

appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

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

PART VI: ISSUES REQUIRING FURTHER CLARIFICATION

- A. Relative efficacy of ^{111}In -labeled leukocytes and $^{99\text{m}}\text{Tc}$ -labeled leukocytes in different clinical conditions.
- B. Radiation effects using $^{99\text{m}}\text{Tc}$ doses greater than 20 mCi on granulocyte viability during $^{99\text{m}}\text{Tc}$ -HMPAO labeling procedure.

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Procedure Guideline for Gallium Scintigraphy in the Evaluation of Malignant Disease

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Note: All 26 SNM-approved procedure guidelines are available on the Society's home page. We encourage you to download these documents via the Internet at <http://www.snm.org>.

PART I: PURPOSE

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting and reporting the results of ^{67}Ga -citrate imaging in the evaluation of patients with malignant disease.

PART II: BACKGROUND INFORMATION AND DEFINITIONS

- A. Gallium-67 is a group IIIA metal which has been used for imaging a variety of solid neoplasms for more than 25 yr (1).
- B. Gallium-67 imaging of neoplastic disease has shown the greatest utility in imaging lymphoma. This guideline will concentrate on the use of this technique in lymphoma, although the technical aspects of image collection and processing may be applied to the imaging of other neoplastic diseases.
- C. Gallium-67 has proven useful in the management of patients with lymphoma for:
 1. Staging the extent of disease (2,3).
 2. Detecting relapse or progression of disease (4).
 3. Predicting response to therapy (5,6).
 4. Predicting outcome (7).
- D. Meaningful compilation of sensitivity and specificity for imaging lymphoma is difficult because of differences in technique (8), differences in reporting the data regarding the number of lesions detected, and the number of cases detected and variations in histopathology reporting and nomenclature.

PART III: COMMON INDICATIONS

- A. Although many tumors take up gallium, the test has been particularly useful in the management of lymphoma (3). A recent review of gallium imaging in lymphomas was published by McLaughlin et al. (2). Observation of the particular utility of gallium in the lymphomas was noted by Anderson et al. (8).
 1. Hodgkin's Disease (HD)

The overall sensitivity and specificity for the detection of Hodgkin's disease is about 90%, exceeding those of other imaging modalities such as CT or MRI. When CT shows residual soft-tissue mass after therapy ^{67}Ga scintigraphy accurately predicts tumor viability (6,9–12).
 2. Non-Hodgkin's Lymphoma (NHL)

In NHL, ^{67}Ga localization correlates with cell type and proliferative rate of the tumor. Diffuse large-cell lymphomas (DLCL) which include diffuse histiocytic lymphoma (DHL) and poorly differentiated lymphocytic lymphoma (PDLL) represent about two-thirds of newly diagnosed lymphomas and are very gallium avid. Kaplan et al. (13) prospectively evaluated the ability of gallium to define residual disease and predict outcomes in 37 consecutive patients with diffuse large-cell lymphoma. They concluded that continued ^{67}Ga uptake during therapy predicted a poor outcome. Most of the intermediate grade lymphomas and all of the high grade lymphomas demonstrate high gallium avidity. For example, small non-cleaved-cell lymphoma (Burkitt's lymphoma) shows avid ^{67}Ga localization (14). In contrast to the other cell types, low-grade lymphomas such as well-differentiated lymphocytic lymphoma (WDLL) have been found to have poor ^{67}Ga avidity.
 3. Recurrence, Restaging, Management and Outcomes in HD and NHL

Histology is almost always known prior to ordering ^{67}Ga imaging. Thus, an optimal test sequence can be tailored to each patient. Furthermore, in advanced stage disease management and outcome can be influenced by the unique information provided by the ^{67}Ga

scan. Henkin et al. (15) first pointed out the usefulness of ^{67}Ga in the follow-up of patients with HD. Front et al. (4) studied the predictive value of ^{67}Ga in approximately 100 patients with HD and NHL. They documented the utility of gallium scanning in restaging patients and predicting survival (1). The test has much to offer in patients with aggressive lesions, advanced stage, or whose management is otherwise problematic. In these patients it is necessary to know: (a) the gallium avidity of the tumor; (b) the response of the tumor to therapy; and (c) the timing of the therapeutic response. Answers to these questions require performance of sequential studies before, during and after therapy (2,5). Any patient for whom the gallium scan is considered part of the work-up of their disease should undergo a baseline study prior to therapy.

