EANM/SNMMI Guideline for ^{18}F-FDG Use in Inflammation and Infection*

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PREAMBLE

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is an international scientific and professional organization founded in 1954 to promote the science, technology and practical application of nuclear medicine. Its 16,000 members are physicians, technologists, and scientists specializing in the research and practice of nuclear medicine. In addition to publishing journals, newsletters, and books, the SNMMI also sponsors international meetings and workshops designed to increase the competencies of nuclear medicine practitioners and to promote new advances in the science of nuclear medicine. The European Association of Nuclear Medicine (EANM) is a professional nonprofit medical association that facilitates communication worldwide between individuals pursuing clinical and research excellence in nuclear medicine. The EANM was founded in 1985.

The SNMMI/EANM will periodically define new guidelines for nuclear medicine practice to help advance the science of nuclear medicine and to improve the quality of service to patients. Existing practice guidelines will be reviewed for revision or renewal as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice guideline, representing a policy statement by the SNMMI/EANM, has undergone a thorough consensus process in which it has been subjected to extensive review. The SNMMI/EANM recognizes that the safe and effective use of diagnostic nuclear medicine imaging requires specific training, skills, and techniques, as described in each document.

The EANM and SNMMI have written and approved these guidelines to promote the use of nuclear medicine procedures with high quality. These guidelines are intended to assist practitioners in providing appropriate nuclear medicine care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the SNMMI/EANM cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by medical professionals taking into account the unique circumstances of each case. Thus, there is no implication that an approach differing from the guidelines, standing alone, is below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of the guidelines.

The practice of medicine involves not only the science but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to these guidelines will not ensure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

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I. INTRODUCTION

^{18}F-fluorodeoxyglucose (^{18}F-2-fluoro-2-deoxyglucose or FDG) positron emission tomography (PET) and PET/CT are noninvasive diagnostic imaging procedures providing tomographic images for the determination of localized metabolic activity. Fluorine-18 (^{18}F) is a cyclotron-produced radioisotope with a half-life of 109.7 min that undergoes positron decay. ^{18}F-FDG is an analog of glucose and is taken up by living cells via cell membrane glucose transporters and subsequently phosphorylated with hexokinase inside most cells. ^{18}F-FDG has been proposed for imaging infection/inflammation in part because it has been seen at sites of infection/inflammation during routine ^{18}F-FDG imaging of cancer patients. Further studies showed that cells involved in infection and inflammation, especially neutrophils and the monocyte/macrophage family, are able to express high levels of glucose transporters, especially GLUT1 and GLUT3, and hexokinase activity (*1–5*). From limited experimental studies, it seems that the ability of the procedure to identify sites of inflammation and infection is related to the glycolytic activity of the cells involved in the inflammatory response. Many types of cells are involved in this process although no single cell was found specifically and consistently involved in all models. In addition, enhanced glucose consumption and subsequent ^{18}F-FDG uptake can also be the result of a stress reaction of the affected cells in response to cell damage (metabolic flare) (*6*).

II. GOALS

The aim of this guideline is to provide general information about performing ^{18}F-FDG PET or PET/CT in inflammation and infection. We provide evidence for efficacy where it is available, but the use of ^{18}F-FDG imaging in inflammation and infection is rapidly evolving and these guidelines cannot be seen as definitive. Therefore, the indications mentioned within this guideline should be regarded as current advice and areas for clinical research rather than as fully approved clinical indications. Despite the limited literature available on the use of ^{18}F-FDG imaging in these indications, it is clear that the use of metabolic imaging using ^{18}F-FDG, together with morphologic imaging, that is, PET/CT or fusion of PET and CT data (further referred to as ^{18}F-FDG imaging), is becoming the scintigraphic method of choice. It can be expected that after further validation, PET/CT may become a first-line tool in these nononcologic indications.

This guideline complements the EANM and SNMMI guidelines for the use of ^{18}F-FDG PET for tumor imaging (*7,8*) and, to avoid duplication, will not reproduce any statements that overlap. These include information concerning PET or PET/CT camera performance and quality control, general acquisition parameters, radiopharmaceutical acceptance, and general basic and clinical aspects of ^{18}F-FDG imaging that may apply to both tumor and infection/inflammation imaging. The present guideline aims to provide the user with basic knowledge of and competence in the use of ^{18}F-FDG imaging in the field of inflammatory and infectious disorders.

III. DEFINITIONS

This section is not applicable.

IV. COMMON CLINICAL INDICATIONS

No appropriateness criteria have been developed to date for this procedure. The development of ^{18}F-FDG in this field is rapidly evolving, especially since the emergence of PET/CT. Table 1 summarizes the indications that have been reported in the literature with various success rates. The list is based on an evaluation of scientific peer-reviewed publications (at least with an abstract in English allowing the evaluation of the study) from 1994 to December 2011. Only original publications with more than 10 patients and with the possibility of calculating the diagnostic sensitivity, specificity, and accuracy were taken into consideration.

Although there is still insufficient literature for this to be described as an evidence-based indication, we can conclude, on the basis of a cumulated reported accuracy (>85%) and expert opinion that major indications for ^{18}F-FDG PET/CT in infection and inflammation are as follows:

- Sarcoidosis (*9–15*).
- Peripheral bone osteomyelitis (nonpostoperative, non–diabetic foot) (*16–23*).
- Suspected spinal infection (spondylodiskitis or vertebral osteomyelitis, nonpostoperative) (*24–28*).

TABLE 1
Published Studies with More Than 10 Patients Before December 2011

Disease	Considered papers	Sensitivity	Specificity	Accuracy	References
Sarcoidosis	7 (173 patients)	93.5% (7 papers)	Data not available	95.5% (1 papers)	*9–15*
Osteomyelitis	8 (287 patients)	94.6% (8 papers)	91.5% (8 papers)	94.5% (6 papers)	*16–23*
Spondylodiskitis	5 (136 patients)	100.0% (5 papers)	89.3% (5 papers)	91.0% (4 papers)	*24–28*
FUO	15 (758 patients)	90.6% (15 papers)	76.9% (15 papers)	86.4% (10 papers)	*29–44*
Vasculitides	12 (283 patients)	80.4% (12 papers)	89.3% (12 papers)	85.0% (3 papers)	*45–56*
Diabetic foot	5 (220 patients)	70.6% (5 papers)	84.4% (5 papers)	80.0% (5 papers)	*88–92*
Prosthesis (knee + hip)	17 (770 patients)	95.0% (17 papers)	98.0% (17 papers)	78.0% (8 papers)	*93–109*
Vascular grafts	5 (189 patients)	88.9% (5 papers)	64.6% (4 papers)	74.5% (4 papers)	*110–114*

- Evaluation of fever of unknown origin (FUO) (*29–44*), including true FUO (defined according to the criteria of Durack and Street (*44*)), postoperative fever and recurrent sepsis, immunodeficiency (both induced and acquired)-related FUO, neutropenic fever, and isolated acute-phase inflammation markers (persistently raised C-reactive protein and/or erythrocyte sedimentation rate).
- Evaluation of metastatic infection and of high-risk patients with bacteremia (*32*).
- Primary evaluation of vasculitides (e.g., giant cell arteritis) (*45–56*).

Other well-described applications, but without sufficient evidence-based indication, include the following:

- Evaluation of potentially infected liver and kidney cysts in polycystic disease (*56–63*).
- Suspected infection of intravascular devices, pacemakers, and catheters (*64–71*).
- AIDS-associated opportunistic infections, associated tumors, and Castleman disease (*72–83*).
- Assessment of metabolic activity in tuberculosis lesions (*84–87*).

Considering the available published data, it is unclear if ^{18}F-FDG imaging offers any significant advantage over radiolabeled white blood cells or antigranulocyte monoclonal antibodies in the following situations:

- Diabetic foot infections (*88–92*).
- Joint prosthetic infections (*93–109*).
- Vascular prosthetic infections (*110–114*).
- Inflammatory bowel diseases (*115,116*).
- Endocarditis (*117–119*).

It must be emphasized that large prospective studies comparing different nuclear medicine procedures are often lacking. Nevertheless, the level of evidence available at this time for many of these indications remains insufficient to strongly advise the use of ^{18}F-FDG imaging as a first-line diagnostic tool. The level of evidence is at best at Cochrane grade B, especially for true FUO, spinal infection, and vasculitis. The level of evidence is lower (Cochrane C or D) for other indications. It must be kept in mind that the choice between ^{18}F-FDG imaging and an alternative technique may depend on the need for rapid diagnosis and local availability of equipment and labeled agents. For example, some specific indications such as the evaluation of vascular prostheses and the diabetic foot absolutely require the use of hybrid PET/CT for precise anatomic localization of the ^{18}F-FDG uptake.

