

Society of Nuclear Medicine Procedure Guideline for Gallium Scintigraphy in Inflammation

Version 3.0, approved June 2, 2004

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I. Purpose

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting, and reporting the results of ^{67}Ga inflammation scintigraphy. Alternative techniques, such as labeled leukocytes, should be considered if clinically indicated.

II. Background Information and Definitions

^{67}Ga scintigraphy may include regional, whole-body, planar, and SPECT scintigrams, or any combination performed after intravenous injection of ^{67}Ga -citrate.

III. Examples of Clinical or Research Applications

- A. Whole-body survey to localize source of fever in patients with fever of unknown origin (FUO).
- B. Detection of pulmonary and mediastinal inflammation/infection, especially in the immunocompromised patient.
- C. Evaluation and follow-up of active lymphocytic or granulomatous inflammatory processes, such

as sarcoidosis or tuberculosis.

- D. Diagnosing osteomyelitis and/or disk space infection. ^{67}Ga is preferred over labeled leukocytes for disk space infection and vertebral osteomyelitis.
- E. Diagnosis and follow-up of medical treatment of retroperitoneal fibrosis.
- F. Evaluation and follow-up of drug-induced pulmonary toxicity (e.g., bleomycin, amiodarone).

IV. Procedure

A. Patient Preparation

Bowel preparation with oral laxatives and/or enemas before imaging will usually decrease the amount of activity within the bowel and reduce radiation dose. Routine use of a bowel preparation is recommended unless the patient is too ill or unable to eat solid food.

B. Information Pertinent to Performing the Procedure

1. Recent hemolysis or blood transfusion, which can alter ^{67}Ga localization.
2. Recent surgery, diagnostic procedures, or trauma.
3. Recent chemotherapy, radiation therapy, or

The Society of Nuclear Medicine (SNM) has written and approved these guidelines as an educational tool designed to promote the cost-effective use of high-quality nuclear medicine procedures or in the conduct of research and to assist practitioners in providing appropriate care for patients. The guidelines should not be deemed inclusive of all proper procedures nor exclusive of other procedures reasonably directed to obtaining the same results. They are neither inflexible rules nor requirements of practice and are not intended nor should they be used to establish a legal standard of care. For these reasons, SNM cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment about the propriety of any specific procedure or course of action must be made by the physician when considering the circumstances presented. Thus, an approach that differs from the guidelines is not necessarily below the standard of care. A conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in his or her reasonable judgment, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the guidelines.

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.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

gadolinium administration for MRI.

4. History of chronic infections, immune suppression, or malignancy.
5. Results of radiographs and other diagnostic tests.

C. Precautions

Lactation and pregnancy are relative contraindications. If the patient is willing to permanently discontinue breast-feeding and the gallium study is not emergent, the patient should be asked to stop breast-feeding 2 wk before the gallium injection. This precaution will significantly decrease the radiation dose to the breast.

If the examination is urgent, the breast-feeding patient must be asked to discontinue breast-feeding for approximately 2–4 wk after the gallium injection. This precaution will significantly decrease the radiation dose to the nursing infant.

D. Radiopharmaceutical

1. ^{67}Ga -citrate has a physical half-life of 78 h. The principal photopeaks are: 93 keV (40%), 184 keV (24%), 296 keV (22%), and 388 keV (7%). For the adult, the usual administered activity is 150–220 MBq (4–6 mCi) intravenously, and up to 330 MBq (9 mCi) is suggested in large patients. The usual administered activity in children is 1.5–2.6 MBq/kg (0.04–0.07 mCi/kg) with a minimum dose of 9–18 MBq (0.25–0.5 mCi). The maximum administered activity in children should not exceed the maximum administered activity for adults.
2. Normal distribution: About 10%–25% of the injected dose is excreted by the kidneys during the first 24 h after injection. After this time, the principal route of excretion is the gastrointestinal tract. By 48 h after injection, about 75% of the injected dose remains in the body and is equally distributed among the liver, bone and bone marrow, and soft tissues. Normal distribution is variable, with increased localization in the nasopharynx, lacrimal glands, thymus, breasts, liver, and spleen.

E. Image Acquisition

1. A large-field-of-view multipeak gamma camera equipped with a medium-energy parallel-hole collimator is preferred. A low-energy collimator cannot be used. Energy discrimination is accomplished by using 15%–20% windows centered around 2 (93 and 184 keV) or 3 (93, 184, and 296 keV) of the principal photopeaks. The 93-keV window is usually not used within 24–36 h of a $^{99\text{m}}\text{Tc}$ tracer injection or in very obese patients.
2. Scintigrams are generally obtained 24–72 h after injection of the radiopharmaceutical. De-

layed scintigrams at 96 h or later may be necessary for accurate interpretation and are particularly helpful in the abdomen when normal colonic and renal activity can make scintigram interpretation difficult. Early 3–4-h scintigrams can be helpful in cases of acute inflammation to avoid extensive bowel activity.

