Comparison of Gallium-67-Citrate and Thallium-201 Scintigraphy in Peripheral and Intrathoracic Lymphoma

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We performed this study in an attempt to reconcile the differences with respect to ^{67}Ga uptake as a function of tumor grade and type in the literature, as well as to determine the sensitivity of ^{201}Tl uptake in both Hodgkin's and non-Hodgkin's lymphoma. **Methods:** Thirty-six (9 with low-grade lymphoma, 11 with intermediate-grade lymphoma, 4 with high-grade lymphoma and 12 with Hodgkin's lymphoma) patients underwent both ^{67}Ga and ^{201}Tl scintigraphy. Biopsies were done on all patients. A semiquantitative rating system was used to make statistical comparisons for thallium versus gallium in all lymphoma subgroups, as well as comparisons of thallium and gallium to themselves in all subgroups. **Results:** Patient sensitivity was only 56% and site sensitivity was 32% in patients with low-grade lymphoma. Conversely, ^{201}Tl sensitivity was 100%, respectively, for patients and sites. The difference between ^{201}Tl and ^{67}Ga sensitivity in patients with low-grade lymphoma on a site basis was statistically significant. When compared to itself in lymphoma subgroups, ^{201}Tl was found to be statistically more avid for low-grade lymphoma than for intermediate, high or Hodgkin's lymphoma. Gallium-67 sensitivity for low-grade lymphoma was significantly less than for Hodgkin's and intermediate grade lymphomas. No significant differences were found when ^{201}Tl and ^{67}Ga were compared in the intermediate, high or Hodgkin's lymphoma groups. **Conclusion:** Thallium-201 demonstrates significantly greater tumor avidity in the low-grade lymphoma group compared to ^{67}Ga citrate. Gallium-67-citrate appears relatively nonavid for low-grade lymphoma compared to ^{201}Tl and is statistically inferior in detecting low-grade lymphoma in comparison to its ability to detect intermediate or high-grade lymphomas. Gallium-67-citrate should not be considered dependable in evaluating patients with low-grade lymphoma. Neither ^{201}Tl or ^{67}Ga is dependable in the evaluation of low-grade lymphoma within the abdomen, since gallium avidity for low-grade lymphoma is low and gastrointestinal excretion of ^{201}Tl is poorly controlled.

Key Words: gallium-67-citrate; thallium-201; lymphoma; scintigraphy

J Nucl Med 1996; 37:46–50

Gallium-67-citrate has been extensively used in evaluating patients with lymphoma (*1–22*). The statistical information regarding sensitivity and specificity generated for lymphoma have been reported for Hodgkin's lymphoma and non-Hodgkin's lymphoma, with only minimal attention focused on sensitivity and specificity based upon tumor grade or type. Gallium-67 tumor avidity has been used to determine tumor viability in diffuse large-cell lymphoma and Hodgkin's disease (*14–21*). In contrast, ^{67}Ga tumor avidity has not been used to evaluate tumor viability in low-grade lymphoma. There is some controversy in the few studies which have addressed the issue of ^{67}Ga uptake according to tumor grade or type (*8,9*). There is limited information on ^{201}Tl accumulation in lymphoma as a general topic (*23–27*). We performed this study to reconcile differences with regard to ^{67}Ga uptake in lymphoma in the literature, as well as to determine the efficacy of ^{201}Tl uptake in both Hodgkin's and non-Hodgkin's lymphoma.

Received Dec. 2, 1993; revision accepted Oct. 24, 1994.
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MATERIALS AND METHODS

Thirty-six patients with a biopsy-proven diagnosis of lymphoma were enrolled in the study. Nine patients were diagnosed as having low-grade lymphoma, 11 with intermediate-grade, 4 with high-grade, and 12 with Hodgkin's lymphoma. Biopsies were obtained on each patient from the least invasive site necessary to make the diagnosis of lymphoma. Most frequently, biopsies were done in the cervical, supraclavicular or inguinal regions. When necessary, biopsies were done invasively using CT-guided biopsy techniques or by direct surgical exploration.

Scintigraphic studies were performed within 14 days of the biopsy, with several patients biopsied following scintigraphy. If uptake was noted at the biopsy site, it was considered as a biopsy effect, as opposed to tumor, unless multiple areas at the site were present. Biopsies were limited to one site per patient.