V. REGULATORY ISSUES

There is consistent progress in the field, with regular new literature and registration of ^{18}F-FDG for several indications by the European Medicines Agency. In the United States ^{18}F-FDG is not approved by the Food and Drug Administration for indications other than oncology, cardiology, and epilepsy (*120*).

VI. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

In the United States, see the SNMMI Guideline for General Imaging and the SNMMI Guideline for Tumor Imaging with ^{18}F-FDG PET/CT (*8*). In Europe, the certified nuclear medicine physician who performed the study and signed the report is responsible for the procedure, according to national laws and rules.

VII. PROCEDURE/SPECIFICATIONS OF THE EXAMINATION

A. Request

The request for the examination should include sufficient medical information to demonstrate medical necessity and should include the diagnosis, pertinent history, and questions to be answered. The medical record should be reviewed. Relevant laboratory tests should be considered. When available, the results of prior imaging studies should be reviewed, including plain-film radiography, CT, MRI, bone scanning, and ^{18}F-FDG PET/CT. Relevant prior studies should be directly compared with current imaging findings when possible.

B. Patient preparation and precautions

The major goals of preparation are to minimize tracer uptake in normal tissues, such as the myocardium, skeletal muscle, and urinary tract, while maintaining uptake in target tissues.

1. Pregnancy (suspected or confirmed)

   In the case of a diagnostic procedure in a patient who is known or suspected to be pregnant, a clinical decision is necessary to consider the benefits against the possible harm of performing any procedure. The International Committee for Radiation Protection (ICRP) reports that the administration of 259 MBq (7 mCi) of ^{18}F-FDG results in an absorbed radiation dose of 4.7 mGy to the nongravid uterus (i.e., 1.8×10^{-2} mGy/MBq) (*121*). Direct measurements of ^{18}F-FDG uptake in a case study suggested higher doses to the fetus than currently provided in standard models (*122*). A pregnancy test may help with the decision, provided the 10-d postovulation blackout is understood. In case of doubt and in the absence of any emergency, the 10-d rule should be adopted.

2. Breastfeeding

   The ICRP does not recommend interruption of breast feeding after ^{18}F-FDG administration since little ^{18}F-FDG is excreted in the milk (*121*). However, the suggestion may be made that contact between mother and child be limited for 12 h after injection of ^{18}F-FDG to reduce the radiation dose that the infant receives from external exposure from the mother. It is recommended that the infant be breastfed just before injection, to maximize the time between the injection and the next feeding.

3. Diabetes and serum glucose level before ^{18}F-FDG administration

   It has been advocated that high serum glucose levels may interfere with the targeting of inflammatory and infectious sites because of competitive inhibition of ^{18}F-FDG uptake by D-glucose. After sporadic reports of patients with glucose levels higher than 2 g/L (10 mmol/L) who were studied successfully, it has recently been demonstrated (in a series including 123 patients with suspected infection) that neither diabetes nor hyperglycemia at the time of the study had any significant impact on the false-negative rate in this clinical scenario (*123*). This is different from tumor imaging, especially of pancreatic and lung cancers, for which reduced ^{18}F-FDG uptake has been observed at 1.4 g/L (8 mmol/L) (*124*). Although efforts should be made to decrease blood glucose to the lowest possible level, if the study is normally indicated in those with unstable ("brittle") or poorly controlled diabetes (often associated with infection), hyperglycemia should not represent an absolute contraindication for performing the study. Therefore we recommend the same advice and suggest registering blood glucose level and any other information that could be relevant for scan interpretation.
4. Kidney failure

   ^{18}F-FDG imaging can be performed in patients with kidney failure, although the image quality may be suboptimal and prone to interpretation pitfalls (*125*).
5. Instructions to patients

   The technologist, nurse, or physician should give the patient a thorough explanation of the test. Patients must fast (although intake of noncaloric beverages, such as water or coffee, is allowed) for at least 4 h before ^{18}F-FDG imaging, during which time they should be encouraged to drink sufficient water to ensure hydration and promote diuresis (*7*). In specific situations (e.g., endocarditis), a longer fast is recommended to optimize the reduction of myocardial uptake.

   Necessary medications are allowed and must be recorded. Ideally, the scan may be scheduled 3–4 h after breakfast in diabetic patients who have received their insulin early in the morning (e.g., 7:00 AM). Diabetic patients should take their medications early in the morning, and the ^{18}F-FDG imaging should be scheduled for late morning. Detailed instructions can be found in the EANM guidelines for tumor imaging. It is strongly advised that commencement of steroid treatment be avoided between the request date for the study and the appointment. The use of steroid treatment could result in a false-negative result, especially in giant cell arteritis and other systemic vasculitides (*126*). Because the effect of antibiotics on ^{18}F-FDG uptake is unknown, it is important to be aware of ongoing antibiotic treatment, but no general recommendation on withdrawal can be stated.

   The patient should be advised to avoid strenuous physical exercise within 24 h before injection. Patients should void before being positioned on the PET/CT table.
6. Preinjection clinical evaluation by the nuclear medicine physician

   ^{18}F-FDG imaging recently showed high performance in critically ill patients with suspected infection (*41*). The management of such patients is, however, time consuming and technically challenging, requiring high-level multidisciplinary skills. If ^{18}F-FDG imaging is scheduled in such a patient, issues concerning logistics, nursing care, and medical care should be anticipated and reviewed carefully.

   The nuclear medicine physician should have available and take into account all information that could facilitate the interpretation of ^{18}F-FDG imaging (CT, MRI, and other previously performed diagnostic imaging, including any previous PET study). In particular, the following parameters should be checked:

   - Fasting state (except in some diabetics who received insulin, see "Instructions to Patients: Medications").
   - History of diabetes.
   - Patient weight and height (weight should be measured in very ill patients if feasible and if standardized uptake values [SUVs], are needed).
   - Fever or elevation of acute inflammatory markers such as erythrocyte sedimentation rate or C-reactive protein.
   - Trauma, recent surgery, or recent invasive diagnostic procedures (at least within the last 4 wk).
   - History of a neoplastic disorder, recent chemotherapy (many patients with previously known cancer or under treatment for cancer may be candidates for ^{18}F-FDG imaging for nonmalignant indications), or radiation therapy (at least within the last 3 mo); bone marrow, spleen, and gastrointestinal biodistribution of ^{18}F-FDG may vary.
   - Presence of a known infectious or inflammatory condition or immunosuppressive status.
   - Pathophysiologic disturbances and symptoms, such as diarrhea and localized pain, especially in the extremities (e.g., knee, for appropriate choice of field of view).
   - Presence of benign disease with high tissue proliferation.
   - Pregnancy or suspected pregnancy, breastfeeding, and date of the last menses.
   - Blood glucose level.
7. Patient relaxation.

   Before ^{18}F-FDG administration, the patient should relax in a waiting room to minimize muscular activity and thereby physiologic uptake of ^{18}F-FDG in muscles. The waiting room should be at an adequate temperature (20°C–22°C), and drafts should be prevented in order to reduce uptake in brown fat. In selected cases, prevention of brown fat uptake may be enhanced by the use of β-blocking agents. Hyperventilation may cause uptake in the diaphragm, and stress-induced tension may result in increased ^{18}F-FDG uptake in the trapezius and paraspinal muscles. Some authors have proposed administration of benzodiazepines to obtain muscle relaxation: this should be restricted to very active patients and those in whom evaluation of the neck is essential. If benzodiazepines are given, it is wise to ensure first that the patient will not drive or undertake activity that requires the patient to be alert after the procedure. Patients should avoid talking or chewing immediately before and after ^{18}F-FDG administration to minimize ^{18}F-FDG uptake in laryngeal and masticatory muscles.

Some of the measures mentioned above may be superfluous for small-field-of-view acquisitions, such as a limited acquisition for the evaluation of a localized infection.

C. Radiopharmaceutical

1. ^{18}F-FDG administered activity in Europe

   The injected activity of ^{18}F-FDG to obtain good imaging with a PET scanner operated in 3-dimensional mode is in the range of 2.5–5.0 MBq/kg, that is, 175–350 MBq or 4.7–9.5 mCi in a 70-kg standard adult, although the required dose may depend on the imaging device and the acquisition time used (*6*). Activities should be reduced for infants and children according to the EANM pediatric dosage card issued in 2008 (*127,128*) (www.eanm.org/docs/dosagecard.pdf). Higher injected activities may be required in overweight and obese patients. National limits may be less than these figures, in which case the relevant national limit should be applied. ^{18}F-FDG should be administered intravenously, using a minimum 21-gauge indwelling catheter (or Abbott butterfly) to ensure good venous access.

