Revised 2009 (Res. 15)*

ACR–SNM–SPR PRACTICE GUIDELINE FOR THE PERFORMANCE OF SCINTIGRAPHY FOR INFLAMMATION AND INFECTION

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic 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 American College of Radiology 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 the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was 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. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

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 assure 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.

I. INTRODUCTION

This guideline was revised collaboratively by the American College of Radiology (ACR), the Society for Pediatric Radiology (SPR), and the Society of Nuclear Medicine (SNM).

It is intended to guide interpreting physicians in performing scintigraphy for inflammation and infection. Properly performed imaging with radiopharmaceuticals that localize in inflamed or infected tissue is an effective means of detecting and evaluating many overt or occult infections. Correlation with clinical findings and other imaging modalities is imperative for maximum diagnostic yield.

For this guideline, discussion is limited solely to agents that are not organ specific. The reader is referred to the guidelines covering scintigraphy of specific organs (e.g., the ACR Practice Guideline for the Performance of Adult and Pediatric Skeletal Scintigraphy for osteomyelitis and the ACR–SPR Practice Guideline for the Performance of Adult and Pediatric Hepatobiliary Scintigraphy for acute cholecystitis) for a discussion of those organs.

Application of this guideline should be in accordance with the ACR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals.

II. GOAL

The goal of scintigraphy for inflammation and infection is to enable the interpreting physician to detect and evaluate foci of inflamed or infected tissue.

III. INDICATIONS AND CONTRAINDICATIONS

Clinical indications for scintigraphy of inflammation and infection include, but are not limited to:

1. Musculoskeletal infections: disc space and joint space infections, osteomyelitis superimposed on existing bone pathology, osteomyelitis in diabetic patients, painful joint prostheses.
2. Fever of unknown origin (FUO).
3. Localization of an unknown source of sepsis (occult infection).
4. Detection of additional site(s) of infection in patients with persistent or recurrent fever and a known site of infection.
5. Postoperative infections.
6. Cardiovascular infections (e.g., prosthetic grafts, mycotic aneurysms).
7. Differentiation of infection from tumor.
8. Opportunistic infections.
9. Pulmonary inflammation due to therapeutic or environmental agents.
10. Sarcoidosis.
11. Tuberculosis.
12. Interstitial nephritis.
13. Inflammatory bowel disease.

For the pregnant or potentially pregnant patient, see the ACR Practice Guideline for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation.

IV. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the ACR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals.

V. SPECIFICATIONS OF THE EXAMINATION

The written or electronic request for scintigraphy for inflammation and infection should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance and interpretation.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state's scope of practice requirements. (ACR Resolution 35, adopted in 2006)

A. Radiopharmaceuticals

1. Gallium-67 citrate

   Gallium-67 citrate in the carrier-free state, given intravenously, binds to plasma transferrin and is transported to inflamed and infected tissues, where it traverses the porous capillary endothelium. Uptake of gallium in infection also may depend in part on bacterial uptake, both direct and indirect via siderophores, as well as macrophage binding. A small amount of gallium is probably transported bound to circulating neutrophils. It also accumulates in certain tumors (especially in lymphomas and lung carcinoma; see the ACR–SPR Practice Guideline for the Performance of Tumor Scintigraphy [with Gamma Cameras]) and in traumatized tissue.

   Imaging usually is performed 18 to 72 hours after tracer administration**;** however, if appropriate, imaging may be performed as early as 4 hours or as late as 7 days after injection. Imaging at multiple time points may be useful to reduce false positive and false negative studies related to bowel and renal activity. Single photon emission computed tomography (SPECT) imaging of relevant sites also may be useful in selected cases.

   Administered activities of 5.0 to 10.0 millicuries (185 to 370 MBq) may be given to adults. Administered activity for children is 0.04 to 0.07 millicurie/kg (1.5 to 2.6 MBq/kg), with a minimum of 0.25 millicurie (9 MBq). Administered activity for children should be determined based on body weight and should be as low as reasonably achievable for diagnostic image quality.

2. Radiolabeled leukocytes (indium-111 oxine or technetium-99m-exametazime [HMPAO])

   In vitro labeling of leukocytes is an exacting process that requires isolation of the cells from the patient's blood (or from a donor in unusual circumstances in which the patient is severely leukopenic), separation of the cells from plasma, labeling of the cells, resuspension in plasma, and reinjection as soon as possible after labeling.