All patients underwent ^{67}Ga and ^{201}Tl scintigraphic studies prior to chemo- or radiation therapy. The studies were performed within one week of each other. Twenty-five patients, however, had more than a single region demonstrating abnormality on ^{201}Tl or ^{67}Ga. These additional areas were not confirmed with biopsy. A site was considered as positive on ^{201}Tl or ^{67}Ga images if confirmation was obtained with CT, MRI, x-ray, physical examination or biopsy.

All patients had at least one area of adenopathy demonstrated on physical examination, x-ray, CT or MRI. Patients with recurrent lymphoma, only central nervous system lymphoma or only abdominal disease were excluded from the study.

Thallium Scintigraphy

Images were acquired with a large field of view Anger camera with high-resolution collimation beginning 2 min postinjection of 3 mCi ^{201}Tl. Two sequential anterior images of the chest with the arms raised above the head were obtained. These were followed by images of the abdomen and pelvis with a final image of the chest acquired approximately 1 hr postinjection. When necessary, 10-min oblique projections with the arms raised above the head were obtained to separate underlying structures such as the heart from suspected tumor areas.

Data were acquired using an 80-keV photopeak with a 20% window. Digital images were acquired and displayed using a 256 × 256 matrix.

Gallium Scintigraphy

Immediately following the ^{201}Tl study, patients were injected with 6–10 mCi ^{67}Ga-citrate and scanned 2 and 4 days postinjection. Gallium-67 photopeaks of 93, 184 and 296 keV with a 20% window were used to acquire the data. Images were acquired and displayed using a 256 × 256 matrix. Anterior and posterior total-body scans were obtained at a scan speed of 10 cm/min. High-resolution spot images of the chest, abdomen and pelvis were obtained when necessary using a preset time of 10 min.

Table 1
Sensitivity for Thallium-201 and Gallium-67 in Lymphoma by Cell Type

Lymphoma Type	^{210}Tl		^{67}Ga	
	Sensitivity (Patient)	Sensitivity (Site)	Sensitivity (Patient)	Sensitivity (Site)
Low Grade	9/9 (100%)	34/34 (100%)	5/9 (56%)	11/34 (32%)
Intermediate Grade	11/11 (100%)	38/46 (83%)	11/11 (100%)	33/46 (72%)
High Grade	3/4 (75%)	8/9 (89%)	4/4 (100%)	7/9 (78%)
Hodgkin's	12/12 (100%)	25/28 (89%)	12/12 (100%)	21/28 (75%)

Total Patients = 36
Sites = 17

Rating System for Thallium-201 and Gallium-67 Comparative Studies

A semiquantitative rating system was used to compare ^{67}Ga and ^{201}Tl studies. Background activity in the axillary area was compared with ^{201}Tl and ^{67}Ga activity within the abnormal sites. A five-point rating system was used in which zero indicated activity within the lesion to be equivalent to background within the axilla (no detectable lesion): 1+ = equivocal, 2+ = definite lesion activity greater than the axillary soft-tissue background (1+ and 2+ values are for both thallium and gallium). For ^{201}Tl, 3+ = activity within the lesion equal to thyroid activity on the initial image (2–12 min postinjection) and 4+ = activity greater than thyroid. For ^{67}Ga, 3+ = activity equal to sternum and 4+ = ^{67}Ga uptake in the lesion greater than sternum.

All studies were graded by three physicians who were blinded to all patient data. An average value was then determined for each site.

Pathologic Tumor Grading

The biopsy specimens were graded by an experienced pathologist according to the working formulation for non-Hodgkin's lymphomas. The grades included low, intermediate and high. The diagnosis for Hodgkin's was established pathologically by accepted criteria.

Statistical Analysis

Sensitivity was calculated for each subgroup of lymphoma. Data were analyzed with respect to patient sensitivity and specificity, as well as site sensitivity.

The data were analyzed to determine the relationship of ^{201}Tl to ^{67}Ga avidity in each of the lymphoma subgroups, including high-grade, intermediate grade, low-grade and Hodgkin's. In addition, the relationship of ^{201}Tl activity within a specific subgroup compared to other subgroups was studied as well as the relationship of ^{67}Ga within a specific subgroup compared to activity within other subgroups.

Comparison of ^{201}Tl and ^{67}Ga within each group was studied using Wilcoxon's sign rank procedure. Wilcoxon's procedure was used since the data were not normally distributed and Wilcoxon's procedure has no requirement for normal distribution.

Comparisons of ^{201}Tl and ^{67}Ga for the different groups were studied using the Kruskal-Wallis procedure. In addition, Konover's procedure was used to examine any individual group differences determined by the Kruskal-Wallis procedure. A Spearman's rank correlation procedure was used to measure the relationships between ^{201}Tl and ^{67}Ga within each group to see if correlations within each group existed.