3. For whole-body scintigraphy, anterior and posterior scintigrams are obtained. These scintigrams should be acquired for 1.5–2.0 million counts/whole-body, or 25–35 min, whichever comes first. For adults, this corresponds to a minimum scan speed of 6–8 cm/min. For regional scintigrams of the chest, they are obtained for 250,000–1,000,000 total counts (5–20 min). Regional scintigrams of the remainder of the body should be obtained for the same time. The large range in counts obtained (and the maximum time per image) is necessary because what is practical depends on (a) the time after the injection that the images are obtained, and (b) the ability of the patient to cooperate.
4. SPECT Imaging
See the Society of Nuclear Medicine Procedure Guideline for General Imaging.

F. Interventions

None. Bowel preparation is optional.

G. Processing

See the Society of Nuclear Medicine Procedure Guideline for General Imaging.

H. Interpretation Criteria

Accurate interpretation of gallium scintigraphy requires knowledge of the normal and abnormal variants of ^{67}Ga localization.

1. Pulmonary Infection
Immunocompromised patients (AIDS and postchemotherapy patients and transplant recipients).
 - a. In a nontreated patient, a negative gallium scan excludes infection with a high degree of certainty.
 - b. Negative gallium scintigraphy in an AIDS patient with an abnormal chest x-ray suggests the diagnosis of Kaposi's sarcoma.
 - c. Increased hilar and mediastinal lymph node activity is frequently caused by *Mycobacterium avium intracellulare*, *Mycobacterium tuberculosis*, and lymphoma.
 - d. Focal increased pulmonary parenchymal activity usually indicates neoplasm or bacterial pneumonia. *Pneumocystis carinii* pneumonia (PCP) may occasionally present in this fashion.

Radiation Dosimetry: Adults*

Radiopharmaceuticals	Administered activity MBq (mCi)	Organ receiving the largest radiation dose mGy/MBq (rad/mCi)	Effective dose equivalent mSv/MBq (rem/mCi)
⁶⁷ Ga-citrate	150–220 iv (4–6)	0.2 Lower large intestine (0.74)	0.12 (0.44)

* International Commission on Radiological Protection. *Radiation Dose to Patients from Radiopharmaceuticals*. ICRP Publication 53. London, UK: ICRP; 1988:142.

MIRD Committee Dose Estimate Report No. 2, Radiation Absorbed Dose for Ga-66, Ga-67, Ga-68, and Ga-72 Citrate. *J Nucl Med*. 1973;14:755–756.

Radiation Dosimetry: Children* (5 Years Old)

Radiopharmaceuticals	Administered activity MBq/kg (mCi/kg)	Organ receiving the largest radiation dose mGy/MBq (rad/mCi)	Effective dose equivalent mSv/MBq (rem/mCi)
⁶⁷ Ga-citrate	1.5–2.6 iv (0.04–0.07)	0.72 Lower large intestine (2.7)	0.40 (1.5)

* International Commission on Radiological Protection. *Radiation Dose to Patients from Radiopharmaceuticals*. ICRP Publication 53. London, UK: ICRP; 1988:142.

MIRD Committee Dose Estimate Report No. 2, Radiation Absorbed Dose for Ga-66, Ga-67, Ga-68, and Ga-72 Citrate. *J Nucl Med*. 1973;14:755–756.

- e. Diffuse increased pulmonary activity
 - i. The intensity of activity usually corresponds to the degree of active inflammation and may be graded relative to hepatic localization. (Note: hepatic uptake may be decreased in AIDS and acute lymphocytic leukemia.)
 - ii. In general, more intense activity is likely to be PCP. Although less intense activity can be seen in PCP, it is also associated with other opportunistic infections such as cytomegalovirus, fungal pneumonia, and partially treated PCP.
 - iii. Increased pulmonary activity predominantly in the upper lungs is associated with PCP in patients receiving aerosolized pentamidine. Increased pulmonary activity confined to the upper lungs is also associated with mycobacterial disease, but there are usually corresponding chest x-ray abnormalities.
2. Abnormal pulmonary localization in patients with a suspected inflammation and/or FUIO
 - a. Additional causes for diffuse increased pulmonary activity include idiopathic pulmonary fibrosis, sarcoidosis, interstitial pneumonitis, drug toxicity, radiation pneumonitis, lymphangitic metastatic cancer, and reaction to contrast (lipiodol) in the lungs.
 - b. Additional causes for increased hilar and mediastinal lymph node activity include sarcoidosis, tuberculosis, and lymphoma.
 - c. Mild-to-moderate perihilar uptake can also be seen as a normal variant in patients who are smokers or after recent chemotherapy.