   It is imperative that the labeled leukocytes (as with any blood product) be administered only to the patient for whom they are intended. There must be a written policy for the handling of radiolabeled blood products that will ensure that all samples are positively identified as to source and that reinjection of these agents occurs only into the correct patient.

   a. Indium-111 oxine-labeled leukocytes

      Imaging normally is performed at 18 to 24 hours after injection. However, the performance of an early (1 to 3 hours) study, especially when inflammatory bowel disease is suspected, may be appropriate. Additional imaging may be done at 48 hours. SPECT imaging of relevant sites also may be useful in selected cases.

      The usual adult administered activity is 500 microcuries (18.5 MBq). Administered activity for children should be determined based on body weight and should be as low as reasonably achievable for diagnostic image quality. The administered activity for children is 0.0075 to 0.015 millicurie/kg, with a minimum of 0.050 millicurie (1.8 MBq).

   b. Technetium-99m exametazime-labeled leukocytes

      Images may be acquired as early as 0.5 to 3 hours and as late as 24 hours after injection. The 6-hour physical half-life of technetium-99m effectively precludes delayed imaging beyond 24 hours.

      Hydrophilic technetium-99m complexes formed by tracer elution from leukocytes appear in the urinary tract shortly after injection, and may appear in normal bowel on images obtained as early as 3 hours after injection. Activity occasionally also is seen in the normal gall bladder.

      Administered activity of 10 to 20 millicuries (370 to 740 MBq) may be given to adults. The administered activity for children is 0.1 to 0.2 millicurie/kg (3.7 to 7.4 MBq/kg), with a minimum of 0.5 millicurie (18 MBq). Administered activity for children should be determined based on body weight and should be as low as reasonably achievable for diagnostic image quality.

3. ^{18}F-fluorodeoxyglucose (FDG)

   FDG is transported into cells via glucose transporters and phosphorylated to ^{18}F-2-FDG-6 phosphate, but it is not metabolized. Cellular uptake of FDG is related to the cellular metabolic rate and to the number of glucose transporters. Activated leukocytes demonstrate increased glucose transporter expression, and the affinity of these glucose transporters for deoxyglucose is thought to be increased.

   Images obtained with positron emission tomography using PET (FDG-PET) have a distinctly higher spatial resolution than those obtained with single photon emitting tracers. Results are available within 1 to 2 hours after tracer administration. Physiologic FDG uptake in most normal organs, except the brain, heart, and genitourinary tract, is quite low resulting in relatively high target to background ratios. Under normal conditions, the bone marrow has a low glucose metabolism, potentially facilitating the differentiation of inflammatory cellular infiltrates from hematopoietic marrow. Compared to infection, degenerative bone changes usually demonstrate only mildly increased FDG uptake. Patient preparation, tracer dose, and imaging protocols for FDG-PET imaging of inflammation and infection have not been established.

B. Patient-Related Issues

When gallium-67 citrate is used, bowel activity may obscure detail in the abdomen. Preparation of the colon using enemas and/or a mild laxative is of questionable value. For this reason, gallium-67 citrate may not be optimal for patients whose disease is in the abdomen. In patients with diminished plasma transferrin or iron overload, altered biodistribution may occur, resulting in impaired localization of sites of inflammation or infection. Gallium-67 citrate is useful for evaluating the patient with a FUO, most opportunistic infections, discitis/spinal osteomyelitis, and pulmonary inflammation due to drug toxicity, sarcoidosis, tuberculosis, and interstitial nephritis. Gallium-67 citrate is superior to radiolabeled leukocytes for discitis/spinal osteomyelitis,

tuberculosis, and some bacterial, fungal, and chronic, infections.

Labeled leukocyte imaging is useful in patients with a FUO (especially when infection is a likely etiology), inflammatory bowel disease, and cardiovascular and postoperative infections. It is also useful for differentiating infection from tumor, and for musculoskeletal infections, except in the spine. Removal of dressings contaminated with wound drainage can reduce false positive results. Correlation of labeled leukocyte images with bone marrow images (performed with technetium-99m sulfur colloid) appears to improve the accuracy of the test for diagnosing osteomyelitis.

There are advantages and disadvantages to both indium-111 labeled and technetium-99m labeled leukocytes. Advantages of technetium-99m labeled leukocytes include photon energy optimal for gamma camera imaging, higher resolution images, lower patient radiation dose and the ability to detect abnormalities within a few hours after injection. Disadvantages include urinary tract activity, which appears shortly after injection, and colonic activity, which appears by 3 to 4 hours after injection. The instability of the label and the short half-life of technetium-99m are disadvantages when delayed 24-hour imaging is needed.

