Gallium-67 Scintigraphy Evaluation of Therapy in Non-Hodgkin's Lymphoma

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Patients with diffuse large cell lymphoma may achieve complete remission (CR) after chemotherapy, and the time to reach CR may be predictive of treatment outcome. Partial remission, or recurrence from CR, is associated with poor survival. Gallium-67 imaging has proven to be useful in evaluating lymphoma patients. In tumor models, this radiotracer is an indicator of tumor viability. Gallium-67 uptake is seen only in avid and viable lymphoma tissue, not in fibrotic or necrotic tissue. In this study, we prospectively assessed the ability of this radiotracer to define residual disease. In addition, we evaluated the possibility of predicting the clinical outcome in patients with diffuse cell lymphoma on the basis of scan positivity during chemotherapy. **Methods:** Thirty-three consecutive patients with histologically proven diffuse large cell lymphoma were investigated with ^{67}Ga scintigraphy 48–72 hr after injection of 185–259 MBq ^{67}Ga-citrate for staging and during follow-up after four to six cycles of intensive chemotherapy. Patients were monitored for a mean of 56.0 mo (range 7–90 mo), and they were restaged using physical examination, CT and all necessary imaging modalities. **Results:** Patients were divided into two groups according to the positivity or negativity of ^{67}Ga scan after four to six cycles of chemotherapy. Of the 33 patients studied, 14 (42.4%) showed persistent abnormal uptake of ^{67}Ga-citrate after four to six cycles of chemotherapy. In this group, 9 patients (64.2%) died of lymphoma at a mean of 24.3 mo from presentation with the diagnosis (range 7–71 mo). Four patients had no evidence of disease at an average of 71.7 mo after diagnosis, and 1 patient was considered to be in partial remission. In the second group of 19 ^{67}Ga-negative patients, after four to six cycles of chemotherapy, 4 died and 15 are alive and considered to be in CR. A statistical analysis of the association between ^{67}Ga scan results after four to six cycles of chemotherapy and survival was performed using the log-rank test; there was a statistically significant association between scan results and survival ($p = 0.00125$). **Conclusion:** We conclude that ^{67}Ga scintigraphy is an excellent predictor of residual tumor viability in lymphoma patients and that persistent positivity of the scan predicts poor outcome and may justify a change in treatment.

Key Words: gallium scintigraphy; non-Hodgkin's lymphoma; chemotherapy

J Nucl Med 1998; 39:1586–1590

Multidrug chemotherapy has transformed aggressive non-Hodgkin's lymphoma (NHL) from a fatal disease into one that is often curable (*1,2*). However, many patients still die of it, and we need a more accurate method of prospectively identifying patients with different long-term prognoses. The identification of different risk groups could have important therapeutic implications. Patients at high risk who are not effectively treated with current regimens may benefit from new experimental approaches, whereas those at low risk may do well with standard therapy.

Patients with diffuse large cell lymphoma (DLCL) can achieve complete remission (CR) after chemotherapy, and the time to reach CR may be predictive of treatment outcome. Partial remission (PR), or relapse of disease after CR, is associated with poor survival. The possibility of further predicting outcome during early treatment might lead to a change in therapy, with a potential improvement in survival.

Differentiation of tumor from fibrosis within residual radiographic masses represents an important diagnostic problem in these patients. The presence of a residual mass after treatment may not always indicate residual disease (*3–5*); conventional radiologic studies often show a mass when the patient is in CR (*6–8*). The reverse situation, when the disease has disappeared clinically and radiologically but the patient shows recurrence very soon after the end of treatment or in due course, is also seen (*9*).

CT gives information about tumor size and distribution of lesions but is sometimes unable to differentiate fibrosis from active lymphoma (*10*). MRI seems to have a valuable role in initial staging (*11*) and in assessing residual disease (*12*), because active malignant tissue has been reported to have different signal characteristics from normal tissues or fibrosis (*13–15*).