3. Osteomyelitis, which may be complicated by other osseous pathology. In general, for diagnosing osteomyelitis, ^{67}Ga scintigrams are interpreted together with $^{99\text{m}}\text{Tc}$ bone scintigrams according to the following criteria:
 - a. The combined bone/gallium study is negative for infection in untreated patients when (1) gallium scintigraphy is negative, regardless of the bone scintigraphy results; or (2) the distribution activity on both studies is spatially congruent and the relative intensity of gallium activity is less than that of bone activity.
 - b. The combined bone/gallium study is positive for infection when (1) the distribution of activity on both studies is spatially congruent and the relative intensity of gallium activity is greater than that of bone activity; or (2) the distribution of activity on both studies is spatially incongruent, with gallium activity exceeding bone activity in at least 1 area.
 - c. The combined bone/gallium study is equivocal for infection when the distribution of activity on both studies is spatially congruent and the relative intensity of the gallium activity is equal to the bone activity. This result can occur in patients who are taking antibiotics and are partially treated.

Note: In the presence of generalized increased intensity of skeletal activity, focal inflammatory or neoplastic lesions of the skeleton may not be apparent on images.
4. Other nonosseous sites of abnormal ^{67}Ga localization can also signify the presence of infection/inflammation (e.g., sinusitis, infected renal or hepatic cysts, intraabdominal abscess, joint sepsis, etc.). Detection of occult sites of infection/inflammation in patients with FUO is a common indication for ^{67}Ga scintigraphy.

I. Reporting

The report should include the following information:

1. Indication for the study
2. Procedure
 - a. Dose of radiopharmaceutical.
 - b. Time(s) of acquisition postinjection.
 - c. Type of images (total body, regional, SPECT).
3. Findings
 - a. Site(s) of abnormal localization.
 - b. Degree of localization compared with liver, bone, or bone marrow uptake and whether it increases over time if delayed images were obtained.

- c. Comparison of site and extent of uptake with other available scintigraphic images (i.e., bone scan).
4. Study limitations or confounding factors
5. Impression (e.g., positive, negative, indeterminate)
 - a. The clinical significance of the findings.
 - b. If appropriate, differential clinical diagnosis.

J. Quality Control

^{67}Ga is available in unit dose or multidose vials as ^{67}Ga -citrate, ready for injection. Refer to the Society of Nuclear Medicine Procedure Guideline for Use of Radiopharmaceuticals for more details. Gamma camera quality control measures will vary from camera to camera. Spatial registration of photons detected must be checked periodically. Refer to the Society of Nuclear Medicine Procedure Guideline for General Imaging for more details.

K. Sources of Error

1. Residual bowel activity is probably the most common cause for both false-positive and false-negative interpretations.
2. Hilar nodal localization (usually low-grade) can be seen as a normal variant in adult patients, particularly in smokers.
3. In children and teenagers, increased activity can be seen in thymic hyperplasia after chemotherapy. Below 2 y of age, increased thymic activity is common.
4. Gadolinium administered for MRI enhancement within 24 h before gallium injection has been observed to decrease gallium localization.
5. Saturation of iron-binding transferrin sites (e.g., hemolysis or multiple blood transfusions) causes altered gallium distribution.
6. ^{67}Ga uptake at sites of bone repair secondary to healing fractures or prior orthopedic hardware sites, loose prostheses, or after successful treatment of osteomyelitis may complicate interpretation in patients with suspected osteomyelitis.
7. Recent chemotherapy and radiation therapy.
8. Desferoxamine therapy.
9. Increased breast activity.
10. Hilar, submandibular and diffuse pulmonary localization in patients with lymphoma during therapy.
11. Radiation sialadenitis causing increased localization.
12. Uptake in a variety of tumors (lymphoma, hepatoma, lung cancer).

V. Issues Requiring Further Clarification

- A. Efficacy related to use of ^{111}In -leukocyte or $^{99\text{m}}\text{Tc}$ -leukocyte in many infections.
- B. Minimum administered activity in children.
- C. Efficacy related to use of ^{18}F -FDG PET in patients with FUO.

VI. Concise Bibliography

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