Advantages of the indium-111 label are a very stable label and a normal distribution of activity limited to the liver, spleen, and bone marrow. The 67-hour half-life of indium-111 allows for delayed imaging, which may be valuable for musculoskeletal infection. Patients with musculoskeletal infection often require bone or marrow scintigraphy, which can be performed while the patient's cells are being labeled, as simultaneous dual isotope acquisitions, or immediately after completion of the indium-labeled leukocyte study. When technetium-99m is the radiolabel used, an interval of at least 48 hours, and preferably 72 hours, is required between the labeled leukocyte and bone or bone marrow scans. Disadvantages of the indium label include less than ideal photon energies, lower resolution images, higher patient radiation dose and the fact that an 18 to 24-hour interval between injection and imaging generally is required.

Technetium-99m labeled leukocytes are best suited to imaging acute inflammatory conditions, such as inflammatory bowel disease, while indium-111 labeled leukocytes may be preferable for more indolent conditions, such as prosthetic joint infection.

FDG's exquisite sensitivity suggests that it may be useful in a FUO, an entity with diverse etiologies. In addition to tumor and infection, other conditions that may present as a FUO, including vasculitis, thromboembolic disease, sarcoidosis, and chronic granulomatous disease, are associated with increased FDG uptake. FDG-PET appears to be sensitive for detecting focal infection and may be useful for detecting infected prosthetic vascular grafts, mycotic aneurysms, lung abscesses and intra-abdominal infections. FDG-PET also may be useful for diagnosing musculoskeletal infection, especially in the setting of previous trauma and metallic implants. The fact that increased uptake of FDG occurs in many neoplasms is both a relative advantage and a relative disadvantage.

VI. EQUIPMENT SPECIFICATIONS

A gamma camera equipped with a medium-energy collimator is used for imaging gallium-67 and indium-111 leukocytes. A low-energy, all-purpose/general all-purpose (LEAP/GAP) collimator or a high-resolution collimator may be used with technetium-99m leukocytes. While a small-field-of-view (SFOV) camera (250 to 300 mm) may be used, the detector head must be shielded adequately if the isotope used is gallium-67 or indium-111. A large-field-of-view (LFOV) camera (≥400 mm) head is preferable, especially when imaging a large area of the body.

For each of the 3 radiopharmaceuticals, images may be obtained either as multiple spot views or as whole-body surveys. The following techniques are suggested (assuming adult administered activity):

Radiopharmaceuticals	SFOV Camera	LFOV Camera
Gallium-67		
Spot images	50,000 to 300,000 counts	100,000 to 500,000 counts
Whole body		5 cm/min (40 min maximum)
Indium-111 leukocytes		
Spot images	30,000 to 60,000 counts	50,000 to 100,000 counts
Whole body		5 cm/min (40 min maximum)
Technetium-99m leukocytes		
Spot image	50,000 to 300,000 counts	100,000 to 500,000 counts
Whole body		5 cm/min (40 min maximum)

SPECT may be performed. If a single-head camera is used with gallium-67, a 6 degree sampling angle, 360 degree rotation, 64 x 64 matrix, and 20 to 25 seconds per stop (50,000 to 80,000 counts per stop) are suggested. If a multihead (2 or more) system is used with gallium-67, one should use a 3 degree sampling angle, 64 x 64 matrix, and 20 to 25 seconds per stop (50,000 to 80,000 counts per stop). SPECT/CT imaging also may be helpful.

VII. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Guideline for Communication of Diagnostic Imaging Findings.

The report should include the radiopharmaceutical used and the dose and route of administration, as well as any other pharmaceuticals administered, also with dose and route of administration.

VIII. RADIATION SAFETY

Radiologists, imaging technologists, and all supervising physicians have a responsibility to minimize radiation dose to individual patients, to staff, and to society as a whole, while maintaining the necessary diagnostic image quality. This concept is known as "as low as reasonably achievable (ALARA)."

Facilities, in consultation with the radiation safety officer, should have in place and should adhere to policies and procedures for the safe handling and administration of radiopharmaceuticals, in accordance with ALARA, and must comply with all applicable radiation safety regulations and conditions of licensure imposed by the Nuclear Regulatory Commission (NRC) and by state and/or other regulatory agencies. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol.

IX. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *Position Statement on QC & Improvement, Safety, Infection Control, and Patient Education* on the ACR web page (http://www.acr.org/guidelines).

Equipment performance monitoring should be in accordance with the ACR Technical Standard for Medical Nuclear Physics Performance Monitoring of Gamma Cameras.

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Suggested Reading (Additional articles that are not cited in the document but that the committee recommends for further reading on this topic)

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*Guidelines and standards are published annually with an effective date of October 1 in the year in which amended, revised or approved by the ACR Council. For guidelines and standards published before 1999, the effective date was January 1 following the year in which the guideline or standard was amended, revised, or approved by the ACR Council.

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