Several studies have examined the potential use of PET with biological tracers for tumor detection (*16,17*), mostly using enhanced glycolysis of vital tumor cells as defined by fluorodeoxyglucose (FDG) uptake. Although nonspecific FDG accumulation in macrophages (*18*) and hypoxia-induced FDG uptake (*19*) could be confounding factors, FDG seems to be an attractive radiopharmaceutical for monitoring response to therapy.

Gallium-67 imaging has proved useful for evaluating lymphoma patients. In tumor models, this radiotracer is an indicator of tumor viability (*20*). Gallium-67 uptake is seen only in avid and viable lymphoma tissue, not in fibrotic or necrotic tissue. There is now convincing evidence that ^{67}Ga scintigraphy has become an important and essential procedure in evaluating cancer patients. It is somewhat paradoxical, therefore, that ^{67}Ga has not yet been generally accepted by the nuclear medicine community.

In this study, we prospectively assessed the ability of ^{67}Ga scintigraphy to define residual disease. In addition, we evaluated the ability to predict clinical outcome in patients with DLCL on the basis of scan positivity during chemotherapy.

MATERIALS AND METHODS

Patient Selection

Thirty-three consecutive patients (16 males and 17 females) with histologically proven DLCL entered the study (working formulation—intermediate grade, Group E = 4, Group F = 3 and Group G = 26). The median age was 47.2 yr (range 14–72 yr). The patients were assessed by physical examination and routine labo-

Received Jul. 21, 1997; revision accepted Dec. 2, 1997.

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TABLE 1
Patient Characteristics

Characteristic	Number of patients
Total	33
Sex	16
M	
F	17
Histology	
NHL	4
E	
F	3
G	26
Stage	12
I	
II	7
III	5
IV	9
Site of disease	23
Above diaphragm	
Below diaphragm	10
Treatment	8
Chemotherapy	
Chemotherapy + radiotherapy	25

Mean age of patients = 47.2 yr.
NHL = non-Hodgkin's lymphoma.

ratory and imaging studies, including chest radiography, CT, MRI, lymphangiography, bone marrow biopsy and eventually gastrointestinal and urographic examinations.

Thirty-two patients were treated with polychemotherapy for the first time at National Cancer Institute of Milan (Italy). One patient had been treated for Hodgkin's disease 8 yr before the current diagnosis.

Chemotherapy consisted of cyclophosphamide, Adriamycin, vincristine and prednisone (CHOP) for 18 patients; cyclophosphamide, etoposide, Adriamycin, vePesid and prednisone (CEEP) for 5 patients; or Adriamycin, vePesid, Endoxan, and prednisone (first part)—Ara C, bleomycin, vincristine and methotrexate (second part) (proMACE/cytaBOM) for 10 patients. Radiation therapy was added in 25 patients after the end of chemotherapy treatment.

Patients were monitored for an average of 56 mo (range 7–90 mo), and they were restaged with ^{67}Ga scan after four to six cycles of chemotherapy, according to the stage of the disease and the treatment scheme. In particular, 19 patients were restaged after the fourth cycle of therapy, 12 after the sixth cycle and 2 after the fifth cycle, due to stopping the treatment for bone marrow toxicity. The restaging workup included physical examination and all imaging modalities that were performed during the staging procedure, to have the same imaging studies done before and after treatment. All examinations were performed during the same period (approximately 15 days). Patient data are listed in Table 1.

Imaging

Gallium-67 scanning (75 examinations) was performed 48 hr and sometimes 72 hr after intravenous injection of 185–259 MBq ^{67}Ga-citrate (Mallinckrodt Medical Systems, Petten, The Netherlands). Two large-field-of-view digital SPECT cameras (Toshiba CGA-901A, Toshiba Medical Systems, Inc., Tokyo, Japan; Picker Prism 3000; Picker International, Cleveland, OH) with medium-energy, general-purpose collimators and three energy peaks of 93, 184 and 296 keV (20% window) were used. Total-body images in anterior and posterior views (scan speed 10 cm $\times$ min^{-1}, matrix acquisition 128 $\times$ 512) were supplemented with appropriate planar views of the thorax and abdomen (0.5–10 $\times$ 10^6 counts). SPECT was performed in 30 patients on a 64 $\times$ 64 or 128 $\times$ 128 matrix, collecting 60 projections in a 360° circular orbit at a rate of 40–45 sec per projection. After uniformity correction, 8-mm transaxial, coronal and, in some cases, sagittal tomograms were reconstructed using a medium filter (cutoff frequency = 0.4 pixel^{-1}) with intermediate characteristics between Sheep and Logan and Chesler and suppresses the high frequencies (Toshiba camera). The Picker three-head images were reconstructed using a Wiener filter. SPECT was used in 16 patients.