2. ^{18}F-FDG administered activity in the United States

   The ^{18}F-FDG administered activity should be 370–740 MBq (10–20 mCi) for adults and 3.7–5.2 MBq/kg (0.10–0.14 mCi/kg) for children. Administered activity for children should be based on body weight and should be as low as reasonably achievable for diagnostic imaging. For more specific guidance on pediatric dosing, please refer to "Pediatric Radiopharmaceutical Administered Doses: 2010 North American Consensus Guidelines" (*129*).

   When feasible, the radiopharmaceutical should be injected intravenously at a site contralateral to sites of known or suspected disease. With PET/CT, the radiation dose to the patient is the combination of the dose from the PET radiopharmaceutical and the dose from the CT portion of the study. Lower administered activities, however, may be appropriate with advancements in PET/CT technology.

3. Uptake period after injection

   After administration of ^{18}F-FDG, the patient should remain quiet until the start of image acquisition and void the urinary bladder as often as possible to limit radiation to the urinary tract. A minimum 60-min interval between ^{18}F-FDG injection and acquisition is recommended to obtain adequate ^{18}F-FDG biodistribution. During this time, the patient should drink at least 1 L of water or receive this amount intravenously to promote diuresis, if there are no contraindications. Patients should void immediately before image acquisition begins.

4. Postprocedure recommendations

   No other recommendations (other than normal radiation protection advice) are to be made after the imaging is finished and the technical quality of the study has been checked. The patient is free to resume normal activities without further precautions, except when benzodiazepines or other depressant medications were administered or if the patient is actively breastfeeding (see "Patient Preparation and Precautions"). Patients who ask about the report should be informed that a detailed report will be produced after thorough evaluation of the ^{18}F-FDG study and all available information.

5. Radiation dosimetry

   The organ that receives the highest radiation dose is the urinary bladder. High absorbed doses are expected in the lactating breast, but figures are not available from the literature. The effective dose is 1.9 10^{-2} mSv/MBq for the PET examination (ICRP 106 (*121*)) in addition to CT dose, which may vary according to the type of study performed.

D. Image acquisition

It is not the aim of this guideline to discuss the performance of current PET/CT scanners. Reference is made to the 2009 EANM guideline for FDG PET and PET/CT for tumor imaging (*7*) and the SNMMI Guideline for Tumor Imaging with ^{18}F-FDG PET/CT (*8*).

With current PET/CT scanners, the acquisition is performed in whole-body mode, using steps of 1.5–3 min per bed position. Whole-body acquisition is usually defined as a field of view covering the head to mid thigh, starting in the pelvic area, when the bladder is empty. This field of view may not be sufficient in patients with FUO, in whom continuation of the scan down to the feet may be useful, depending on the clinical suspicion.

Conversely, a limited field of view may be used, with imaging confined only to the region of the clinical problem (e.g., a hip prosthesis, an infected vascular graft, or a diabetic foot).

Although dynamic scanning has been described in orthopedic indications, it has not proven widely useful and hence is not advised at present in clinical practice. This applies also to dual-time-point early and late imaging protocols. From the available literature, dual-time-point imaging does not reliably help in differentiating infection from cancer.

CT acquisition parameters are detailed in the EANM and SNMMI tumor imaging guidelines. For PET/CT, low-dose CT should be performed for attenuation correction and anatomic localization.

For diagnostic CT, acquisition parameters should be determined according to specific radiologic society guidelines. Injection of iodinated contrast may be indicated to obtain a full PET/CT scan with a diagnostic CT sequence. However, there are not enough data to support the use of intravenous contrast in the clinical setting of infection/inflammation imaging. The use of contrast is probably indicated in FUO, postoperative fever, and vascular prostheses but not in vasculitis and orthopedic infection. In cases of contrast-enhanced CT, a low-dose CT scan before contrast injection should be obtained for attenuation correction. An alternative to acquiring 2 CT scans could be to apply contrast compensation when considering Hounsfield units.

E. Image analysis and interpretation

1. Physiologic ^{18}F-FDG distribution

   Accumulation of ^{18}F-FDG can normally be seen in the brain, heart, kidneys, and urinary tract at 60 min after injection. The brain has a high uptake of ^{18}F-FDG (7% of injected activity). The myocardium in a typical fasting state primarily uses free fatty acids but after a glucose load uses glucose. In the fasting state, ^{18}F-FDG uptake in the myocardium should be low, but this is variable. Unlike glucose, ^{18}F-FDG is excreted by the kidneys into the urine and accumulates in the urinary tract. ^{18}F-FDG may also be seen in muscles, depending on recent motor activity and insulin. Uptake in the gastrointestinal tract varies from patient to patient and may be increased in patients taking metformin (*130*). Uptake is common in the lymphoid tissue of the Waldeyer ring and in the lymphoid tissue of the terminal ileum and cecum (*131,132*). Physiologic thymic uptake may be present, especially in children and young adults (*133*). Uptake in brown fat may be observed mainly in young patients and when the ambient temperature is low. No physiologic uptake is noted in the bone itself (unless free ^{18}F-fluoride is present as a contaminant), but especially in infected or inflamed patients, bone marrow uptake can be noted to a variable level. This is also true in patients with hematopoietic regeneration, such as after chemotherapy, either spontaneously or after administration of hematopoietic growth factors (e.g., granulocyte–macrophage colony-stimulating factor) (*134*).

2. Qualitative analysis

   PET images are visually analyzed by looking for increased ^{18}F-FDG uptake, taking into consideration the pattern (focal, linear, diffuse), intensity, and relationship to areas of physiologic distribution. PET information is compared with morphologic information obtained by CT. It must be kept in mind that the sensitivity of ^{18}F-FDG for infection is not absolute and that even in the case of negative PET results, a thorough interpretation of the CT scan is essential.

3. Quantitative analysis (SUV)

   In contrast to its use in oncology, SUV has not been validated in inflammation and infection. Therefore, SUV in this field should be used with caution in clinical practice. In a single study, though, in spondylodiskitis, an SUV cutoff greater than 3 has been suggested to avoid false-positive findings (*26*). This criterion, however, cannot be applied for other diseases. Maximum SUV data were also analyzed for sarcoidosis (*27*). Although correlations were found with other parameters of disease activity, no real cutoff was derived for interpretation.

4. General interpretation criteria

   To evaluate ^{18}F-FDG imaging, the following should be taken into consideration:

   - Clinical question raised in the request for ^{18}F-FDG imaging.
   - Clinical history.
   - Scanning protocol (with or without attenuation correction).
   - Physiologic distribution of ^{18}F-FDG, and its individual variations in the specific patient evaluated.
   - Localization of the abnormal uptake according to anatomic imaging data.
   - Intensity of ^{18}F-FDG uptake (e.g., maximum SUV and/or peak SUV).
   - Correlation with data from previous clinical, biochemical, and morphologic examinations.
   - Presence of potential causes of false-negative results (lesion size, low metabolic rate, hyperglycemia, lesions masked by adjacent high physiologic uptake, concomitant drug use interfering with uptake, such as ongoing steroid therapy in systemic disorders).
   - Presence of potential causes of false-positive results (injection artifacts and external contamina-

tion, reconstruction artifacts from attenuation correction, normal physiologic uptake, pathologic uptake not related to infection or inflammation).

Care should be taken in the interpretation of PET data corrected for attenuation using a low-dose CT scan (particularly when metallic material or implants are present). Assessment of both attenuation-corrected and non–attenuation-corrected images is recommended.

5. Interpretation criteria for specific disorders

   There are no general criteria published for all inflammatory and infectious disorders. Most research articles on the subject have defined interpretation criteria for the purposes of the study. Some authors have reported specific interpretation criteria that can be used, although no definitive consensus has been agreed on.

   - Joint prostheses: some interpreting criteria have been proposed by Reinhartz et al. (*106*) for painful hip arthroplasties. The use of their criteria results in overall accuracy of 95% but has not been confirmed by others. Visual interpretation using these criteria may be more reliable than quantitative (SUV) analysis, which is not recommended.
   - Sarcoidosis: sarcoidosis can mimic malignancies and especially lymphoma. Keijsers et al., however, reported that a high parenchymal lung uptake (with elevated SUV) was predictive of severe disease activity, especially if the mediastinum and hilum maximum SUV was low (*135*). Conversely, the same authors reported that the absence of metabolic activity in the lung parenchyma was related to low-activity disease and justifies a wait-and-see policy (*136*).
   - Vascular prostheses: because physiologic uptake is often visible in vascular prostheses, patterns of interpretation have been discussed. It is now felt that linear, diffuse, and homogeneous uptake is not likely to represent infection whereas focal or heterogeneous uptake with projection over the vessel on CT is highly suggestive of infection (*111*).
   - Vasculitis: Hautzel et al. (*137*) and Meller et al. (*138*) both proposed criteria for the diagnosis of active giant cell arteritis. The criteria of Meller et al. are based on visual comparison of uptake in the aorta with that in the liver or brain but have not been used or reproduced by others. Using receiver-operating-characteristic curve analysis, Hautzel et al. defined an optimal cutoff of 1.0 for aorta-to-liver ratio to differentiate patients with giant cell arteritis from healthy patients. Although this cutoff resulted in good diagnostic performance, this parameter has also not been further evaluated by other authors.

