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The American College of Radiology will periodically define new practice parameters and technical standards for radiologic practice to help advance the science of radiology and to improve the quality of service to patients throughout the United States. Existing practice parameters and technical standards will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice parameter and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review and approval. The practice parameters and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice parameter and technical standard by those entities not providing these services is not authorized.

Revised 2018 (Resolution 28)*

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

PREAMBLE

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care¹. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents 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 practitioner in light of all the circumstances presented. Thus, an approach that differs from the guidance in this document, 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 this document 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 this document. However, a practitioner who employs an approach substantially different from the guidance in this document 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 the guidance in this document 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 this document is to assist practitioners in achieving this objective.

¹ Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing, ___ N.W.2d ___ (Iowa 2013) Iowa Supreme Court refuses to find that the *ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures* (Revised 2008) sets a national standard for who may perform fluoroscopic procedures in light of the standard’s stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, Stanley v. McCarver, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that “published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation” even though ACR standards themselves do not establish the standard of care.

I. INTRODUCTION

This practice parameter was revised collaboratively by the American College of Radiology (ACR) and the Society for Pediatric Radiology (SPR).

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 occult or overt inflammatory and infectious conditions. Correlation with clinical findings and/or other imaging modalities is imperative for maximum diagnostic yield.

For this practice parameter, discussion is limited solely to radiopharmaceuticals that are not organ-specific. The reader is referred to the practice parameters covering scintigraphy of specific organs (eg, the [ACR–SPR Practice Parameter for the Performance of Skeletal Scintigraphy \(Bone Scan\)](#) for osteomyelitis and the [ACR–SPR Practice Parameter for the Performance of Hepatobiliary Scintigraphy](#) for acute cholecystitis) for a discussion of those organs [1,2].

Application of this practice parameter should be in accordance with the [ACR–SPR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals](#) [3].

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

II. INDICATIONS AND CONTRAINDICATIONS

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

1. Musculoskeletal infections such as disc space, joint space, prosthetic joint and other orthopedic hardware, osteomyelitis superimposed on existing bone pathology, osteomyelitis in diabetic patients, and differentiating osteomyelitis from bone infarction
2. Fever of unknown origin (FUO)
3. Detection and localization of an unknown source of sepsis (occult infection)
4. Detection of an additional site of infection in patients with persistent or recurrent fever and a known site of infection
5. Postoperative infections
6. Cardiovascular infections (eg, prosthetic vascular graft, mycotic aneurysms, infective endocarditis involving native and prosthetic valves, cardiac implantable electronic devices)
7. Differentiation of infection from tumor
8. Mycobacterial infections (eg, tuberculosis)
9. Opportunistic infections
10. Pulmonary inflammation due to therapeutic or environmental agents.
11. Granulomatous diseases (eg, sarcoidosis)
12. Interstitial nephritis
13. Inflammatory bowel disease

The [ACR–SPR Practice Parameter for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation](#) provides useful information on radiation risks to the fetus regardless of source. Information on managing pregnant or potentially pregnant patients undergoing nuclear medicine procedures is available from the International Commission on Radiological Protection [4-6].

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the [ACR–SPR Technical Standard for Diagnostic Procedures Using Radiopharmaceuticals](#) [3].

IV. 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 – revised in 2016, Resolution 12-b)

Radiopharmaceuticals and Imaging

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. Gallium uptake in infection also may depend in part on bacterial uptake, as well as macrophage binding and binding to the leukocyte-derived tissue lactoferrin.

A small amount of gallium probably is transported bound to circulating leukocytes. Gallium also accumulates in certain tumors (especially in lymphomas and lung carcinomas) and in traumatized tissue [7].

Imaging usually is performed 18 to 72 hours after radiopharmaceutical 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 [7]. Single photon emission computed tomography (SPECT) and SPECT/CT of relevant sites also may be useful in selected cases [8].

Administered activities of 4.0 to 6.0 mCi (150 to 220 MBq) may be given to adults. The usual administered activity in children is 1.5 to 2.6 MBq/kg (0.04 to 0.07 mCi/kg) with a minimum administered activity of 9 to 18 MBq (0.25 to 0.5 mCi).

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 FUO; most opportunistic infections to include pneumocystis jiroveci pneumonia and other pulmonary conditions (eg, drug toxicity, sarcoidosis, mycobacterium, early radiation pneumonitis, vasculitis, pneumoconioses, idiopathic pulmonary fibrosis, connective tissue disease); discitis/spinal osteomyelitis; skull base osteomyelitis/malignant otitis externa; and interstitial nephritis [9]. Gallium-67 citrate is superior to radiolabeled leukocytes for discitis/spinal osteomyelitis, tuberculosis, and some bacterial, fungal, and chronic infections [7].