Abnormal ^{67}Ga tumor uptake was defined as any focal or diffuse area of increased activity in a location incompatible with normal anatomy.

CT scans were performed in 22 patients (total 42 examinations) before and after treatment, whereas the other 11 patients were investigated with MRI (29 examinations). The main criterion of a positive CT scan was the presence of an abnormal mass in the body and a change in tumor size over time; CT assessment of lymphoma activity is predicated on anatomic criteria.

MRI was considered positive for active disease (lesion composed primarily of active tumor tissue) when an homogeneous active pattern, with low signal intensity on T2-weighted imaging and high signal intensity on T1-weighted imaging, was present. Homogeneous inactive pattern, with low signal intensity on T1- or T2-weighted imaging corresponded to lesions composed primarily of fibrosis.

After restaging, the patients were categorized as (a) having achieved CR with no evidence of disease on the basis of clinical, laboratory and imaging studies or (b) having uncertain CR when showing no clinical evidence of lymphoma, but having some persistent abnormality on imaging studies at the site of previous disease.

The results of ^{67}Ga gallium scintigraphy, CT or MRI were matched with clinical findings; an imaging finding that agreed with clinical status was considered to be either true-positive or true-negative.

RESULTS

Of the 75 ^{67}Ga scans performed, 48 (64%) showed abnormal uptake and 27 (36%) were considered negative. In the group of positive scans, there was 1 false-positive result, whereas 4 false-negative findings were recorded in the group of negative scans.

The patients were divided into two groups according to the positivity or negativity of ^{67}Ga scan after four to six cycles of chemotherapy. Of the 33 patients studied, 14 (42.4%) (Table 2) showed persistent abnormal uptake of ^{67}Ga-citrate after four to six cycles of chemotherapy (^{67}Ga positivity group). At staging, ^{67}Ga scan was positive in all patients. During follow-up one false-positive result was recorded by scintigraphy and MRI. A 17-yr-old male patient showed persistent abnormal uptake of the radiotracer behind the sternum after the sixth cycle of chemotherapy; this finding was confirmed by MRI (Fig. 1). Subsequent surgery revealed the presence of thymic hyperplasia. The patient was considered to be in CR 12 mo after presentation.

In this group of 14 patients with abnormal uptake, 9 patients (64.3%) died of lymphoma at a mean of 24.3 mo after presentation (range 7–71 mo). Four patients had no evidence of disease (at 74, 80, 85 and 90 mo from the beginning of treatment). These patients were considered to be in CR 9–12 mo after the beginning of treatment. In particular, in Patients 4, 7 and 13 (Table 2) the ^{67}Ga scan became negative after the radiation treatment. Patient 12 is the 17-yr-old mentioned above who underwent surgery.

The last living patient, a 51-yr-old woman with a sacrum localization of NHL, was considered to be in CR after 8 mo but

TABLE 2
Gallium-67 Positivity After Four to Six Cycles of Chemotherapy

Patient no.	Stage	Site of disease	Follow-up	Clinical outcome
1	IVB	Inguinal nodes, left cervical nodes	CR after 8 mo	Died 26 mo after presentation
2	IIIsB	Mediastinum	PR after 7 mo; no CR	Died 16 mo after presentation
3	IVB	Mediastinum, left lung	PR after 10 mo; no CR	Died 20 mo after presentation
4	IEA	Sacrum	CR after 8 mo	Alive in CR 85 mo after presentation
5	IIIB	Bilateral inguinal nodes	No CR	Died 20 mo after presentation
6	IEA bulky	Right maxillary bone	PR after 7 mo	Died 19 mo after presentation
7	IVB	Sacrum, L3–L4	CR after 8 mo	Alive in CR 80 mo after presentation
8	IEA	Right maxillary bone	CR after 8 mo	Died 71 mo after presentation
9	IVA	Sacrum	PR after 8 mo; no CR	Alive 79 mo after presentation
10	IV	Liver	No PR	Died 24 mo after presentation
11	IVB	Right axilla, iliac bone	No PR	Died 7 mo after presentation
12	IIIB	Mediastinum	CR after 12 mo	Alive 74 mo after presentation
13	IIIEB bulky	Sternum	CR after 12 mo	Alive 90 mo after presentation
14	IB	Mediastinum	No PR	Died 14 mo after presentation