VIII. DOCUMENTATION/REPORTING

A. Direct communication

Significant abnormalities should be verbally communicated to the appropriate health care provider if a delay in treatment might result in significant morbidity. An example of such an abnormality would be a lesion with a high risk of pathologic fracture. Other clinically significant unexpected findings should also be communicated verbally.

Reporting of abnormalities requiring urgent attention should be consistent with the policy of the interpreting physician's local organization. Written documentation of verbal reporting should be made in the medical record, usually as part of the PET/CT report.

B. Contents of the written report

1. Study identification

   The report should include the full name of the patient, medical record number, and date of birth. The name of the examination should also be included, with the date and time it is performed. The electronic medical record should provide these data, as well as a unique study number.
2. Clinical information

   At a minimum, the clinical history should include the reason for referral and the specific question to be answered. If known, the diagnosis and a brief treatment history should be provided. The results of relevant diagnostic tests and prior imaging findings should be summarized.

   The type and date of comparison studies should be stated. If no comparison studies are available, a statement should be made to that effect.
3. Procedure description

   Study-specific information should include the name of the radiopharmaceutical, the dose in megabecquerels or millicuries, the route of administration (intravenous), and the date and time of administration. The site of administration is optional. The name, dose, and route of administration of regulated nonradioactive drugs and agents should also be stated. The type of camera should be specified, but specific equipment information is optional.

   A description of the procedure should include the time the patient was scanned or the time interval between administration of ^{18}F and the start time of the scan. The part of the body that is scanned should be described from the starting to the ending point. The position of the patient (supine or prone), and the position of the arms (elevated or by the sides) should be stated if nonstandard.

   Description of the CT part of the examination may be limited to a statement that a low-mAs CT was performed for attenuation correction and anatomic registration of the emission images. However, findings should be reported. If CT was optimized for diagnosis, then a more complete description of the CT protocol and anatomic findings should be provided.

Routine processing parameters are usually not stated in the report, but any special circumstances requiring additional processing, such as motion correction, should be described.

4. Description of the findings

Significant findings should be described in a logical manner. Findings may be grouped by significance or described by body region. An integrated PET/CT report is preferred, although CT optimized for diagnosis may be reported separately. For important ^{18}F-FDG findings, the location, extent, and intensity of abnormal uptake should be described, as well as the relevant morphologic CT findings at the site of ^{18}F-FDG abnormalities. SUV may be used as a purely descriptive means of reporting, but the measurement should not be used to render a specific diagnosis. The integrated PET/CT report should include any detected incidental findings on the CT scan that are relevant to patient care.

Limitations should be addressed. Where appropriate, factors that can limit the sensitivity and specificity of the examination should be identified. In patients with known cancer evaluated for an episode of pyrexia, the interpretation should try to separate uptake within a site of cancer from uptake in a site of inflammation or infection. Possible sources of error include a small lesion, a low-grade infection, physiologic uptake around or along exogenous material (i.e., a foreign body aseptic reaction, such as that associated with a vascular graft), artifacts (in particular, those related to overcorrection of attenuation after contrast injection or due to metallic implants, devices, and prosthesis), physiologic uptake of ^{18}F-FDG (in brain; myocardium and other muscles; brown fat; urinary, gastrointestinal, and oropharyngeal tracts; thymus), uptake in known or unknown malignant disease, treatment-related uptake (after chemotherapy and radiation therapy and in healing surgical wounds up to 8 wk, scars, stoma, and tube placements), and aseptic inflammatory reactive ^{18}F-FDG uptake (lymph node uptake in sterile arthritis such as rheumatoid arthritis, reactive lymph nodes in HIV-positive patients, and following immunization; atherosclerotic plaques, bone fractures, granulation tissue).

5. Impression

The most probable diagnosis should be given whenever possible. A differential diagnosis should be given when appropriate. When appropriate, follow-up and additional diagnostic studies should be recommended to clarify or confirm the impression.

C. Issues requiring further clarification

Controversy still remains on the role of ^{18}F-FDG in infection and inflammation in the presence of artifacts caused by metallic implants and prostheses and the added value of SUV in improving the diagnostic accuracy of reporting. Strategies for differentiating infection from sterile inflammation need to be developed. The utility of ^{18}F-FDG in monitoring response to antibacterial or antiinflammatory therapy is not known.

IX. EQUIPMENT SPECIFICATION

See SNMMI Guideline for Tumor Imaging with ^{18}F-FDG PET/CT.

X. QUALITY CONTROL AND IMPROVEMENT; SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with national rules in Europe and with the SNMMI policies on quality control, and patient education in the United States, where appropriate.

In all patients, the lowest exposure factors should be chosen that will produce images of diagnostic quality.

Equipment performance monitoring should be in accordance with “ACR Technical Standard for Medical Nuclear Physics Performance Monitoring of PET/CT Imaging Equipment” in the United States and in accordance with national rules in Europe.

See also “FDG PET and PET/CT: EANM Procedure Guidelines for Tumour PET Imaging: version 1.0,” the SNMMI Guideline for General Imaging, the SNMMI Guideline for Use of Radiopharmaceuticals, and the SNMMI

TABLE 2
Radiation Dosimetry for Adults (*121*)

	Administered activity (intravenously)		Bladder (organ receiving largest radiation dose)*		Effective dose	
Radiopharmaceutical	MBq	mCi	mGy/MBq	rad/mCi	mSv/MBq	rem/mCi
^{18}F-FDG	370–740	10–20	0.13	0.48	0.019	0.070

*Voiding interval, 3.5 h. Changes in bladder wall dose are approximately linear with changes in voiding interval; therefore, for voiding interval of 2.0 h, dose to bladder wall would change by factor of 2/3.5.

TABLE 3
Radiation Dosimetry for Children (5 Years Old) (*121*)

Radiopharmaceutical	Administered activity (intravenously)		Bladder (organ receiving largest radiation dose)*		Effective dose	
	MBq/kg	mCi/kg	mGy/MBq	rad/mCi	mSv/MBq	rem/mCi
^{18}F-FDG	5.18–7.4	0.14–0.20	0.34	1.3	0.056	0.21

*Voiding interval, 2.0 h.

Guideline for Tumor Imaging with ^{18}F-FDG PET/CT for equipment performance guidelines and quality control.

XI. RADIATION SAFETY IN IMAGING

See the SNMMI Guideline for General Imaging, "FDG PET and PET/CT: EANM Procedure Guidelines for Tumour PET Imaging: version 1.0," and Tables 2 and 3.

A. The pregnant or potentially pregnant patient (Table 4)

The ICRP reports that the administration of 259 MBq (7 mCi) of ^{18}F-FDG results in an absorbed radiation dose of 4.7 mGy to the nongravid uterus (i.e., 1.8×10^{-2} mGy/MBq) (*121*). Direct measurements of ^{18}F-FDG uptake in 1 case study suggested somewhat higher doses than currently provided in standard models (*120*). More detailed information, including information on changes with the stage of gestation, has been previously reported (*130,131*).

B. The breastfeeding patient

The ICRP does not recommend interruption of breastfeeding after ^{18}F-FDG administration since little ^{18}F-FDG is excreted in the milk (*121*). However, the suggestion may be made that contact between mother and child be limited for 12 h after injection of ^{18}F-FDG to reduce the radiation dose the infant receives from external exposure to breast uptake in the mother. It is recommended that the infant be breastfed just before injection, to maximize the time between the injection and the next feeding. Milk pumped from the breast may also be fed to the infant via a bottle to avoid close contact with ^{18}F decay in breast tissue.

C. Issues related to the CT radiation dose from PET/CT

With PET/CT, the radiation dose to the patient is the combination of the radiation dose from the PET radiopharmaceutical and the radiation dose from the CT portion of the study. Radiation dose in diagnostic CT has attracted considerable attention in recent years, in particular for pediatric examinations. It can be misleading to quote a "representative" dose for a CT scan because of the wide diversity of applications, protocols, and CT systems. This also applies to the CT component of a PET/CT study. For example, a body scan may include protocols to reduce the radiation dose to the patient or to optimize the CT for diagnostic purposes. The effective dose could range from approximately 5 to 80 mSv (0.5–8.0 rem) for these options. It is therefore advisable to estimate the CT dose specific to the CT system and protocol.