Determination of Regional Abnormalities

To compare ^{201}Tl and ^{67}Ga activity in abnormal tissue, the body was divided into selected areas. The areas or sites included were the right and left cervical-supraclavicular region, right and left axilla, right and left mediastinum, right and left inguinal region and the extremities. The brain was not included in this series because of blood-brain barrier considerations; the abdomen was not included because of unpredictable gastrointestinal activity which significantly impaired interpretation of the ^{201}Tl studies.

An area with multiple focal abnormalities was considered as having a single site abnormality for statistical evaluation. In addition, if a site abnormality was recorded for isotope A and read as normal for isotope B, then isotope B was recorded as a 0 and was considered to have missed the tumor. These false-negative readings were confirmed with other imaging modalities such as CT, MRI or radiography, as well as clinical examination.

RESULTS

The results are summarized in Table 1. Patient sensitivity for ^{67}Ga, defined as at least one positive site in any given patient, was low in the low-grade lymphoma subgroup with no detectable abnormalities in four of nine patients. Conversely, ^{201}Tl abnormalities in these four patients were observed in more than one location. Site sensitivity for ^{67}Ga in low-grade lymphoma patients was only 32% (11/34). For intermediate, high-grade and Hodgkin's lymphoma, ^{67}Ga sensitivity on a per patient basis was high, with 27 of 27 patients demonstrating at least one abnormality.

Comparison by sites of ^{201}Tl and ^{67}Ga activity within each lymphoma subgroup using the Wilcoxon's sign rank procedure demonstrated ^{201}Tl ratings for the low-grade non-Hodgkin's lymphoma group to be significantly higher than ^{67}Ga ($p < 0.0005$). The ^{201}Tl and ^{67}Ga ratings were not significantly different for the intermediate, high or Hodgkin's lymphoma groups.

Thallium-201 and ^{67}Ga scans from a patient with low-grade lymphoma are compared in Figure 1. The blind reading of the ^{67}Ga scan was initially interpreted as normal while the ^{201}Tl scan demonstrated multiple sites of abnormality with high intensity relative to background activity. Following a review of the ^{67}Ga study, and after correlation with the ^{201}Tl scan, low-level ^{67}Ga activity could be detected in the neck and axilla. Many of the sites contained more than one lesion.

A comparison of a ^{67}Ga and ^{201}Tl in a patient with an intermediate grade lymphoma is depicted in Figure 2. The groin abnormalities are best visualized with ^{201}Tl, whereas the neck and chest findings are similar with both isotopes. Figure 3 illustrates the superiority of ^{67}Ga detection in the chest, but superior ^{201}Tl detection in the inguinal region, in a 84-yr-old man with high-grade immunoblastic lymphoma.

Comparison of ^{201}Tl and ^{67}Ga in Hodgkin's disease is shown in Figure 4 in a patient with cervical and mediastinal tumors. The findings are similar with both agents. There is improvement in the neck evaluation on the delayed ^{201}Tl study due to washout of surrounding soft tissue, including thyroid.

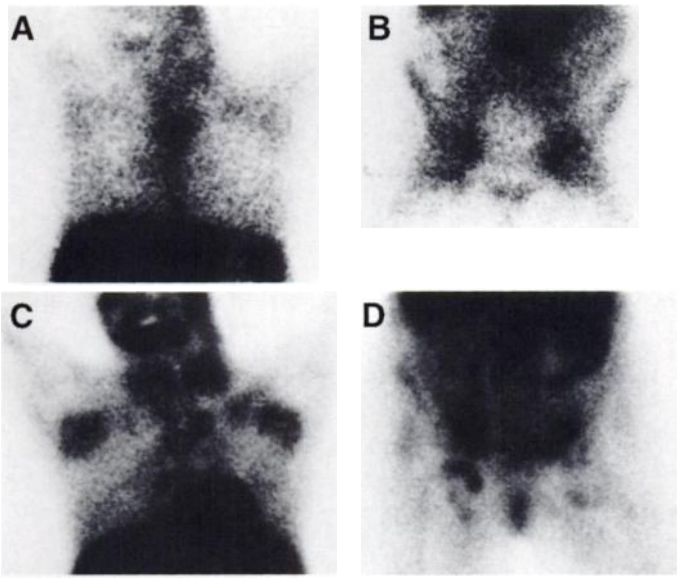

FIGURE 1. Patient with a low-grade non-Hodgkin's lymphoma. Comparison of ^{67}Ga chest and pelvic views (A, B) with ^{201}Tl (C, D). There is low level ^{67}Ga accumulation in the left neck as well as in the axillary regions bilaterally. The ^{201}Tl study demonstrates intense cervical activity bilaterally as well as bilateral axillary and mediastinal accumulation, with intense uptake in the pelvis and inguinal areas.