CR = complete remission; PR = partial remission.

relapsed 31 mo after presentation with evidence of node metastases in the left supraclavear region. Regarding follow-up of these patients (Table 2), 7 of the deceased never reached CR and 2 were considered to be in CR 8 mo after presentation but relapsed at 3 and 34 mo, respectively. The 5 living patients were considered to be in CR at a mean of 9.6 mo after presentation, and in 4 of these patients the disease was localized in the bone.

In the second group of 19 patients, ^{67}Ga scan at staging was positive in 16 and negative in 3. We had one false-negative result in a woman with lymphoma of the breast and axillary lymph nodes. The ^{67}Ga scan was negative at presentation and after the fourth cycle of therapy but became positive when the patient relapsed 9 mo after the primary diagnosis. She died due to progression of the disease 7 mo after the local recurrence. In the other 2 patients, the ^{67}Ga scan showed a negative pattern after surgery of the primary site involved (thyroid gland and axillary lymph nodes, respectively). In these 2 patients the results of CT of thorax and abdomen were also negative.

In this group of ^{67}Ga-negative patients, 4 patients died after four cycles of chemotherapy. The primary sites of lymphoma were the breast and axillary nodes, the lumbar-aortic lymph nodes, the thyroid gland and the retroperitoneum region. They died at 16, 19, 24 and 58 mo, respectively, due to disease progression. Two of these patients were considered to be in CR 4 mo after diagnosis and local relapse was seen 9 and 11 mo after the primary diagnosis; in another patient, scintigraphy showed ^{67}Ga uptake in the liver, which was confirmed by CT and ultrasonography after 10 mo PR. In another female patient

