tumor and postoperative changes.

**Immunological conditions:** Sarcoidosis is a chronic inflammatory condition of unknown etiology. Asymptomatic disease is the most common presentation. FDG-PET is the gold standard for diagnosing osseous and soft tissue malignancies.

FDG-PET shows promise in several nonosseous conditions:

- Acquired immunodeficiency syndrome.

**FDG uptake by normal cortical bone is quite low, and patients often have large quantities of glucose and hence, FDG. Unfortunately, increased uptake of FDG is also associated with inflammatory arthritis, acute fractures, and normally healing bone.**

Since FDG accumulates in the bone marrow, increased marrow uptake also may be related to localized hyperemia.

While reports about the value of FDG-PET for diagnosing osteomyelitis in general are encouraging, extensive investigations focused on specific indications are needed to define its role in managing patients with orthopedic hardware. Nearly 500,000 lower extremity joint replacements for its use must be developed.

In otherwise normal bone, three-phase bone scintigraphy is both sensitive and specific for diagnosing osteomyelitis, with accuracy comparable to that of In-111-labeled leukocytes. The radionuclide study of the central nervous system, it is not possible to distinguish infection from tumor with FDG. In the CNS, however, FDG-PET is very sensitive early in the course of an illness, while toxoplasmosis is not.

The standardized uptake values of toplasmosis are significantly lower than those of lymphoma, with virtually no overlap of the uptake values between these two groups.

The radionuclide study of choice for diagnosing spinal osteomyelitis is the radionuclide study of choice for diagnosing spinal osteomyelitis. It is sensitive to motion degrada-
tion, however, and patients with movement disorders may not be suitable candidates for imaging.

FDG-PET imaging performed on a 60-year-old woman with history of renal cell carcinoma, persistent fevers, and no localizing signs demonstrated a hypermetabolic right kidney, consistent with hydronephrosis, corresponding to CT-identified left nephrolithiasis. Renal scans confirmed bilateral renal stones.

The role of FDG-PET in the evaluation of painless elevated serum alkaline phosphatase and the need for further investigation is uncertain. Persistent uptake of FDG in uninfected surgical margins is diagnostic of infection. Persistent uptake of FDG in uninfected surgical margins is diagnostic of infection. Persistent uptake of FDG in uninfected surgical margins is diagnostic of infection.
FDG uptake in 76% of 25 patients with proven temporal arthritis or polyarthritis rheumatics. Thrombo-aryctyuria had a positive predictive value of 93% and a negative predictive value of 80%. Melzer et al. compared FDG PET with MRI in 15 patients with vasculitis and found that the radiologic study detected more sites of involvement than MRI and was more effective in the diagnosis and follow-up of patients with arthritis.

Endocarditis. The clinical value of the radiologic diagnosis of infective endocarditis has never been established. A recent pilot study suggests, however, that FDG-PET accurately postulates infective endocarditis and may become a useful adjunct to echocardiography (Figure 5).

CONCLUSION

Despite the fact that few data are available on its role in infection and inflammation imaging, PET/CT will undoubtedly be useful, especially for evaluating the musculoskeletal system when it is not always possible to use radiolabeled imaging alone, to determine whether infection involves bone, soft tissue, or both (Figure 6). PET/CT is likely to have a major impact on the workup of patients with fever of unknown origin. These patients undergo numerous anatomic and functional imaging tests, and PET/CT has the potential to greatly reduce the number of tests performed. While a negative study may suggest that it is unlikely that a morphologic complication exists, a positive study obtained, and intervention undertaken, can be concordantly during the same imaging session.

Although its role is still evolving, PET/CT is a promising modality in the diagnosis of infection and inflammation. While this technique will probably be of limited utility for differentiating infection from tumor and in monitoring response to therapy, it is likely that for FUDG, optical spectroscopy, and inflammatory processes, such as vasculitis and sepsis, FDG-PET will become increasing important, perhaps even becoming the procedure of choice in some or all of these entities.

UPTAKE MECHANISMS

NUCLEAR MEDICINE

Uptake mechanisms of F-18 FDG in infection and inflammation

1. Describe uptake mechanisms of F-18 FDG in infection and inflammation.
2. Name at least two indicators for infection/inflammation imaging in which F-18 FDG may replace current agents.
3. Explain why it may be difficult, using F-18 FDG, to distinguish the infected from the aseptically loosened joint replacement.
4. Describe the potential role of FDG-PET in this patient with vasculitis.

NUCLEAR MEDICINE

Infection and Inflammation with F-18 FDG-PET

Christopher J. Palestro, M.D.