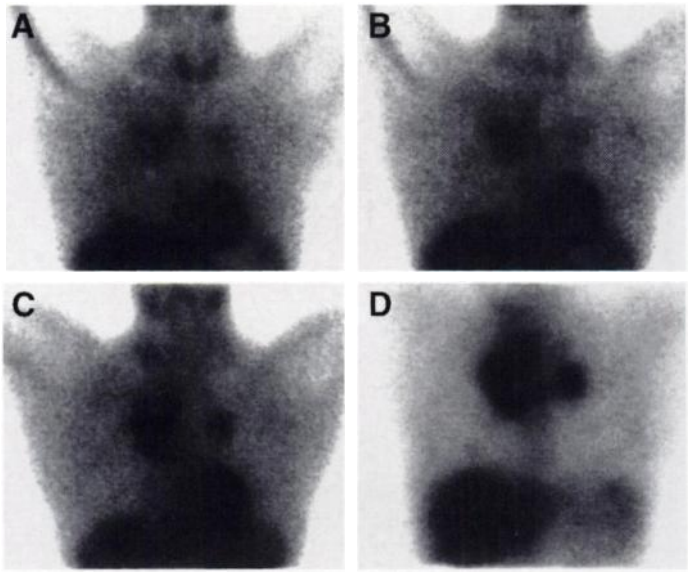

FIGURE 3. High-grade immunoblastic lymphoma in a patient with a mediastinal mass on CT and palpable inguinal nodes. Notice the mixed pattern of superior ^{201}Tl detection of inguinal nodes but superior mediastinal detection with ^{67}Ga.

Comparison of ^{201}Tl uptake for different groups using the Kruskal-Wallis procedure demonstrated that ^{201}Tl avidity for low-grade lymphoma was significantly higher than for intermediate, high or Hodgkin's lymphoma ($p = 0.002$). Thallium uptake for intermediate, high or Hodgkin's groups did not demonstrate a statistically significant difference.

A comparison of ^{67}Ga for different groups was also performed using the Kruskal-Wallis procedure. Gallium-67 sensitivity for low-grade lymphoma was significantly less than for Hodgkin's and intermediate grade lymphomas ($p = 0.007$). Gallium sensitivities for intermediate, high or Hodgkin's lymphoma were not significantly different.

There was no correlation of ^{201}Tl to ^{67}Ga within specific tumor subgroups based on Spearman's range correlation.

DISCUSSION

Thallium accumulation has been described in a number of tumors, including lymphoma (*23–43*). The mechanism of

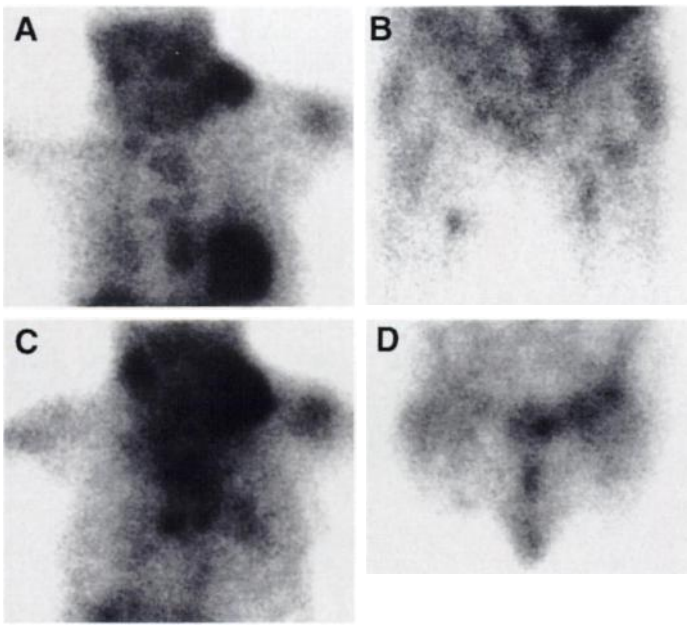

FIGURE 2. Patient with an intermediate grade lymphoma (diffuse large-cell type). Thallium-201 anterior chest and pelvic images (A, B) are compared with ^{67}Ga projections (C, D). There are extensive abnormalities in the neck and chest on both sets of images, but the ^{201}Tl images demonstrate multiple abnormalities in the right and left groin regions that are not well defined on ^{67}Ga.

