^{67}Ga-Citrate Imaging

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Since the development of clinical scanning, researchers and clinicians alike have been interested in the technique as a means of locating tumors. This interest has promoted a wide search for a tumor-specific scanning agent, especially an agent that will concentrate in all tumors irrespective of type of location. In 1969 Edwards and Hayes (*1*) noted on a skeletal scan the accumulation of ^{67}Ga-citrate in the neck lymph nodes of a patient with Hodgkin's disease.

The sequence of research findings that led these investigators to use carrier-free ^{67}Ga-citrate as a tumor scanning agent were: (A) The radiochemical characteristics of ^{68}Ga and ^{72}Ga do not lend themselves to good scanning agents; the half-life of ^{68}Ga is too short, and the gamma emissions of ^{72}Ga are too high for proper collimation; (B) ^{67}Ga has better characteristics as a scanning agent than either of the other two. It has a convenient 78-hr half-life and gamma emissions that are suited for commercially available imaging systems. (C) Radionuclides of gallium concentrate in bone only when administered along with a proper amount of cold gallium as a carrier (*2,3*). When carrier is omitted, these nuclides show diffuse, total-body distribution. (D) It was decided from these facts that ^{67}Ga, administered with carrier added, would be a better bone scanning agent than ^{68}Ga. Using ^{67}Ga meant that scans could be performed days after its administration, thus providing a better bone-to-soft tissue ratio. (E) It was during these studies that Edwards and Hayes noted that *carrier-free* ^{67}Ga would concentrate in soft tissue tumors (*3,4,5*).

Since the initial observations by these investigators, the affinity of carrier-free ^{67}Ga-citrate has been proven by a number of authors (*6-15*). Positive gallium retention was observed in the scans of patients with a variety of malignant neoplasms. Reticulum cell sarcoma, lymphoblastoma, and poorly differentiated adenocarcinoma gave the most consistent positive results. In these studies, ^{67}Ga was found to localize most in viable tumor cells and less in fibrotic or neocrotic tumor, and isotope retention was diminished after effective radiation therapy and/or chemotherapy.

Langhammer, et al (*16*) have summarized the results of four European university centers* in visualizing the distribution of ^{67}Ga-citrate in 246 patients with different neoplasma and non-neoplastic disease. Their greatest accuracy was

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*Universities of Amsterdam, Berlin, Giessen, and Munich.

Table 1. Total ^{67}Ga-Citrate Examinations

Disease	Examinations
Leukemias	
Acute lymphocytic	2
Multiple myeloma	1
Lymphomas	
Hodgkins	67
Lymphocytic	8
Histocytic	12
Burketts	1
Adenocarcinoma	
Lung	1
Thyroid	1
Breast	5
Epidermoid carcinoma	
Bronchus	3
Mesenchymal tumors	
Mesenchyomoma	1
Neuroblastoma	2
Osteogenic sarcoma	2
Inflammatory lesions	
Sarcoidosis	1
Benign nodule	1
Tuberculosis	1
Lymphadenopathy	1
Total	110

Table 2. Distribution of Positive and Negative Examinations with Diagnosed Lymphoma

	Number	Positive	Negative
Hodgkins	67	38	29
Lymphocytic	8	4	4
Histocytic	12	9	3
Burketts	1	1	0
Total	88	52	36

Table 3. Patients with NED Lymphomas

	Number	Image results			+Image accuracy	
		+	−	±	True	False
Hodgkins	23	7	14	2	6	1
Histocytic and lymphocytic	6	5	1	0	4	—
Total	29	12	15	2	10	1

found in patients with bronchial, thyroid, and gastric carcinomas, malignant melanoma, and metastases of unknown primary tumors.

Higasi, et al (*17*) have presented data on the distribution of ^{67}Ga in 149 patients with a variety of neoplasma and inflammatory lesions. Their best results were found in the diagnosis of primary and metastatic lung cancer (23 of 29 patients had positive images), breast cancer (8 of 16 patients had positive images), and maxillary cancer (8 of 8 patients had positive images). These investigators also found that ^{67}Ga imaging is most useful in evaluating the effectiveness of treatment and the susceptability of tumor cells to irradiation.

Results

In Table 1 our total ^{67}Ga-citrate examinations are listed by disease type. The only disease category with a sufficient number of examinations to evaluate is the lymphomas, a total of 88 examinations. Table 2 shows the distribution of positive and negative examinations on patients with diagnosed lymphoma. On further examination of these patient's charts we found that 29 of these clinically had no evidence of disease (NED) on the last visit to their physician. Table 3 shows the 29 NED patients from Table 2 and their image results. We believe that from the reviews stated and our experience ^{67}Ga-citrate imaging can be a valuable tool in the diagnosis and follow-up of cancer patients.

From the observation of these investigators one might think ^{67}Ga-citrate is the ultimate agent for cancer localization. But there are two problems that can be recognized immediately: (A) localization of ^{67}Ga-citrate in the bowel, and (B) the extent of contrast enhancement due to total-body distribution of the ^{67}Ga-citrate if you have no method for "after-the-fact" contrast enhancement.