- B. Additional tumors that are gallium-avid include: lung carcinoma, melanoma, hepatocellular carcinoma, sarcomas, testicular tumors, multiple myeloma, head and neck tumors and neuroblastoma. The utility of ^{67}Ga scanning in patients with these tumors has not been thoroughly demonstrated and is not addressed in this guideline.

PART IV: PROCEDURE

- A. Patient Preparation
 1. Bowel preparation is optional. (See section IV.D.)
 2. Oral laxatives prior to imaging may decrease activity in the bowel. Bulk in the diet facilitates transit of ^{67}Ga through the gastrointestinal tract.
- B. Information Pertinent to Performing the Procedure
 1. A relevant history and physical examination are prerequisites to ^{67}Ga tumor imaging. Relevant pathological, radiological and laboratory data should be correlated.
 2. Specific attention should be directed to:
 - a. Tumor cell type, size and location.
 - b. Degree of transferrin saturation (e.g., hemolysis or recent transfusion).
 - c. Interfering drugs such as recent chemotherapy (16,17), treatment with iron preparations (18), chelation therapy or recent MRI with gadolinium contrast agent (19). A more complete list of drugs that may affect ^{67}Ga distribution has been published (20).
 - d. Recent surgery, radiotherapy, diagnostic procedures or trauma (21).
 - e. Presence of any inflammatory lesions or infectious processes.
- C. Precautions
None.
- D. Radiopharmaceutical
 1. Gallium-67 has a half-life of 78 hr. It is supplied as the soluble citrate salt in the +3 oxidation state. The principal photo peaks of ^{67}Ga are 93.3 (37.0%), 184.6 (20.4%), 300 (16.6%) and 393.5 (4.64%) keV. The organ receiving the largest radiation dose (0.2 mSv/MBq [740 mR/mCi]) is the lower large intestine. In children, the largest organ dose is in the physes (growth plates) (22). The recommended activity in adults is 370 MBq (10 mCi) intravenously. The usual administered activity in children is 4.2 MBq/kg (0.110 mCi/kg). The minimum activity administered in children is 18.5 MBq (0.5 mCi).

2. Normal biodistribution: About 10%–15% of the injected dose is excreted by the kidneys during the first 24 hr after injection. After this the principal route of excretion is via the bowel.
3. By 48 hr postinjection, about 75% of the dose remains in the body and is distributed among the liver, bone and bone marrow and soft tissues. The normal distribution is variable and also includes nasopharyngeal, lacrimal, salivary, breast (especially lactating or stimulated), thymus and spleen.

TABLE 1
Radiation Dosimetry in Adults

Radiopharmaceutical	Administered activity MBq (mCi)	Organ receiving the largest radiation dose* mGy (rad)	Effective dose* mSv (rem)
⁶⁷ Ga†	185–370 (5–10)	0.59 Bone surface (2.2)	0.12 (0.44)

*per MBq (per mCi).
†ICRP 53, p. 142.

TABLE 2
Radiation Dosimetry in Children (5 yr old)

Radiopharmaceutical	Administered activity MBq/kg (mCi/kg)	Organ receiving the largest radiation dose* mGy (rad)	Effective dose* mSv (rem)
⁶⁷ Ga†	3.7–7.4 (0.1–0.2)	2.3 Bone surface (8.5)	0.38 (1.4)

*per MBq (per mCi).
†From Treves ST. Internal dosimetry in pediatric nuclear medicine. In: *Pediatric Nuclear Medicine*. New York: Springer-Verlag; 1995:564.

4. Mechanism of localization
 - a. Uptake of ⁶⁷Ga appears to correlate with the presence of the transferrin receptor, CD71, which may be a marker for gallium avidity (23,24).
 - b. Lactoferrin also binds ⁶⁷Ga.

5. Radiation Dosimetry (Tables 1 and 2).

E. Image Acquisition

1. A large field of view multipeak gamma camera with adequate shielding of the head should be used. A medium- (preferred) or high-energy collimator is used to perform planar or SPECT imaging. Newer instruments are well suited for gallium imaging and produce excellent clinical studies compared to older equipment (8). Photopeak settings should be as recommended by the manufacturer or on site determination. Use of 20% window at 93 keV and 15% at 187 keV was best in one phantom study (25).
2. Initial images are obtained at 48–72 hr postinjection. Later images obtained 5–10 days after injection may be helpful as this allows clearance of nonspecific activity from the body and enhanced target-to-background in the images.