Pediatric and adolescent patients should have their CT examinations adjusted for patient size, since radiation dose to the patient increases significantly as the diameter of the patient decreases.

The effective dose for whole-body CT performed for attenuation correction and registration of emission images is in the range of 3.2 mSv (0.32 rem), using the following parameters: voltage of 120 kV, current of 30 mAs, rotation of 0.5 s, and pitch of 1. In all cases, adaptive CT dose tools (as now proposed by most manufacturers) are recommended to reduce the radiation exposure, especially in young patients.

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TABLE 4
^{18}F-FDG Dose Estimates to Fetus (*139,140*)

Stage of gestation	mGy/MBq	rad/mCi	mGy	rad
Early	0.022	0.081	8.1–16	0.81–1.6
3 mo	0.022	0.081	8.1–16	0.81–1.6
6 mo	0.017	0.063	6.3–13	0.63–1.3
9 mo	0.017	0.063	6.3–13	0.63–1.3

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XIII. REFERENCES

1. Mochizuki T, Tsukamoto E, Kuge Y, et al. FDG uptake and glucose transporter subtype expressions in experimental tumor and inflammation models. *J Nucl Med.* 2001;42:1551–1555.
2. Kubota R, Yamada S, Kubota K, Ishiwata K, Tamahashi N, Ido T. Intratumoral distribution of fluorine-18-fluorodeoxyglucose in vivo: high accumulation in macrophages and granulation tissues studied by microautoradiography. *J Nucl Med.* 1992;33:1972–1980.
3. Yamada S, Kubota K, Kubota R, Ido T, Tamahashi N. High accumulation of fluorine-18-fluorodeoxyglucose in turpentine-induced inflammatory tissue. *J Nucl Med.* 1995;36:1301–1306.
4. Gamelli RL, Liu H, He LK, Hofmann CA. Augmentations of glucose uptake and glucose transporter-1 in macrophages following thermal injury and sepsis in mice. *J Leukoc Biol.* 1996;59:639–647.
5. Fukuzumi M, Shinomiya H, Shimizu Y, Ohishi K, Utsumi S. Endotoxin-induced enhancement of glucose influx into murine peritoneal macrophages via GLUT1. *Infect Immun.* 1996;64:108–112.
6. Mortimer JE, Dehdashti F, Siegal BA, et al. Metabolic flare: indicator of hormone responsiveness in advanced breast cancer. *J Clin Oncol.* 2001;19:2797–2803.
7. Boellaard R, O'Doherty MJ, Weber WA, et al. FDG PET and PET/CT: EANM procedure guidelines for tumor PET imaging: version 1.0. *Eur J Nucl Med Mol Imaging.* 2010;37:181–200.
8. Delbeke D, Coleman RE, Guiberteau MJ, et al. Procedure guideline for tumor imaging with ^{18}F-FDG PET/CT 1.0. *J Nucl Med.* 2006;47:885–895.
9. Braun JJ, Kessler R, Constantinesco A, Imperiale A. ^{18}F-FDG PET/CT in sarcoidosis management: review and report of 20 cases. *Eur J Nucl Med Mol Imaging.* 2008;35:1537–1543.
10. Braun JJ, Imperiale A, Riehm S, Veillon F. Imaging in sinonasal sarcoidosis: CT, MRI, ^{67}gallium scintigraphy and ^{18}F-FDG PET/CT features. *J Neuroradiol.* 2010;37:172–181.
11. Keijsers RG, Thomeer M, Du Bois RM, et al. Imaging the inflammatory activity of sarcoidosis: sensitivity and inter observer agreement of ^{67}Ga imaging and ^{18}F-FDG PET. *Q J Nucl Med Mol Imaging.* 2011;55:66–71.
12. Keijsers RG, Verzijlbergen FJ, Oyen WJ, et al. ^{18}F-FDG PET, genotype-corrected ACE and sIL-2R in newly diagnosed sarcoidosis. *Eur J Nucl Med Mol Imaging.* 2009;36:1131–1137.
13. Mostard RL, Vöö S, van Kroonenburgh MJ, et al. Inflammatory activity assessment by F18 FDG-PET/CT in persistent symptomatic sarcoidosis. *Respir Med.* 2011;105:1917–1924.
14. Okumura W, Iwasaki T, Toyama T, et al. Usefulness of fasting ^{18}F-FDG PET in identification of cardiac sarcoidosis. *J Nucl Med.* 2004;45:1989–1998.
15. Yamada Y, Uchida Y, Tatsumi K, et al. Fluorine-18-fluorodeoxyglucose and carbon-11-methionine evaluation of lymphadenopathy in sarcoidosis. *J Nucl Med.* 1998;39:1160–1166.
16. de Winter F, van de Wiele C, Vogelaers D, de Smet K, Verdonk R, Dierckx RA. Fluorine-18 fluorodeoxyglucose-position emission tomography: a highly accurate imaging modality for the diagnosis of chronic musculoskeletal infections. *J Bone Joint Surg Am.* 2001;83-A:651–660.
17. Guhlmann A, Brecht-Krauss D, Suger G, et al. Chronic osteomyelitis: detection with FDG PET and correlation with histopathologic findings. *Radiology.* 1998;206:749–754.
18. 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.* 1998;39:2145–2152.
19. Hartmann A, Eid K, Dora C, Trentz O, von Schulthess GK, Stumpe KD. Diagnostic value of ^{18}F-FDG PET/CT in trauma patients with suspected chronic osteomyelitis. *Eur J Nucl Med Mol Imaging.* 2007;34:704–714.
20. Hakim SG, Bruecker CW, Jacobsen HCh, et al. The value of FDG-PET and bone scintigraphy with SPECT in the primary diagnosis and follow-up of patients with chronic osteomyelitis of the mandible. *Int J Oral Maxillofac Surg.* 2006;35:809–816.
21. Meller J, Köster G, Liersch T, et al. Chronic bacterial osteomyelitis: prospective comparison of ^{18}F-FDG imaging with a dual-head coincidence camera and ^{111}In-labelled autologous leucocyte scintigraphy. *Eur J Nucl Med Mol Imaging.* 2002;29:53–60.
22. Stumpe KD, Dazzi H, Schaffner A, von Schulthess GK. Infection imaging using whole-body FDG-PET. *Eur J Nucl Med.* 2000;27:822–832.
23. Zhuang H, Duarte PS, Pourdehand M, Shnier D, Alavi A. Exclusion of chronic osteomyelitis with F-18 fluorodeoxyglucose positron emission tomographic imaging. *Clin Nucl Med.* 2000;25:281–284.
24. De Winter F, Gemmel F, Van De Wiele C, Poffijn B, Uyttendaele D, Dierckx R. 18-fluorine fluorodeoxyglucose positron emission tomography for the diagnosis of infection in the postoperative spine. *Spine (Phila Pa 1976).* 2003;28:1314–1319.
25. Gratz S, Dörner J, Fischer U, et al. ^{18}F-FDG hybrid PET in patients with suspected spondylitis. *Eur J Nucl Med Mol Imaging.* 2002;29:516–524.
26. Schmitz A, Risse JH, Textor J, et al. FDG-PET findings of vertebral compression fractures in osteoporosis: preliminary results. *Osteoporos Int.* 2002; 13:755–761.
27. Schmitz A, Risse JH, Grünwald F, Gassel F, Biersack HJ, Schmitt O. Fluorine-18 fluorodeoxyglucose positron emission tomography findings in spondylodiscitis: preliminary results. *Eur Spine J.* 2001;10:534–539.
28. Stumpe KD, Zanetti M, Weishaupt D, Hodler J, Boos N, Von Schulthess GK. FDG positron emission tomography for differentiation of degenerative and infectious endplate abnormalities in the lumbar spine detected on MR imaging. *AJR.* 2002;179:1151–1157.
29. Becerra Nakayo EM, García Vicente AM, Soriano Castrejón AM, et al. Analysis of cost-effectiveness in the diagnosis of fever of unknown origin and the role of ^{18}F-FDG PET-CT: a proposal of diagnostic algorithm. *Rev Esp Med Nucl*. December 5, 2011 [Epub ahead of print].
30. Bleeker-Rovers CP, Vos FJ, Mudde AH, et al. A prospective multi-centre study of the value of FDG-PET as part of a structured diagnostic protocol in patients with fever of unknown origin. *Eur J Nucl Med Mol Imaging.* 2007;34:694–703.
31. Bleeker-Rovers CP, de Kleijn EM, Corstens FH, van der Meer JW, Oyen WJ. Clinical value of FDG PET in patients with fever of unknown origin and patients suspected of focal infection or inflammation. *Eur J Nucl Med Mol Imaging.* 2004;31:29–37.
32. Bleeker-Rovers CP, Vos FJ, Wanten GJ, et al. ^{18}F-FDG PET in detecting metastatic infectious disease. *J Nucl Med.* 2005;46:2014–2019.
33. Ferda J, Ferdová E, Záhlava J, Matejovic M, Kreuzberg B. Fever of unknown origin: a value of ^{18}F-FDG-PET/CT with integrated full diagnostic isotropic CT imaging. *Eur J Radiol.* 2010;73:518–525.
34. Keidar Z, Gurman-Balbir A, Gaitini D, Israel O. Fever of unknown origin: the role of ^{18}F-FDG PET/CT. *J Nucl Med.* 2008;49:1980–1985.
35. Kjaer A, Lebech AM, Eigtved A, Højgaard L. Fever of unknown origin: prospective comparison of diagnostic value of ^{18}F-FDG PET and ^{111}In-granulocyte scintigraphy. *Eur J Nucl Med Mol Imaging.* 2004;31:622–626.
36. Kubota K, Nakamoto Y, Tamaki N, et al. FDG-PET for the diagnosis of fever of unknown origin: a Japanese multi-center study. *Ann Nucl Med.* 2011;25:355–364.
37. Meller J, Sahlmann CO, Lehmann K, et al. F-18-FDG hybrid camera PET in patients with postoperative fever [in German]. *Nuklearmedizin.* 2002;41:22–29.
38. Meller J, Altenvoerde G, Munzel U, et al. Fever of unknown origin: prospective comparison of [^{18}F]FDG imaging with a double-head coincidence camera and gallium-67 citrate SPET. *Eur J Nucl Med.* 2000;27:1617–1625.
39. Balink H, Collins J, Bruyn GA, Gemmel F. F-18 FDG PET/CT in the diagnosis of fever of unknown origin. *Clin Nucl Med.* 2009;34:862–868.
40. Sheng JF, Sheng ZK, Shen XM, et al. Diagnostic value of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in patients with fever of unknown origin. *Eur J Intern Med.* 2011;22:112–116.