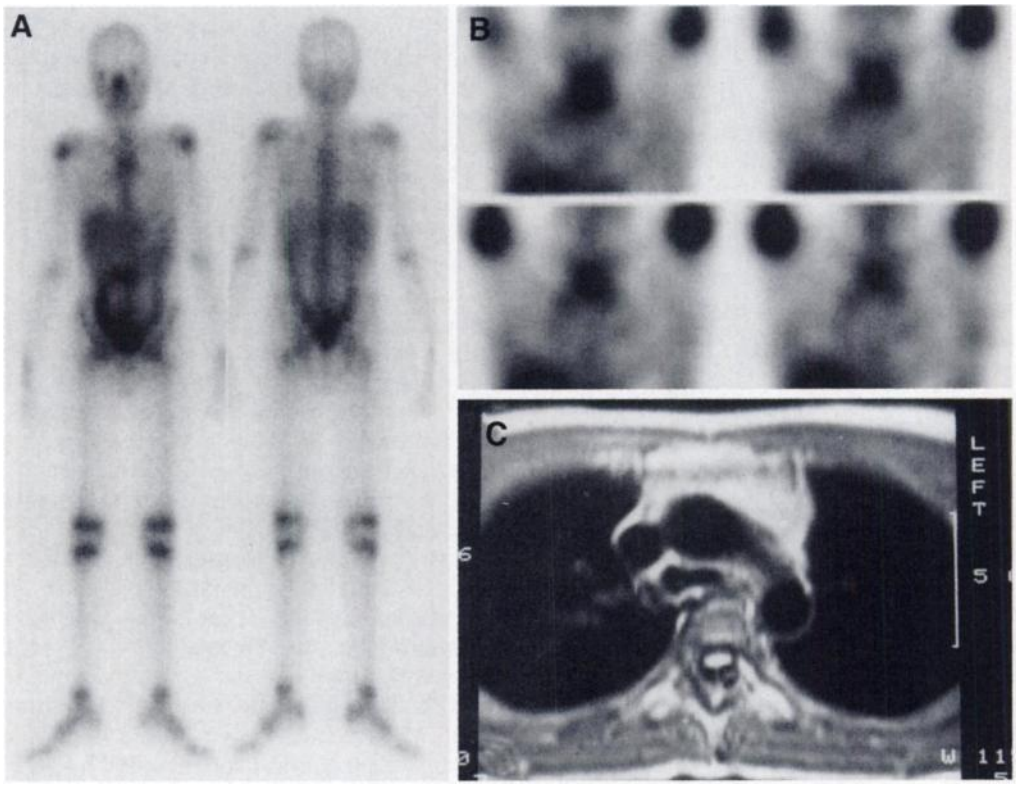

FIGURE 1. (A) Total-body image (anterior view) obtained 48 hr after injection of 185 MBq ^{67}Ga-citrate in 17-yr-old male patient with NHL. Note faint uptake in retrosternal region that is suspicious for persistent disease. (B) SPECT image of thorax shows important uptake of radiotracer, with extension near the paramediastinal region. (C) MRI also confirmed the presence of malignant tissue (proton-density image).

TABLE 3
Results of Gallium-67 Scintigraphy in 33 Patients with Diffuse Large Cell Non-Hodgkin's Lymphoma

Result	CR	PR	Died	Active tumor
Positive	4	0	9	1
Negative	15	0	4	0
Total	19	0	13	1

CR = complete remission; PR = partial remission.

with tumor localization in the thyroid, relapse occurred 50 mo after presentation, and the patient died 8 mo later due to substantial disease progression in the liver and retroperitoneum.

Of the 42 CT examinations, no false-positive results were noticed and only 1 patient had a false-negative result (a patient with subclavian lymph node involvement), whereas of 32 MRI studies performed, a false-positive result was recorded for 2 patients (both had mediastinal disease).

Table 3 summarizes the results of ^{67}Ga scanning. Ninety patients achieved CR on the basis of clinical and imaging criteria; 13 did not achieve CR and died.

A statistical analysis of the association between ^{67}Ga scan results after four to six cycles of chemotherapy and survival was performed using the log-rank test; there was a statistically significant association between scan results and survival ($p = 0.00125$) (Fig. 2). Figure 3 shows the statistical analyses of disease-free interval. Again, a statistically significant association was shown between ^{67}Ga scan results and disease-free interval ($p = 0.003$).

DISCUSSION

Durable CRs and cures may be achieved in a significant number of patients with intermediate and high-grade NHL using aggressive chemotherapy, radiation therapy or both (*21,22*). The inability to obtain a CR is almost always associated with limited survival. During the restaging of NHL patients, persistent masses are not uncommon (*23,24*), but there are no reliable radiographic characteristics that allow differentiation between malignant and fibrotic or necrotic tissue. Persistent tumor may be present despite a normal chest radiograph or CT scan as shown by a 20%–40% relapse rate from CR in a published series (*25*).

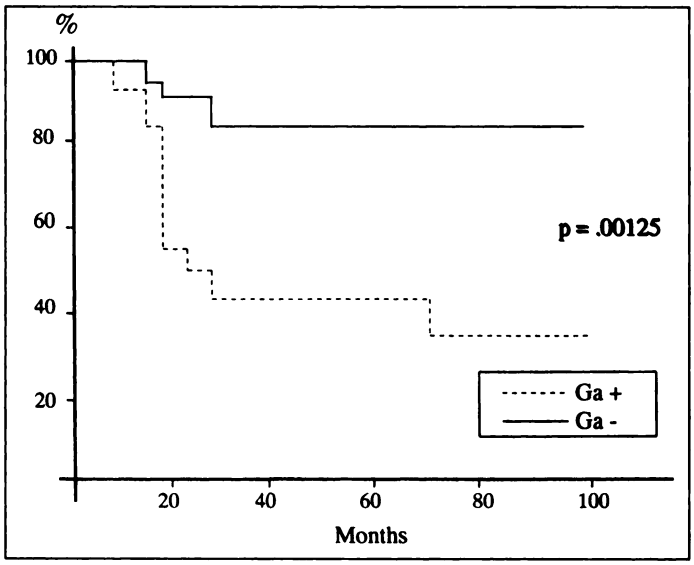

FIGURE 2. Survival curves of patients with NHL with positive and negative ^{67}Ga scintigraphy after four to six cycles of chemotherapy.