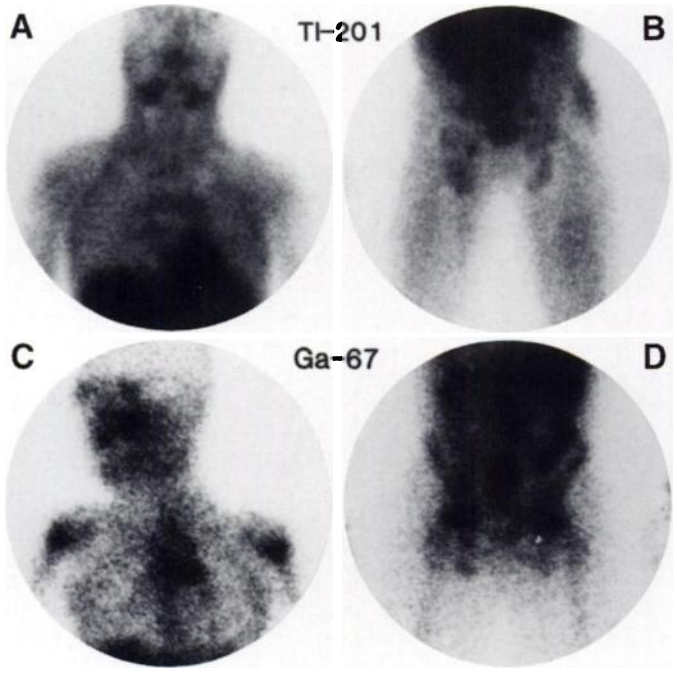

FIGURE 4. A patient with nodular sclerosing Hodgkin's lymphoma of the mediastinum, neck and left axilla demonstrates increased activity on both ^{201}Tl (A, B, C) and ^{67}Ga (D) images. There is visual improvement in the tumor-to-background ratio in the neck when comparing early (2–12 min) postinjection views (A) to intermediate (12–22 min) (B) and delayed views (50–60 min) (C). Thyroid activity had cleared 50–60 min postinjection.

uptake is not clear, but it has been postulated that several mechanisms are involved in tumor accumulation, including the ATP-ase sodium potassium pump, a co-transport system, calcium channel mechanisms, blood flow and tumor viability (*31,33,43,48–55*). The mechanism for ^{67}Ga accumulation in tumors is still uncertain, but several studies indicate that the mechanism for ^{201}Tl and ^{67}Ga accumulation are independent (*53,56–59*). The sole intent of the study was to characterize ^{67}Ga and ^{201}Tl scintigraphy in patients with Hodgkin's as well as non-Hodgkin's lymphoma.

Thallium SPECT imaging was initially evaluated in this series but was discontinued because of the relatively poor image quality obtained from administration of 3 mCi ^{201}Tl. Thallium SPECT images generally resulted in detection of major thallium-avid regions, but image interpretation was considered difficult because of significant noise generated during image reconstruction. The noise was thought to be due to the low photon yield resulting from a 3-mCi injection of ^{201}Tl.

This study demonstrates a significant ($p < 0.0005$) disparity between ^{67}Ga and ^{201}Tl accumulation in the low-grade lymphoma group, with ^{67}Ga demonstrating low or absent uptake and ^{201}Tl moderate to marked avidity. Thallium-201 tumor intensity was also significantly higher in the low-grade lymphoma group when compared to other lymphoma subgroups ($p < 0.002$). In Hodgkin's lymphoma patients, there was a statistically significant difference between ^{201}Tl and ^{67}Ga detection in areas outside the abdomen.

The sensitivity for detection of lymphoma reported in this series was confirmed by biopsy for the patient sensitivity subgroups. Sensitivity for lymphoma subgroups on a site basis was not confirmed by biopsy in all areas because each patient only underwent a single biopsy even though they may have had multiple sites demonstrating ^{201}Tl and/or ^{67}Ga avidity. A true-positive reading was recorded for areas demonstrating ^{201}Tl or ^{67}Ga avidity if the biopsy was positive or if a mass abnormality was detected on CT, MRI, radiograph or physical examination. The potential for sensitivity error in the site subgroup is present and governed by the assumptions that mass abnormalities discovered on x-ray correlative imaging techniques or physical examination represent true-positive findings. If abnormalities observed on ^{201}Tl or ^{67}Ga scintigraphy were not confirmed by biopsy, other correlative imaging techniques or physical examination, then the ^{201}Tl and ^{67}Ga findings were considered to be false-positive and were not included for calculation of sensitivity. Overall, site sensitivity would be falsely reduced for ^{201}Tl and ^{67}Ga by these assumptions.