To help eliminate bowel activity (Fig. 1)) we have chosen to routinely give oral laxatives on three evenings prior to scanning, and enemas are sometimes still required (Fig. 2) before imaging. Since ^{67}Ga-citrate may also be seen in bowel mucosa, it must be noted that laxatives and enemas are not always totally effective for removing activity from the abdominal area. One must also note ^{67}Ga-citrate uptake in unusual areas (Figs. 3 and 4) such as recent surgical scars.

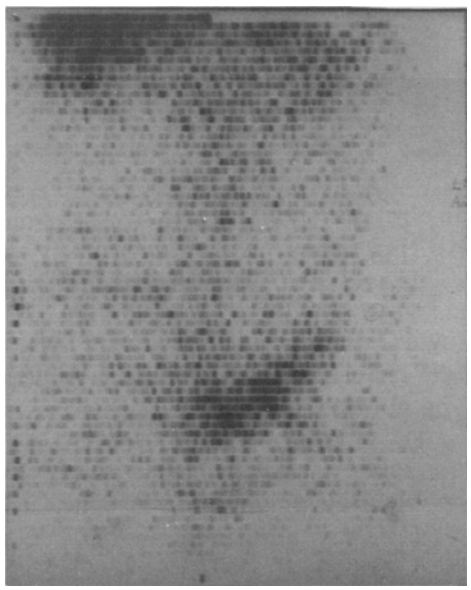

FIG. 1. Image after three oral laxatives.

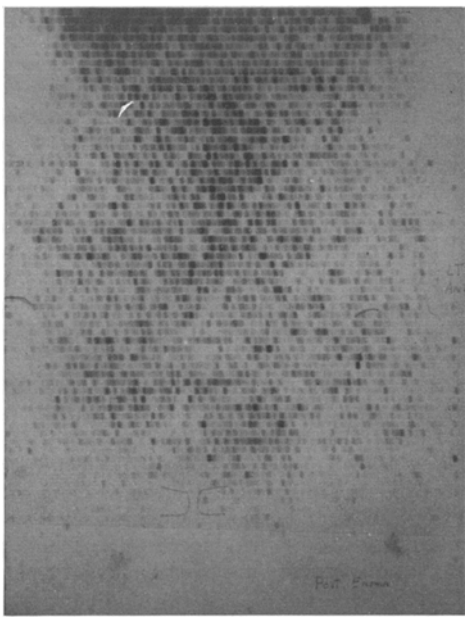

FIG. 2. Image from Fig. 1 after enema.

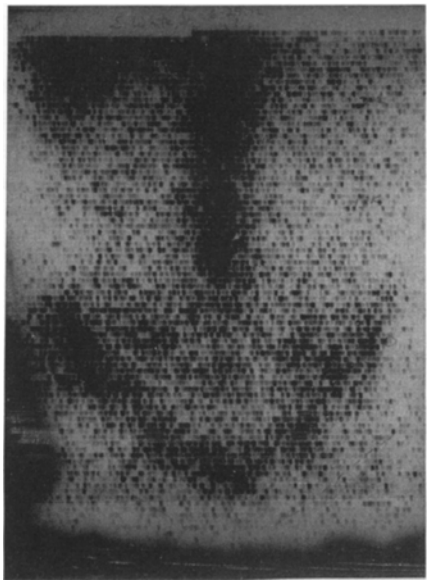

FIG. 3. ^{67}Ga-citrate image illustrating surgical scar.

As for contrast enhancement we have chosen to show the "hot" area (Figs. 1 and 2) in a field of gray, which will demonstrate any activity above body background. These studies were performed on a single 5-in. scanner at an i.d. of 400-500 counts/cm^2. We have found it very important to choose the contrast setting for each patient rather than use an arbitrary one for all images. These images were performed 3 days after the injection of 35 mCi/kg body weight.

Figures 5-7 show additional uses of ^{67}Ga-citrate in our institution.

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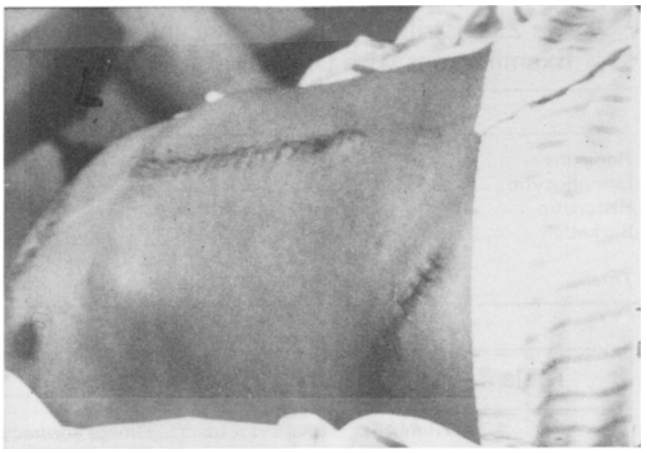

FIG. 4. Surgical scar, 7 days postoperative at time of image.