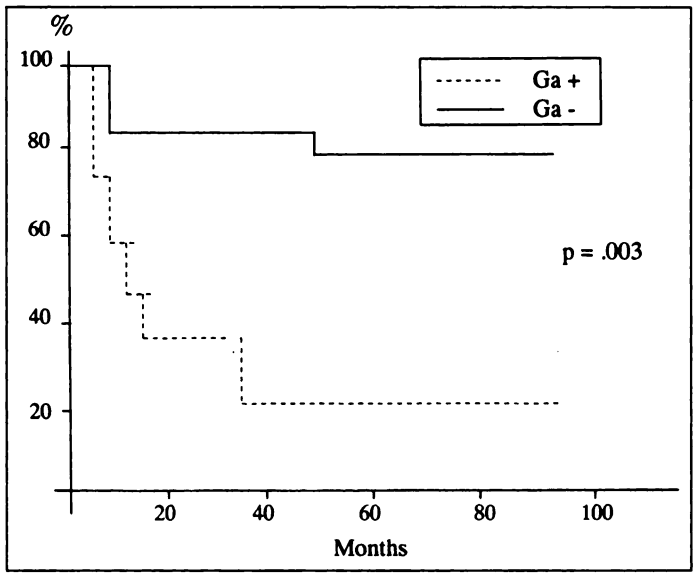

FIGURE 3. Disease-free survival in patients with NHL with positive and negative ^{67}Ga scintigraphy after four to six cycles of chemotherapy.

In a previous report (*13*), we showed that ^{67}Ga scan and MRI were accurate in assessing the activity of residual masses in the mediastinum in patients with Hodgkin's disease after treatment, but MRI often overestimates the presence of malignant tissue. Armitage et al. (*26*) showed with CT scans and radiographs that the rapidity of response is an important prognostic factor in DLCL. In their experience, patients who achieved CR within three cycles of initiating therapy had more durable remissions than patients who required five cycles to achieve remission and thus received two more treatment cycles. In their series, 60% of the patients did not achieve CR before five cycles of treatment relapsed within the 2-yr period of follow-up, whereas when CR was achieved after three cycles of therapy, the relapse rate was only 20%. Kaplan et al. (*27*) demonstrated the clinical utility of gallium scan to predict outcome after initial treatment in 37 consecutive DLCL patients. In their study, persistent ^{67}Ga uptake after four cycles of combination chemotherapy for DLCL predicted a poor outcome. At follow-up, 10 of 17 patients (59%) who were gallium positive halfway through therapy died, whereas in the group of negative patients only 20% (4 of 20) died due to disease progression. The positivity of this radiotracer during chemotherapy could indicate the clinical outcome in patients with DLCL.

Recently, there have been reports on the value of FDG in the evaluation of treatment response in lymphoma (*28,29*). Although it has been shown that ^{67}Ga and FDG are both viability agents (*20*) and that they show a similar behavior in lymphoma after treatment, PET has significantly higher costs and more complicated logistics than the cheaper and more convenient single-photon ^{67}Ga scan. At present, in Italy the cost of a PET scan is about $1500 versus $180 for ^{67}Ga scintigraphy.

In our study of 33 patients, 14 showed persistent ^{67}Ga uptake after four to six cycles of polychemotherapy, and 9 died of disease progression. In the group of patients with negative ^{67}Ga scan results, only 4 patients died and 14 were considered to be in CR; in 1 patient there was persistent disease with a follow-up of 79 mo. Survival time and disease-free interval showed a significant association with results of ^{67}Ga scan, whereas no significant correlation between the time to achieve CR, disease relapse and site of relapse was observed.