41. Simons KS, Pickkers P, Bleeker-Rovers CP, Oyen WJ, van der Hoeven JG. F-18-fluorodeoxyglucose positron emission tomography combined with CT in critically ill patients with suspected infection. *Intensive Care Med.* 2010;36:504–511.
42. Vos FJ, Bleeker-Rovers CP, Sturm PD, et al. ^{18}F-FDG PET/CT for detection of metastatic infection in gram-positive bacteremia. *J Nucl Med.* 2010;51:1234–1240.
43. Zhao K, Dong MJ, Ruan LX, et al. *Zhejiang Da Xue Xue Bao Yi Xue Ban*. 2010;39:174–180.
44. Durack DT, Street AC. Fever of unknown origin: reexamined and redefined. *Curr Clin Top Infect Dis.* 1991;11:35–51.
45. Arnaud L, Haroche J, Malek Z, et al. Is ^{18}F-fluorodeoxyglucose positron emission tomography scanning a reliable way to assess disease activity in Takayasu arteritis? *Arthritis Rheum.* 2009;60:1193–1200.
46. Bleeker-Rovers CP, Bredie SJ, van der Meer JW, Corstens FH, Oyen WJ. F-18-fluorodeoxyglucose positron emission tomography in diagnosis and follow-up of patients with different types of vasculitis. *Neth J Med.* 2003;61:323–329.
47. Blockmans D, Stroobants S, Maes A, Mortelmans L. Positron emission tomography in giant cell arteritis and polymyalgia rheumatica: evidence for inflammation of the aortic arch. *Am J Med.* 2000;108:246–249.
48. Cyran CC, Sourbron S, Bochmann K, et al. Quantification of supra-aortic arterial wall inflammation in patients with arteritis using high resolution dynamic contrast-enhanced magnetic resonance imaging: initial results in correlation to [^{18}F]-FDG PET/CT. *Invest Radiol.* 2011;46:594–599.
49. Förster S, Tato F, Weiss M, et al. Patterns of extracranial involvement in newly diagnosed giant cell arteritis assessed by physical examination, colour coded duplex sonography and FDG-PET. *Vasa.* 2011;40:219–227.
50. Kobayashi Y, Ishii K, Oda K, et al. Aortic wall inflammation due to Takayasu arteritis imaged with ^{18}F-FDG PET coregistered with enhanced CT. *J Nucl Med.* 2005;46:917–922.
51. Lee KH, Cho A, Choi YJ, et al. The role of ^{18}F-fluorodeoxyglucose-positron emission tomography in the assessment of disease activity in patients with takayasu arteritis. *Arthritis Rheum.* 2011;64:866–875.
52. Lee SG, Ryu JS, Kim HO, et al. Evaluation of disease activity using F-18 FDG PET-CT in patients with Takayasu arteritis. *Clin Nucl Med.* 2009;34:749–752.
53. Lehmann P, Buchtala S, Achajew N, et al. ^{18}F-FDG PET as a diagnostic procedure in large vessel vasculitis: a controlled, blinded re-examination of routine PET scans. *Clin Rheumatol.* 2011;30:37–42.
54. Walter MA, Melzer RA, Schindler C, Müller-Brand J, Tyndall A, Nitzsche EU. The value of [^{18}F]FDG-PET in the diagnosis of large-vessel vasculitis and the assessment of activity and extent of disease. *Eur J Nucl Med Mol Imaging.* 2005;32:674–681.
55. Webb M, Chambers A, AL-Nahhas A, et al. The role of ^{18}F-FDG PET in characterising disease activity in Takayasu arteritis. *Eur J Nucl Med Mol Imaging.* 2004;31:627–634.
56. Yamashita H, Kubota K, Takahashi Y, et al. Whole-body fluorodeoxyglucose positron emission tomography/computed tomography in patients with active polymyalgia rheumatica: evidence for distinctive bursitis and large-vessel vasculitis. *Mod Rheumatol*. December 29, 2011 [Epub ahead of print].
57. Sainaresh V, Jain Sh, Patel H, Shah P, Vanikar A, Trivedi H. Post transplant urinary tract infection in autosomal dominant polycystic kidney disease a perpetual diagnostic dilema - 18-fluorodeoxyglucose - positron emission computerized tomography - a valuable tool. *Indian J Nucl Med.* 2011;26:109–111.
58. Agrawal K, Bhattacharya A, Singh SK, Manohar K, Kashyap R, Mittal BR. Polycystic kidney disease: renal cyst infection detected on F-18 FDG PET/CT. *Clin Nucl Med.* 2011;36:1122–1123.
59. Piccoli GB, Arena V, Consiglio V, et al. Positron emission tomography in the diagnostic pathway for intracystic infection in adpkd and “cystic” kidneys: a case series. *BMC Nephrol.* 2011;12:48.
60. Jouret F, Lhommel R, Beguin C, et al. Positron-emission computed tomography in cyst infection diagnosis in patients with autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol.* 2011;6:1644–1650.
61. Jiménez-Bonilla JF, Quirce R, Calabia ER, Banzo I, Martínez-Rodríguez I, Carril JM. Hepatorenal polycystic disease and fever: diagnostic contribution of gallium citrate Ga 67 scan and fluorine F 18 FDG-PET/CT. *Eur Urol.* 2011;59:297–299.
62. Soussan M, Sberro R, Wartski M, Fakhouri F, Pecking AP, Alberini JL. Diagnosis and localization of renal cyst infection by ^{18}F-fluorodeoxyglucose PET/CT in polycystic kidney disease. *Ann Nucl Med.* 2008;22:529–531.
63. Bleeker-Rovers CP, de Sévaux RG, van Hamersvelt HW, Corstens FH, Oyen WJ. Diagnosis of renal and hepatic cyst infections by 18-F-fluorodeoxyglucose positron emission tomography in autosomal dominant polycystic kidney disease. *Am J Kidney Dis.* 2003;41:E18–E21.
64. Miceli MH, Jones Jackson LB, Walker RC, Talamo G, Barlogie B, Anaissie EJ. Diagnosis of infection of implantable central venous catheters by [^{18}F]fluorodeoxyglucose positron emission tomography. *Nucl Med Commun.* 2004;25:813–818.
65. Ploux S, Riviere A, Amraoui S, et al. Positron emission tomography in patients with suspected pacing system infections may play a critical role in difficult cases. *Heart Rhythm.* 2011;8:1478–1481.
66. Bhargava P, Kumar R, Zhuang H, Charron M, Alavi A. Catheter-related focal FDG activity on whole body PET imaging. *Clin Nucl Med.* 2004;29:238–242.
67. Gabaldon D, Xu Z, Sun Y, Servilla KS, Hartshorne MF, Tzamaloukas AH. Hemodialysis catheter infection with unusual presentation and grave outcome. *Hemodial Int.* 2011;15:568–572.
68. Costo S, Hourna E, Massetti M, Belin A, Bouvard G, Agostini D. Impact of F-18 FDG PET-CT for the diagnosis and management of infection in JARVIK 2000 device. *Clin Nucl Med.* 2011;36:e188–e191.
69. Singh P, Wiggins B, Sun Y, et al. Imaging of peritoneal catheter tunnel infection using positron-emission tomography. *Adv Perit Dial.* 2010;26:96–100.
70. Bensimhon L, Lavergne T, Hugonnet F, et al. Whole body [^{18}F]fluorodeoxyglucose positron emission tomography imaging for the diagnosis of pacemaker or implantable cardioverter defibrillator infection: a preliminary prospective study. *Clin Microbiol Infect.* 2011;17:836–844.
71. Turpin S, Lambert R, Poirier N. An unusual looking pacemaker infection imaged with ^{18}F-FDG PET/CT. *Eur J Nucl Med Mol Imaging.* 2010;37:1438.
72. Sathekge M, Goethals I, Maes A, van de Wiele C. Positron emission tomography in patients suffering from HIV-1 infection. *Eur J Nucl Med Mol Imaging.* 2009;36:1176–1184.
73. Masekela R, Gongxeka H, Green RJ, Sathekge M. Positron emission tomography in the prediction of inflammation in children with human immunodeficiency virus related bronchiectasis. *Hell J Nucl Med.* 2012;15:23–27.
74. Wada T, Kubota K, Minamimoto R, et al. FDG uptake by a condylomata acuminata in an HIV-infected patient mimicked urine contamination. *Clin Nucl Med.* 2012;37:420–421.
75. Belkhir L, Jonckheere S, Lhommel R, Vandercam B, Yombi JC. High FDG uptake on FDG-PET scan in HIV-1 infected patient with advanced disease. *Acta Clin Belg.* 2011;66:419–421.
76. Liu Y. Demonstrations of AIDS-associated malignancies and infections at FDG PET-CT. *Ann Nucl Med.* 2011;25:536–546.
77. Sathekge M, Maes A, Kgomo M, Stoltz A, Van de Wiele C. Use of ^{18}F-FDG PET to predict response to first-line tuberculostatics in HIV-associated tuberculosis. *J Nucl Med.* 2011;52:880–885.
78. Sathekge M, Maes A, Kgomo M, Pottel H, Stolz A, Van De Wiele C. FDG uptake in lymph-nodes of HIV+ and tuberculosis patients: implications for cancer staging. *Q J Nucl Med Mol Imaging.* 2010;54:698–703.
79. Lucignani G, Orunesu E, Cesari M, et al. FDG-PET imaging in HIV-infected subjects: relation with therapy and immunovirological variables. *Eur J Nucl Med Mol Imaging.* 2009;36:640–647.
80. Barker R, Kazmi F, Stebbing J, et al. FDG-PET/CT imaging in the management of HIV-associated multicentric Castleman’s disease. *Eur J Nucl Med Mol Imaging.* 2009;36:648–652.
81. Just PA, Fieschi C, Baillet G, Galicier L, Oksenhendler E, Moretti JL. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography in AIDS-related Burkitt lymphoma. *AIDS Patient Care STDS.* 2008;22:695–700.
82. Kösters K, Bleeker-Rovers CP, van Crevel R, Oyen WJ, van der Ven AJ. Aortitis diagnosed by F-18-fluorodeoxyglucose positron emission tomography in a patient with syphilis and HIV coinfection. *Infection.* 2005;33:387–389.
83. Scharko AM, Perlman SB, Pyzalski RW, Graziano FM, Sosman J, Pauza CD. Whole-body positron emission tomography in patients with HIV-1 infection. *Lancet.* 2003;362:959–961.
84. Kosterink JG. Positron emission tomography in the diagnosis and treatment management of tuberculosis. *Curr Pharm Des.* 2011;17:2875–2880.
85. Kim IJ, Lee JS, Kim SJ, et al. Double-phase ^{18}F-FDG PET-CT for determination of pulmonary tuberculoma activity. *Eur J Nucl Med Mol Imaging.* 2008; 35:808–814.
86. Ichiya Y, Kuwabara Y, Sasaki M, et al. FDG-PET in infectious lesions: the detection and assessment of lesion activity. *Ann Nucl Med.* 1996;10:185–191.
87. Sathekge M, Maes A, Kgomo M, Stoltz A, Pottel H, Van de Wiele C. Impact of FDG PET on the management of TBC treatment: a pilot study. *Nuklearmedizin.* 2010;49:35–40.
88. 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;28:465–472.
89. Familiari D, Glaudemans AW, Vitale V, et al. Can sequential ^{18}F-FDG-PET/CT imaging replace WBC imaging in the diabetic foot? *J Nucl Med.* 2011;52:1012–1019.
90. Nawaz A, Torigian DA, Siegelman ES, Basu S, Chryssikos T, Alavi A. Diagnostic performance of FDG-PET, MRI, and plain film radiography (PFR) for the diagnosis of osteomyelitis in the diabetic foot. *Mol Imaging Biol.* 2010; 12:335–342.