There are only limited data for lymph node size which may be detected using ^{201}Tl in patients with low-grade lymphoma. In this series, it was difficult to determine the relationship between thallium avidity and lymph node size. Patients generally underwent biopsy prior to imaging. Therefore, no direct correlation could be made on the lymph nodes removed prior to scintigraphy. In three patients who underwent biopsy following a scintigraphic procedure, the nodes taken from the general area of scan positivity were 4–16 mm. The nodes were matted and probably superimposed on one another during imaging, which made it difficult to define the size of the smallest node that could be detected.

A major disadvantage in the use of ^{201}Tl to evaluate lymphoma was the unpredictability of gastrointestinal secretion which did not appear to clear on multiple delayed images performed 2–7 days postinjection. This may be due to a recycling of ^{201}Tl with continuous bowel excretion. Delayed ^{67}Ga imaging appeared to be a superior technique for evaluating the abdomen in the intermediate and high-grade lymphoma groups.

Kaplan et al. determined ^{67}Ga-citrate to be a predictor of tumor viability in patients with diffuse large-cell lymphoma (*37*). Gallium-67 viability has not been applied to lower grade lymphomas possibly because of the lack of ^{67}Ga accumulation in this lymphoma group.

CONCLUSION

Thallium-201 appears to be a promising radiopharmaceutical for the detection of low-grade lymphoma and warrants further study to evaluate its use as an indicator of therapeutic response.

ACKNOWLEDGMENTS

The author thanks Robin Backer for her support in preparing the manuscript. This study was supported by a grant from Dupont-Merck Pharmaceuticals, Inc.