3. Typical imaging times are 10–20 min per view. For planar images of the chest it is desirable to have as many as 2,000,000 counts while spot views of the abdomen and pelvis should be acquired for 1,500,000 counts. Lateral head and neck views should then be acquired for 600,000 counts. Special attention should be placed in getting the chest and pelvic views without the liver in the field of view.
4. For whole-body imaging, anterior and posterior views are needed. A scanning speed to achieve an information density of greater than 450 counts/cm² or greater than 1,500,000 counts for each view is suggested.
5. The increased contrast resolution of SPECT may be helpful in obtaining studies that allow subtle lesion detection in the chest and abdomen (26–29). SPECT imaging parameters should be as recommended by the instrument manufacturer or site specific protocol. The importance of SPECT is emphasized as the reconstruction of multiple planes are critical in assessing subtle lesions in the chest and abdomen.

F. Interventions

None other than bowel preparation, which is optional.

G. Processing

1. Filter selection for SPECT images is dependent on the equipment and the user. This should be determined on site.
2. Three-dimensional volume images displayed in a cine sequence may be helpful in visualizing abnormalities (dynamic kinetic effect).

H. Interpretation/Reporting

1. Interpretation of the ⁶⁷Ga scan requires knowledge of the physiologic distribution of activity in liver, spleen, bone marrow, bone, gastrointestinal tract, soft tissues and glandular tissues (lacrimal, salivary, nasopharyngeal and mammary).
2. Correlation with other imaging modalities is essential.

I. Quality Control

1. Quality control for the gamma camera and image display are as enumerated by the Society of Nuclear Medicine Procedure Guideline for General Imaging.
2. Demonstration of spatial registration in multiple energy windows may be required to optimize image quality.

J. Sources of Error

1. Other diagnostic studies may be required to define the underlying pathology when either tumor or inflammation may be the cause of the uptake. See the Society of Nuclear Medicine Procedure Guideline for Gallium Scintigraphy in Inflammation.
2. Patient motion frequently occurs with long imaging times. This can be minimized by careful positioning and ensuring patient comfort prior to image acquisition. Motion correction software may be helpful in restoring motion degraded SPECT images.
3. Residual bowel activity may be mistaken for disease or obscure underlying lesions in the abdomen. SPECT may help to distinguish bowel activity from an abdominal or pelvic tumor.
4. Faint pulmonary hilar uptake may be seen in adult patients, particularly smokers. More prominent hilar uptake can also be observed following chemotherapy and radiation therapy.
5. Thymic hyperplasia may be visualized in the anterior mediastinum and is known to occur as a rebound response after chemotherapy. Occasionally, uptake in

the mediastinum and other sites occurs for unknown reasons (30–33).

6. Chemotherapy may decrease gallium uptake (16,17). Gallium studies should be performed prior to induction chemotherapy or at least 3 wk after the last course of chemotherapy.
7. Gadolinium used for MRI contrast enhancement has been observed to decrease ^{67}Ga localization when given within 24 hr of injection (19).
8. Iron administration may alter the biodistribution of ^{67}Ga by competing for transferrin receptor sites in plasma and tissue (18).
9. Bone marrow harvest may cause uptake at the site of the procedure (21).
10. Well-differentiated lymphocytic lymphoma usually does not accumulate ^{67}Ga . Low-grade lymphomas may be better visualized with ^{201}Tl or $^{99\text{m}}\text{Tc}$ -MIBI.

PART V: DISCLAIMER

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different than the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

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

PART VI: ISSUES REQUIRING FURTHER CLARIFICATION

- A. Whether attenuation correction of ^{67}Ga SPECT images is helpful has not been determined. No studies to date have investigated this issue.
- B. What are the economic and therapeutic implications of using ^{67}Ga for imaging the lymphomas?
- C. Is the transferrin receptor (CD71) a reliable marker for gallium avidity in lymphoma and other tumors? If so can this information be used to guide the work-up and management of CD71-positive tumors?
- D. Whether the use of "bowel preparation" is of clinical utility is not agreed upon by experts. Preparation with oral laxatives prior to imaging is controversial (27,32,35). Studies have revealed either no significant difference in ^{67}Ga interference or low rates of compliance. Although in theory, laxatives and high bulk diets may facilitate transit of ^{67}Ga through the bowel and decrease radiation burden, there are no studies which document that this is clinically significant. Further, in the patient who has been treated with chemotherapy or is immunosuppressed, vigorous catharsis may be associated with sepsis due to break down of the intestinal epithelial defense mechanisms.

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Procedure Guideline for Gallium Scintigraphy in Inflammation

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PART I: PURPOSE

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

PART II: BACKGROUND INFORMATION AND DEFINITIONS

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