91. Keidar Z, Militianu D, Melamed E, Bar-Shalom R, Israel O. The diabetic foot: initial experience with ^{18}F-FDG PET/CT. *J Nucl Med.* 2005;46:444–449.
92. Schwegler B, Stumpe KD, Weishaupt D, et al. Unsuspected osteomyelitis is frequent in persistent diabetic foot ulcer and better diagnosed by MRI than by ^{18}F-FDG PET or ^{99m}Tc-MOAB. *J Intern Med.* 2008;263:99–106.
93. Chacko TK, Zhuang H, Stevenson K, Moussavian B, Alavi A. The importance of the location of fluorodeoxyglucose uptake in periprosthetic infection in painful hip prostheses. *Nucl Med Commun.* 2002;23:851–855.
94. Chryssikos T, Parvizi J, Ghanem E, Newberg A, Zhuang H, Alavi A. FDG-PET imaging can diagnose periprosthetic infection of the hip. *Clin Orthop Relat Res.* 2008;466:1338–1342.
95. Chen SH, Ho KC, Hsieh PH, Lee MS, Yen TC. Potential clinical role of ^{18}F FDG-PET/CT in detecting hip prosthesis infection: a study in patients undergoing two-stage revision arthroplasty with an interim spacer. *Q J Nucl Med Mol Imaging.* 2010;54:429–435.
96. Delank KS, Schmidt M, Michael JW, Dietlein M, Schicha H, Eysel P. The implications of ^{18}F-FDG PET for the diagnosis of endoprosthetic loosening and infection in hip and knee arthroplasty: results from a prospective, blinded study. *BMC Musculoskelet Disord.* 2006;7:20.
97. García-Barrecheguren E, Rodríguez Fraile M, Toledo Santana G, Valentí Nín JR, Richter Echevarría JA. FDG-PET: a new diagnostic approach in hip prosthetic replacement [in Spanish]. *Rev Esp Med Nucl.* 2007;26:208–220.
98. Gravius S, Gebhard M, Ackermann D, Büll U, Hermanns-Sachweh B, Mumme T. *Nuklearmedizin.* 2010;49:115–123.
99. Kobayashi N, Inaba Y, Choe H, et al. Use of F-18 fluoride PET to differentiate septic from aseptic loosening in total hip arthroplasty patients. *Clin Nucl Med.* 2011;36:e156–e161.
100. Love C, Marwin SE, Tomas MB, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection ^{18}F-FDG and ^{111}In-labeled leukocyte/^{99m}Tc-sulfur colloid marrow imaging. *J Nucl Med.* 2004; 45:1864–1871.
101. Love C, Pugliese PV, Afriyie MO, Tomas MB, Marwin SE, Palestro CJ. Utility of F-18 FDG imaging for diagnosing the infected joint replacement. *Clin Positron Imaging.* 2000;3:159.
102. Mayer-Wagner S, Mayer W, Maegerlein S, Linke R, Jansson V, Müller PE. Use of ^{18}F-FDG-PET in the diagnosis of endoprosthetic loosening of knee and hip implants. *Arch Orthop Trauma Surg.* 2010;130:1231–1238.
103. Manthey N, Reinhard P, Moog F, Knesewitsch P, Hahn K, Tatsch K. The use of [^{18}F]fluorodeoxyglucose positron emission tomography to differentiate between synovitis, loosening and infection of hip and knee prostheses. *Nucl Med Commun.* 2002;23:645–653.
104. Mumme T, Reinartz P, Alfer J, Müller-Rath R, Buell U, Wirtz DC. Diagnostic values of positron emission tomography versus triple-phase bone scan in hip arthroplasty loosening. *Arch Orthop Trauma Surg.* 2005;125:322–329.
105. Pill SG, Parvizi J, Tang PH, et al. Comparison of fluorodeoxyglucose positron emission tomography and ^{111}indium-white blood cell imaging in the diagnosis of periprosthetic infection of the hip. *J Arthroplasty.* 2006;21(6, suppl 2):91–97.
106. Reinartz P, Mumme T, Hermanns B, et al. Radionuclide imaging of the painful hip arthroplasty: positron-emission tomography versus triple-phase bone scanning. *J Bone Joint Surg Br.* 2005;87:465–470.
107. Vanquickenborne B, Maes A, Nuyts J, et al. The value of ^{18}FDG-PET for the detection of infected hip prosthesis. *Eur J Nucl Med Mol Imaging.* 2003;30:705–715.
108. Van Acker F, Nuyts J, Maes A, et al. FDG-PET, ^{99m}tc-HMPAO white blood cell SPET and bone scintigraphy in the evaluation of painful total knee arthroplasties. *Eur J Nucl Med.* 2001;28:1496–1504.
109. Zhuang H, Duarte PS, Pourdehnad M, et al. The promising role of ^{18}F-FDG PET in detecting infected lower limb prosthesis implants. *J Nucl Med.* 2001;42:44–48.
110. Bruggink JL, Glaudemans AW, Saleem BR, et al. Accuracy of FDG-PET-CT in the diagnostic work-up of vascular prosthetic graft infection. *Eur J Vasc Endovasc Surg.* 2010;40:348–354.
111. Fukuchi K, Ishida Y, Higashi M, et al. Detection of aortic graft infection by fluorodeoxyglucose positron emission tomography: comparison with computed tomographic findings. *J Vasc Surg.* 2005;42:919–925.
112. Spacek M, Belohlavek O, Votrubova J, Sebesta P, Stadler P. Diagnostics of "non-acute" vascular prosthesis infection using ^{18}F-FDG PET/CT: our experience with 96 prostheses. *Eur J Nucl Med Mol Imaging.* 2009;36:850–858.
113. Wassélius J, Malmstedt J, Kalin B, et al. High ^{18}F-FDG uptake in synthetic aortic vascular grafts on PET/CT in symptomatic and asymptomatic patients. *J Nucl Med.* 2008;49:1601–1605.
114. Keidar Z, Engel A, Hoffman A, Israel O, Nitecki S. Prosthetic vascular graft infection: the role of ^{18}F-FDG PET/CT. *J Nucl Med.* 2007;48:1230–1236.