REFERENCES

1. Edwards CL, Hayes RL. Tumor scanning with ^{67}Ga, in *Research Report ORAU-107*, Oak Ridge, TN: Medical Division, Oak Ridge Associated Universities; 1968:110–125.
2. Bakshi S, Bender MA. Use of gallium-67 scanning in the management of lymphoma. *J Surg Oncol* 1973;5:539–549.
3. Johnston G, Buena RS, Teates CD, et al. Gallium-67-citrate imaging in untreated Hodgkin's disease: preliminary report of cooperative group. *J Nucl Med* 1974;15:399–403.
4. Greenlaw RH, Weinstein MB, Brill AB, et al. Gallium-67-citrate imaging in untreated lymphoma: preliminary report of cooperative group. *J Nucl Med* 1974;15:404–407.
5. Levi JA, O'Connel MJ, Murphy WL, et al. Role of gallium-67-citrate scanning in the management of non-Hodgkin's lymphoma. *Cancer* 1975;36:1690–1741.
6. Makoski HB, Teske HK, Becker G. Diagnostic value of gallium-67 in malignant lymphoma. *Acta Radiol (Stockholm)* 1976;12:321–328.
7. Seabold JE, Votaw ML, Keyes JW, et al. Gallium-67-citrate scintigraphy. *NY State J Med* 1976;76:2148–53.
8. Horn NL, Ray GR, Kriss JP. Gallium-67 citrate scanning in Hodgkin's disease and non-Hodgkin's lymphoma. *Cancer* 1976;37:250–253.
9. McCaffrey JA, Rudders RA, Kahn PC, et al. Clinical usefulness of gallium-67 scanning in malignant lymphomas. *Am J Med* 1976;60:523–30.
10. Johnston GS, Go MF, Buena RS, et al. Gallium-67-citrate imaging in Hodgkin's disease: final report of cooperative group. *J Nucl Med* 1977;18:692–698.
11. Rudders RA, McCaffrey JA, Kahn PC. The relative roles of gallium-67-citrate scanning and lymphangiography in the current management of malignant lymphoma. *Cancer* 1977;40:1439–1443.
12. Turner DA, Pinsky SM, Gottschalk A, et al. The use of ^{67}Ga scanning in the staging of Hodgkin's disease. *Radiology* 1982;103:97–101.
13. Tumeh ST, Rosenthal DS, Kaplan WD, et al. Lymphoma: evaluation with ^{67}Ga SPECT. *Radiology* 1987;164:111–114.
14. Wylie BR, Southee, Joshua DE, et al. Gallium scanning in the management of mediastinal Hodgkin's disease. *Eur J Haematol* 1989;42:334–347.
15. Weeks JC, Year JC, Caellos GP, et al. Value of follow-up procedures in patients with large cell lymphoma who achieve a complete remission. *J Clin Oncol* 1991;9:1196–1203.
16. Front D, Israel O, Epelbaum R, et al. Gallium-SPECT in patients with lymphoma before and after treatment: *Radiology* 1990;175:515–519.
17. Kostakoglu L, Yeh SDJ, Portlock C, et al. Validation of gallium-67-citrate single-photon emission computed tomography in biopsy-confirmed residual Hodgkin's disease in the mediastinum. *J Nucl Med* 1992;33:345–350.
18. McLaughlin AF, Magee MA, Greenough R, et al. Current role of gallium scanning in the management of lymphoma. *Eur J Nucl Med* 1990;16:771–775.
19. Hagemeister FB, Fesus SM, Lamki LM, et al. Role of the gallium scan in Hodgkin's disease. *Cancer* 1990;65:1090–1096.
20. Kaplan WD. Residual mass and negative gallium scintigraphy in treated lymphoma: when is the gallium scan really negative? [Abstract]. *J Nucl Med* 1990;31:369–371.
21. Israel O, Front D. Benign mediastinal and parahilar uptake of gallium-67 in treated lymphoma: do we have all the answers? [Abstract]. *J Nucl Med* 1993;34:1330–1332.
22. Kaplan WD, Jochelson MS, Herman TS, et al. Gallium-67 imaging: a predictor of residual tumor viability and clinical outcome in patients with diffuse large-cell lymphoma. *J Clin Oncol* 1990;8:1966–1970.
23. Winzelberg GG, Melada GA, Hydrovitz JD. False-positive thallium-201 parathyroid scan of the mediastinum in Hodgkin's Lymphoma. *AJR* 1986;147:819–821.
24. Waxman AD, Ramanna L, Said J. Thallium scintigraphy in lymphoma: relationship to gallium-67 [Abstract]. *J Nucl Med* 1989;30(suppl):915.
25. Kaplan WD, Southee LM, Annese MS, et al. Evaluating low- and intermediate-grade non-Hodgkin's lymphoma with gallium-67 and thallium-201 imaging [Abstract]. *J Nucl Med* 1990;31:793.
26. Waxman AD, Ramanna L, Eller D. Characterization of lymphoma using thallium and gallium scintigraphy [Abstract]. *J Nucl Med* 1991;32:917–918.
27. Waxman AD. Thallium-201 in nuclear oncology. In: Freeman LM. *Nuclear Medicine Annual*. New York: Raven Press; 1991:193–209.
28. Salvatore M, Carratii L, Porta E. Thallium-201 as a positive indicator for lung neoplasms: preliminary experiments. *Radiology* 1976;21:487–488.
29. Tonami N, Hisda K. Clinical experience of tumor imaging with thallium-201-chloride. *Clin Nucl Med* 1977;2:75–81.