Our data seem to suggest that any abnormal ^{67}Ga uptake should be considered an indicator of residual tumor. In this

context, particular attention must be paid to the technical parameters associated with optimal gallium scanning. High doses (185–296 MBq) will allow increased diagnostic performance, particularly on delayed images because the tumor-to-background ratio increases with time. Acceptable counting rates can be achieved even up to 4–5 days after radionuclide injection.

CONCLUSION

Gallium-67 scanning seems to be the best modality available for evaluating treatment response and predicting outcome in patients with diffuse small and large cell lymphoma. Persistent ^{67}Ga uptake after four cycles of polychemotherapy may justify a change of therapy.

REFERENCES

1. Shipp MA, Harrington DP, Anderson JR, et al. A predictive model for aggressive non-Hodgkin's lymphoma. *N Engl J Med* 1993;329:987–994.
2. DeVita VT, Hubbard SM, Young RC, et al. The role of chemotherapy in diffuse aggressive lymphomas. *Semin Hematol* 1988;25:2–10.
3. Jochelson M, Mauch P, Bilikian J, Rosenthal D, Canellos G. The significance of the residual mediastinal mass in treated Hodgkin's disease. *J Clin Oncol* 1985;3:637–640.
4. Israel O, Front D, Ebelbaum R, et al. Residual mass and negative gallium scintigraphy in treated lymphoma. *J Nucl Med* 1990;31:365–368.
5. Wylie BR, Southee AE, Joshua DE. Gallium scanning in the management of mediastinal Hodgkin's disease. *Eur J Haematol* 1989;42:344–347.
6. Lewis E, Bernardino ME, Salvator PG, Cabanillas FF, Barnes PA, Thomas JL. Post-therapy CT-detected mass in lymphoma patients: is it viable tissue? *J Comput Assist Tomogr* 1982;6:792–795.
7. Chen JL, Osborne BM, Butler JJ. Residual fibrous masses in treated Hodgkin's disease. *Cancer* 1987;60:407–413.
8. Radford JA, Cowan RA, Flanagan M, et al. The significance of residual mediastinal abnormality on the chest radiograph following treatment for Hodgkin's disease. *J Clin Oncol* 1988;6:940–946.
9. Front D, Ben-Haim S, Israel O, et al. Lymphoma: predictive value of Ga-67 scintigraphy after treatment. *Radiology* 1992;182:359–363.
10. Karimjee S, Brada M, Husband J, McCready VR. A comparison of gallium-67 single photon emission computed tomography and computed tomography in mediastinal Hodgkin's disease. *Eur J Cancer* 1992;28A:1856–1857.
11. Tesoro-Tess JD, Balzarini L, Ceglia E, et al. Magnetic resonance imaging in the initial staging of Hodgkin's disease and non-Hodgkin's lymphoma. *Eur J Radiology* 1991;12:81–90.
12. Hill M, Cunningham D, MacVicar D, et al. Role of magnetic resonance imaging in predicting relapses in residual masses after treatment of lymphoma. *J Clin Oncol* 1993;11:2273–2278.
13. Gasparini M, Balzarini L, Castellani MR, et al. Current role of gallium scan and magnetic resonance imaging in the management of mediastinal Hodgkin lymphoma. *Cancer* 1993;72:577–582.
14. Nyman RS, Rehn SM, Glimelius BLG, et al. Residual mediastinal masses in Hodgkin's disease: prediction of size with MR imaging. *Radiology* 1989;170:435–440.
15. Frija J, Bris C, Yarner C, et al. MRI with gadolinium of post therapeutic residual masses in lymphoma [Abstract]. *Eur J Radiol* 1991;1(suppl):17.
16. Okada J, Yoshikawa K, Imazeky K, et al. The use of FDG PET in the detection and management of malignant lymphoma: correlation of uptake with prognosis. *J Nucl Med* 1991;32:686–691.
17. Leskinen-Kallio S, Ruotsalainen U, Nagren K, Teras M, Joensum H. Uptake of carbon-11-methionine and fluorodeoxyglucose in non-Hodgkin's lymphoma: a PET study. *J Nucl Med* 1991;32:1211–1218.
18. Kubota R, Yamada S, Kubota K, Ishiwata K, Ido T. Microautoradiographic study of F-18-FDG: high accumulation in granulation tissues and phagocytes in mouse tumor in vivo [Abstract]. *J Nucl Med* 1992;33:840.
19. Wahl RL, Clavo A, Brown RS, Roessner J. 2-Fluoro-2-deoxy-D-glucose (FDG) uptake into human cancer cell lines is increased by hypoxia [Abstract]. *J Nucl Med* 1992;33:841.
20. Iosilevski G, Front D, Bettman L, et al. Uptake of gallium-67 citrate and [2-H^3]deoxyglucose in the tumor model, following chemotherapy and radiotherapy. *J Nucl Med* 1985;26:278–282.
21. Straus DJ. Modern approaches for Hodgkin's disease. *Curr Opin Oncol* 1993;5:785–790.
22. von Gunten CF, Gordon LI. Treatment of advanced, aggressive non-Hodgkin's lymphoma. *Curr Opin Oncol* 1993;5:791–796.
23. Peylan-Ramu N, Haddy TB, Jones E, et al. High frequency of benign mediastinal uptake of gallium-67 after completion of chemotherapy in children with high-grade non-Hodgkin's lymphoma. *J Clin Oncol* 1989;7:1800–1806.
24. Canellos GP. Residual mass in lymphoma may not be residual disease. *J Clin Oncol* 1988;6:931–933.
25. Stewart FM, Williamson BR, Innes DJ, et al. Residual tumor masses following treatment for advanced histiocytic lymphoma. Diagnostic and therapeutic implications. *Cancer* 1985;55:620–623.
26. Armitage JO, Weisenburger DD, Hutchins M, et al. Chemotherapy for diffuse large cell lymphoma: rapidly responding patients have more durable remissions. *J Clin Oncol* 1986;4:160–164.
27. 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.
28. Newman JS, Francis IR, Kaminski MS, et al. Imaging of lymphoma with PET with 2-[F-18]-fluoro-deoxy-d-glucose: correlation with CT. *Radiology* 1994;190:111–116.
29. Heokstra OS, Ossenkoppele GJ, Golding R, et al. Early treatment response in malignant lymphoma, as determined by planar fluorine-18-fluorodeoxyglucose scintigraphy. *J Nucl Med* 1993;34:1706–1710.