2. Radiolabeled autologous leukocytes (indium-111 oxine or technetium-99m-exametazime)

In vitro labeling of leukocytes is an exacting process that requires isolation of the cells from the patient's blood. This process is performed by separating the leukocytes from plasma, labeling of the cells,

resuspension of the labeled cells in plasma, and reinfusion as soon as possible after labeling. Although this process results in a high labeling efficiency (~95%), the majority of these labeled leukocytes are neutrophils [10].

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 ensures that all samples are positively identified as to source and that of these radiopharmaceuticals occurs only into the correct patient.

Labeled leukocyte imaging is useful in patients with FUO (especially when infection is a likely etiology), inflammatory bowel disease, postoperative infections, and cardiovascular infections including infective endocarditis and cardiac implantable electronic device infections. It is also useful for differentiating infection from tumor and for musculoskeletal infections, except those involving the spine and skull base, the latter when there is concern for malignant otitis externa. 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, improves the accuracy of the examination for diagnosing acute osteomyelitis [11-14].

Technetium-99m-labeled leukocytes are best suited for use in pediatric patients (due to a lower radiation dose to the spleen than indium-111 labeled leukocytes) and for imaging acute inflammatory conditions, such as inflammatory bowel disease, whereas indium-111-labeled leukocytes may be preferable for more indolent conditions, such as prosthetic joint infection [14].

a. Indium-111 oxine-labeled leukocytes

Imaging usually is performed 18 to 30 hours after reinfusion of the labeled cells. However, the performance of early (1 to 3 hours) imaging, especially when inflammatory bowel disease is suspected, may be appropriate. Additional imaging may be done at 48 hours. SPECT and SPECT/CT of relevant sites also may be useful in selected cases [8].

Administered activities of 0.3 to 0.5 mCi (11.1 to 18.5 MBq) may be given to adults. The administered activity for children, which should be based on body weight, is 0.0135 mCi/kg (0.25 MBq/kg), with a minimum of 0.06 mCi (2.3 MBq). The usual administered activity of indium-111 labeled leukocytes in children is 0.15 to 0.25 MBq/kg (0.007 to 0.0135 mCi/kg). Minimum administered activity is 1.85 to 2.3 MBq (0.05 to 0.06 mCi) and maximum administered activity is 18.5 MBq (0.5 mCi).

Advantages of the indium-111 label include a very stable label and a normal biodistribution 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. Complementary bone (technetium-99m methylene diphosphonate [MDP]) or marrow (technetium-99m sulfur colloid) scintigraphy can be performed while the patient's cells are being labeled, as simultaneous dual radiopharmaceutical acquisitions, or immediately after completion of the indium-labeled leukocyte examination [14]. Disadvantages of the indium label include less than ideal photon energies, lower-resolution images, higher patient radiation absorbed dose, and the fact that an 18- to 30-hour interval between reinfusion of labeled leukocytes and imaging generally is required [14].

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 reinfusion of labeled leukocytes. The 6-hour physical half-life of technetium-99m effectively precludes imaging beyond 24 hours [14].

Hydrophilic technetium-99m complexes formed by radiopharmaceutical 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 gallbladder [14].

Administered activity of 5 to 10 mCi (185 to 370 MBq) may be given to adults. The administered activity for children, which should be based on body weight, is 0.2 mCi/kg (7.4 MBq/kg), with a minimum of 2 mCi (37 MBq) [15].

Advantages of the technetium-99m label compared to the indium-111 label include photon energy optimal for gamma camera imaging, higher-resolution images, lower patient radiation absorbed dose, and the ability to detect abnormalities within a few hours after injection [14].

Disadvantages include urinary tract activity, which appears shortly after injection, and bowel 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. Patients with musculoskeletal infection often require bone or marrow scintigraphy. When technetium-99m-labeled leukocytes are used, an interval of 48 to 72 hours is required between the labeled leukocyte and bone or bone marrow scans [13].

3. Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)

Cellular uptake of FDG is governed by three mechanisms: passive diffusion, active transport by a Na-dependent glucose transporter (SGLT), and via GLUT-1 through GLUT-13 transporters, with the GLUT-1 through GLUT-3 transporters being the most important pathway in human cells and granulation tissue. Once inside the cell FDG is phosphorylated to F-18 FDG-6 phosphate but is not metabolized. [16].

Images obtained with positron emission tomography (FDG-PET) have a distinctly higher spatial resolution than those obtained with single photon emitting radiopharmaceuticals. Results are available within 1 to 2 hours after radiopharmaceutical administration. Physiologic FDG uptake in most normal organs, except the brain, heart, and urinary 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. Optimal patient preparation, radiopharmaceutical administered activity, and imaging protocols for FDG-PET imaging of inflammation and infection have not been established, but FDG-PET tumor imaging protocols and dosages may be used. For adults, the administered activity should be 185 to 740 MBq (5 to 20 mCi) of FDG. For children, the administered activity should be determined based on body weight and should be as low as reasonably achievable. The typical pediatric range of administered activity of FDG is 3.7 to 5.2 MBq/kg (0.10 to 0.14 mCi/kg), with a minimum administered activity of 26 MBq (0.7 mCi). For additional details about FDG tumor imaging protocols, see the [ACR-SPR Practice Parameter for Performing FDG-PET/CT in Oncology](#) [17].