30. Hisada K, Tonami H, Miyamae T, et al. Clinical evaluation of tumor imaging with thallium-201-chloride. *Radiology* 1978;129:497–500.
31. Tonami N, Hisada K. Thallium-201 scintigraphy in postoperative detection of thyroid cancer; a comparative study with ^{131}I. *Radiology* 1980;136:461–464.
32. Stoller DW, Waxman AD, Rosen G, et al. Comparison of thallium-201, gallium-67, technetium-99m ADP and magnetic resonance imaging of musculoskeletal sarcoma [Abstract]. *Clin Nucl Med* 1986;12(suppl):P15.
33. Kaplan WD, Takvorian T, Morris JH, et al. Thallium-201 brain tumor imaging: a comparative study with pathological correlation. *J Nucl Med* 1987;28:47–52.
34. Waxman AD, Goldsmith MS, Greif PM, et al. Differentiation of tumor versus sarcoidosis using thallium-201 in patients with hilar mediastinal adenopathy [Abstract]. *J Nucl Med* 1987;28(suppl):561.
35. Ramanna L, Waxman AD, Binney G, et al. Increasing specificity of brain scintigraphy using thallium-201 [Abstract]. *J Nucl Med* 1987;28(suppl):658.
36. Mountz JM, Stafford-Shuck, McLeever P, et al. The tumor/cardiac ratio: a new method to estimate residual high grade astrocytoma using thallium-201 [Abstract]. *J Nucl Med* 1987;28(suppl):706.
37. Hofnagel CA, Delprat CC, Marcus HR, et al. Role of thallium-201 total body scintigraphy in follow-up of thyroid carcinoma. *J Nucl Med* 1988;27:1854–1857.
38. Lee VW, Rosen MP, Baum A, Cohen SE, Cooley T, Liebman HA. AIDS-related Kaposi sarcoma: findings on thallium-201 scintigraphy *AJR* 1988;151:1233–1235.
39. Sehweil AM, McKillop JH, Milroy R, et al. Thallium-201 scintigraphy in the staging of lung cancer, breast cancer and lymphoma. *Nucl Med Comm* 1990;11:263–269.
40. Waxman AD, Ramanna L, Brachman MB, et al. Thallium scintigraphy in primary carcinoma of the breast: evaluation of primary and axillary metastasis [Abstract]. *J Nucl Med* 1989;30(suppl):844.
41. Black KL, Hawkins R, Kim KT, et al. Use of thallium-201 SPECT to quantitate malignancy grade of gliomas. *J Neurosurg* 1989;71:342–346.
42. Tonami N, Shuke N, Kunihiko Y, et al. Use of thallium-201 single-photon emission computed tomography in the evaluation of suspected lung cancer. *J Nucl Med* 1989;30:997–1004.
43. Ramanna L, Waxman AD, Binney G, et al. Thallium-201 scintigraphy in bone sarcoma: comparison with gallium-67 and technetium-MDP in evaluation of chemotherapy response. *J Nucl Med* 1990;31:567–572.
44. Kim KT, Black KL, Marciano D, et al. Thallium-201 SPECT imaging of brain tumors: methods and results. *J Nucl Med* 1990;31:965–969.
45. Waxman AD, Ramanna L, Memsic A, et al. Thallium scintigraphy in differentiating malignant from benign mass abnormalities of the breast [Abstract]. *J Nucl Med* 1990;31(suppl):747.
46. Ramanna L, Waxman AD, Braunstein G. Thallium-201 scintigraphy in differentiated thyroid cancer: comparison with radioiodine scintigraphy and serum thyroglobulin determination. *J Nucl Med* 1991;32:441–446.
47. Waxman AD, Ramanna L, Memsic LD, et al. Thallium scintigraphy in the evaluation of mass abnormalities of the breast. *J Nucl Med* 1993;34:18–23.
48. Gehring PJ, Hammand PB. The interrelationship between thallium and potassium in animals. *J Pharmacol Exp Ther* 1967;155:187–201.
49. Lebowitz E, Greene MW, Greene R, et al. Thallium-201 for medical use: part I. *J Nucl Med* 1975;16:151–155.
50. Bradley-Moore PR, Lebowitz E, Greene MW, Atkins HL, Ansari AN. Thallium-201 for medical use: part II. Biologic behavior. *J Nucl Med.* 1975;16:156–160.
51. Atkins HL, Budinger TF, Lebowitz E, et al. Thallium-201 for medical use: part III. Human distribution and physical imaging properties. *J Nucl Med* 1977;18:133–140.
52. Britten JS, Blank M. Thallium activation of the (Na^+, K^+) activated ATPase of rabbit kidney. *Biochem Biophys Acta* 1968;15:160–166.
53. Muranake A. Accumulation of radioisotopes with tumor affinity, II. Comparison of the tumor accumulation of Ga-67-citrate and thallium-201-chloride in vitro. *Acta Med Okayama* 1981;35:85–101.
54. Sessler MJ, Geek P, Maul FD, et al. New aspects of cellular thallium uptake: Tl+-NA+-2CL(-)-Co-transport is the central mechanism of ion uptake. *Nucl Med* 1986;25:24–27.
55. Ando A, Ando I, Katayama M, et al. Biodistribution of ^{201}Tl in tumor bearing animals and inflammatory lesion-induced animals. *Eur J Nucl Med* 1987;12:567–572.
56. Ito Y, Okuyama S, Sata K, et al. Gallium-67 tumor scanning and its mechanisms: studies in rabbits. *Radiology* 1971;100:357–362.
57. Larson SM. Mechanisms of localization of gallium-67 in tumors. *Semin Nucl Med* 1978;8:193–204.
58. Kriegel H. Biokinetics and metabolism of radiogallium. *Nucl Med* 1984;23:53–57.
59. Hoffer PB, Huberty J, Khayam-Bashi H. The association of ^{67}Ga and lactoferrin. *J Nucl Med* 1977;18:713–717.