Impact of Scatter Correction in Planar Scintimammography: A Phantom Study

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This study examines how scatter correction might affect lesion detection and quantitation of tumor-to-normal breast tissue activity ratio in planar scintimammography. **Methods:** Forty-one phantom acquisitions were performed to mimic a wide variety of scintimammographic imaging conditions in which lesions would be close to the chest wall. For each acquisition, the images corresponding to a 10% energy window (I10) and two scatter correction methods [the Jaszczak (JA) method and a factor analysis (FA)-based method] were obtained in addition to the conventional 20% image (I20). A total of 368 images in which detection of the "tumor" was judged borderline were selected, and 10 independent observers were asked to detect lesions in these images. Receiver operating curve analyses were performed to assess detection performance. Tumor-to-normal tissue activity ratios were calculated for quantitative analysis. **Results:** Detection performance significantly improved for the I10, JA and FA images compared to the I20 images, with an increase in sensitivity up to 8% for FA images. Sensitivity was especially increased for small lesions (13- and 16-mm^3 spheres) and true heart-to-normal tissue activity ratios of >12. Scatter correction also increased the certainty with which the readers gave their judgment. The tumor-to-normal tissue activity ratio was ~8% larger on JA or FA images and 1% larger on the I10 images compared to the I20 images. For a given image, the variability with which this ratio was estimated was reduced by ~4% on JA and FA images. **Conclusion:** Based on these phantom results, scatter correction might be used with benefit in scintimammography.

Key Words: scatter correction; scintimammography; receiver operating curve analysis; quantitation

J Nucl Med 1998; 39:1590–1596

Received Aug. 5, 1997; revision accepted Nov. 24, 1997.

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