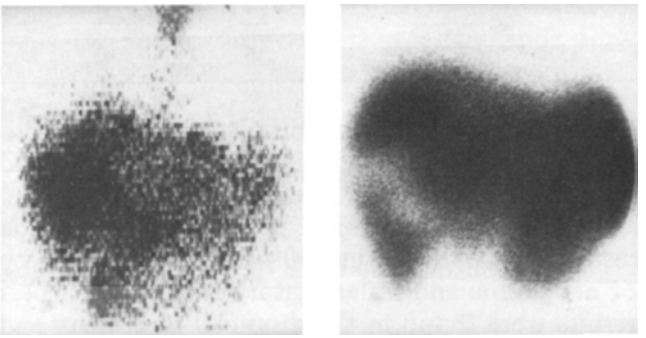

FIG. 5. Left, scan made with ^{67}Ga-citrate; right with ^{99m}Tc-sulfur colloid. In this patient with Hodgkins disease correlation of gallium scan with other images is often helpful.

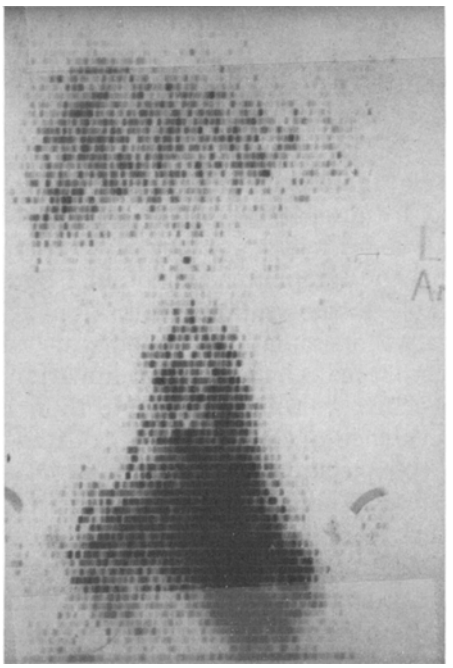

FIG. 6. Image performed on patient with Hodgkins' disease demonstrates usefulness as tool for following up patients. Patient had no evidence of disease on her last physician visit before this image.

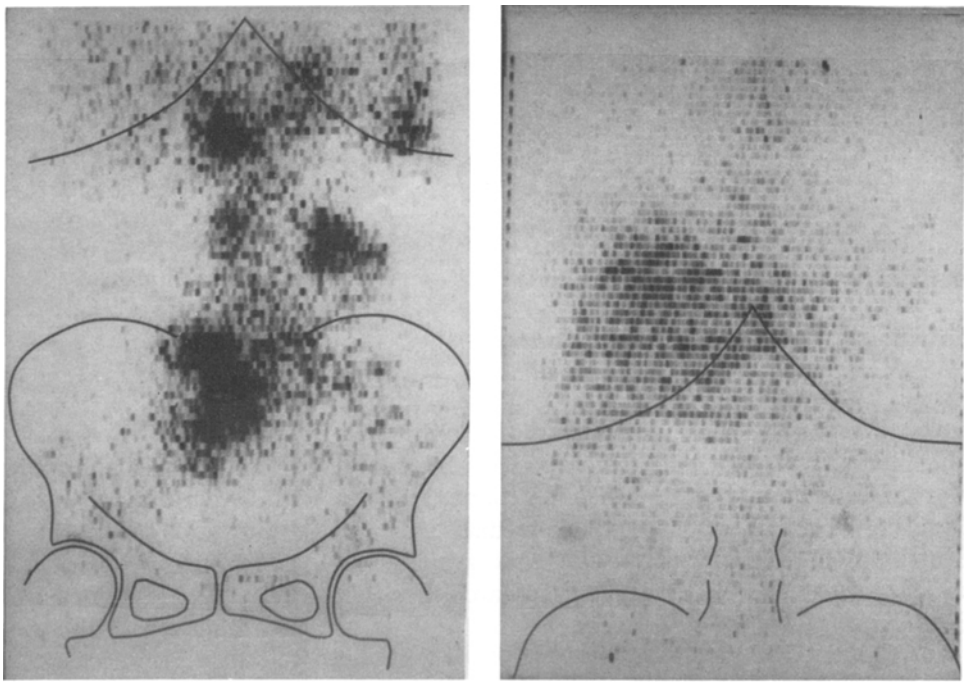

FIG. 7. Left shows scan before treatment; right is after treatment. Possibly most important use of ^{67}Ga-citrate imaging is diagnostic value, as demonstrated in patient thought to have lymphoma. Diagnosis was not confirmed until after ^{67}Ga-citrate image suggested biopsy site which revealed histocytic lymphoma.

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