115. Spier BJ, Perlman SB, Reichelderfer M. FDG-PET in inflammatory bowel disease. *Q J Nucl Med Mol Imaging.* 2009;53:64–71.
116. Glaudemans AW, Maccioni F, Mansi L, Dierckx RA, Signore A. Imaging of cell trafficking in Crohn's disease. *J Cell Physiol.* 2010;223:562–571.
117. Kenzaka T, Shimoshikiryo M, Kitao A, Kario K, Hashimoto M. Positron emission tomography scan can be a reassuring tool to treat difficult cases of infective endocarditis. *J Nucl Cardiol.* 2011;18:741–743.
118. Vind SH, Hess S. Possible role of PET/CT in infective endocarditis. *J Nucl Cardiol.* 2010;17:516–519.
119. Moghadam-Kia S, Nawaz A, Millar BC, et al. Imaging with ^{18}F-FDG-PET in infective endocarditis: promising role in difficult diagnosis and treatment monitoring. *Hell J Nucl Med.* 2009;12:165–167.
120. Product information sheet for METATRACE FDG® (fludeoxyglucose F 18 injection, USP). PETNET Project Toolkit Center Web site. Available at: http://clients.logica3.com/petnet/toolkit/website/library/Documents/04-02.pdf. Accessed September 19, 2012.
121. ICRP. Radiation dose to patients from radiopharmaceuticals: addendum 3 to ICRP Publication 53—ICRP Publication 106. Approved by the Commission in October 2007. *Ann ICRP.* 2008;38:1–197.
122. Zanotti-Fregonara P, Jan S, Taieb D, et al. Absorbed ^{18}F-FDG dose to the fetus during early pregnancy. *J Nucl Med.* 2010;51:803–805.
123. Rabkin Z, Israel O, Keidar Z. Do hyperglycemia and diabetes affect the incidence of false-negative ^{18}F-FDG PET/CT studies in patients evaluated for infection or inflammation and cancer? A comparative analysis. *J Nucl Med.* 2010;51:1015–1020.
124. Langen KJ, Braun U, Rota Kops E, et al. The influence of plasma glucose levels on fluorine-18-fluorodeoxyglucose uptake in bronchial carcinomas. *J. Nucl Med* 1993;34:355–359.
125. Minamimoto R, Takahashi N, Inoue T. FDG-PET of patients with suspected renal failure: standardized uptake values in normal tissues. *Ann Nucl Med.* 2007;21:217–222.
126. Blockmans D, de Ceuninck L, Vanderschueren S, Knockaert D, Mortelmans L, Bobbaers H. Repetitive ^{18}F-fluorodeoxyglucose positron emission tomography in giant cell arteritis: a prospective study of 35 patients. *Arthritis Rheum.* 2006;55:131–137.
127. Lassmann M, Biassoni L, Monsieurs M, Franzius C, Jacobs F. The new EANM paediatric dosage card. EANM Dosimetry and Paediatrics Committees. *Eur J Nucl Med Mol Imaging.* 2007;34:796–798.
128. Lassmann M, Biassoni L, Monsieurs M, Franzius C. The new EANM paediatric dosage card: additional notes with respect to F-18. EANM Dosimetry and Paediatrics Committees. *Eur J Nucl Med Mol Imaging.* 2008;35:1666–1668.
129. Gelfand MJ, Parisi MT, Treves ST. Pediatric radiopharmaceutical administered doses: 2010 North American Consensus Guidelines. *J Nucl Med.* 2011;52:318–322.
130. Gontier E, Fourme E, Wartski M, et al. High and typical ^{18}F-FDG bowel uptake in patients treated with metformin. *Eur J Nucl Med Mol Imaging.* 2008;35:95–99.
131. Jabour BA, Choi Y, Hoh CK, et al. Extracranial head and neck: PET imaging with 2-[F-18]fluoro-2-deoxy-D-glucose and MR imaging correlation. *Radiology.* 1993;186:27–35.
132. Cook GJ, Fogelman I, Maisey MN. Normal physiology and benign pathological variants of 18-fluoro-2-deoxyglucose postitron emission tomography scanning: potential for error in interpretation. *Semin Nucl Med.* 1996;26:308–314.
133. Shammas A, Lim R, Charron M. Pediatric FDG PET/CT: physiologic uptake, normal variants, and benign conditions. *Radiographics.* 2009;29:1467–1486.
134. Kazama T, Swanston N, Podoloff DA, et al. Effect of colony-stimulating factor and conventional- or high-dose chemotherapy on FDG uptake in bone marrow. *Eur J Nucl Med Mol Imaging.* 2005;32:1406–1411.
135. Keijsers RG, Grutters JC, van Velzen-Blad H, van den Bosch JM, Oyen WJ, Verzijlbergen FJ. ^{18}F-FDG PET patterns and BAL cell profiles in pulmonary sarcoidosis. *Eur J Nucl Med Mol Imaging.* 2010;37:1181–1188.
136. Keijsers RG, Verzijlbergen EJ, van den Bosch JM, et al. ^{18}F-FDG PET as a predictor of pulmonary function in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis.* 2011;28:123–129.
137. Hautzel H, Sander O, Heinzel A, Schneider M, Müller HW. Assessment of large-vessel involvement in giant cell arteritis with ^{18}F-FDG PET: introducing an ROC-analysis-based cutoff ratio. *J Nucl Med.* 2008;49:1107–1113.
138. Meller J, Strutz F, Siefker U, et al. Early diagnosis and follow-up of aortitis with [^{18}F]FDG PET and MRI. *Eur J Nucl Med Mol Imaging.* 2003;30:730–736.
139. Russell JR, Stabin MG, Sparks RB, Watson E. Radiation absorbed dose to the embryo/fetus from radiopharmaceuticals. *Health Phys.* 1997;73:756–769.
140. Stabin MG. Proposed addendum to previously published fetal dose estimate tables for ^{18}F-FDG. *J Nucl Med.* 2004;45:634–635.

XIV. APPROVAL

This practice guideline was approved by the Board of Directors of the SNMMI on November 15, 2012.