The exquisite sensitivity of FDG makes this radiopharmaceutical very useful in FUO, an entity with diverse etiologies. In addition to tumor and infection, other conditions that may present as FUO, including vasculitis, thromboembolic disease, sarcoidosis, and chronic granulomatous disease, are associated with increased FDG uptake [18,19]. FDG is sensitive for detecting focal infection and may be useful for detecting infective endocarditis, cardiac implantable electronic device infections, prosthetic vascular graft infections, mycotic aneurysms, lung abscesses, and intra-abdominal infections [20-22]. FDG also may be useful for diagnosing musculoskeletal infection, especially spinal infections [13].

V. 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, preferably, a high-resolution collimator is used with technetium-99m leukocytes. Although a small-field-of-view (SFOV) camera

(250 to 300 mm) may be used, the detector head must be shielded adequately if the radiopharmaceutical 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):

<u>Gallium-67</u>	<u>SFOV Camera</u>	<u>LFOV Camera</u>
Spot Images	50,000 to 300,000 counts	100,000 to 500,000 counts
Whole body		5 cm/min (40 min maximum)

SPECT: Data should be acquired for 20 to 25 seconds per angular sampling (50,000 to 80,000 counts per sample) over a 360-degree rotation using a 64×64 matrix.

<u>Indium-111</u>	<u>SFOV Camera</u>	<u>LFOV Camera</u>
leukocytes	30,000 to 60,000 counts	50,000 to 100,000 counts
Spot images		
Whole body		5 cm/min (40 min maximum)

SPECT: Because of the low count rate, a dual or multidetector unit is recommended. For head and body, data should be acquired for 25 to 30 seconds per angular sampling over a 360-degree rotation, using a 64×64 matrix. For the extremities, especially the feet, acquisition time should be increased to 45 to 60 seconds per angular sampling. Iterative reconstructions with collimator corrections specific to indium-111 improve image quality.

<u>Technetium-99m leukocytes</u>	<u>SFOV Camera</u>	<u>LFOV Camera</u>
Spot image	50,000 to 300,000 counts	100,000 to 500,000 counts
Whole body		5 cm/min (40 min maximum)

SPECT: Data should be acquired for 30 seconds per angular sampling using a 128×128 matrix over a 360-degree rotation. Iterative reconstruction with collimator corrections specific to technetium-99m, along with scatter and attenuation corrections may improve image quality.

VI. DOCUMENTATION

Reporting should be in accordance with the [ACR Practice Parameter for Communication of Diagnostic Imaging Findings](#) [23].

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

VII. RADIATION SAFETY

Radiologists, medical physicists, registered radiologist assistants, radiologic technologists, and all supervising physicians have a responsibility for safety in the workplace by keeping radiation exposure to staff, and to society as a whole, “as low as reasonably achievable” (ALARA) and to assure that radiation doses to individual patients are appropriate, taking into account the possible risk from radiation exposure and the diagnostic image quality necessary to achieve the clinical objective. All personnel that work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection and application of dose limits) and the principles of proper management of radiation dose to patients (justification, optimization and the use of dose reference levels)

http://www-pub.iaea.org/MTCD/Publications/PDF/Pub1578_web-57265295.pdf.

Facilities and their responsible staff should consult with the radiation safety officer to ensure that there are policies and procedures for the safe handling and administration of radiopharmaceuticals and that they are adhered to in accordance with ALARA. These policies and procedures 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

Nationally developed guidelines, such as the ACR's [Appropriateness Criteria](#)[®], should be used to help choose the most appropriate imaging procedures to prevent unwarranted radiation exposure.

Additional information regarding patient radiation safety in imaging is available at the Image Gently[®] for children (www.imagegently.org) and Image Wisely[®] for adults (www.imagewisely.org) websites. These advocacy and awareness campaigns provide free educational materials for all stakeholders involved in imaging (patients, technologists, referring providers, medical physicists, and radiologists).

Radiation exposures or other dose indices should be measured and patient radiation dose estimated for representative examinations and types of patients by a Qualified Medical Physicist in accordance with the applicable ACR Technical Standards. Regular auditing of patient dose indices should be performed by comparing the facility's dose information with national benchmarks, such as the ACR Dose Index Registry, the NCRP Report No. 172, Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States or the Conference of Radiation Control Program Director's National Evaluation of X-ray Trends. (ACR Resolution 17 adopted in 2006 – revised in 2009, 2013, Resolution 52).

VIII. 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 website (<https://www.acr.org/Clinical-Resources/Practice-Parameters-and-Technical-Standards>).

Equipment performance monitoring should be in accordance with the [ACR–AAPM Technical Standard for Nuclear Medical Physics Performance Monitoring of Gamma Cameras](#) [24].

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