Gallium Imaging in Metastatic and Recurrent Soft-Tissue Sarcoma

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Fifty-six patients with metastatic or recurrent soft-tissue sarcoma were evaluated by ^{67}Ga-citrate imaging. Prior to entry on the therapy protocol, 52/56 (93%) patients had true-positive ^{67}Ga studies. Two of four patients with liposarcoma, one of twelve with leiomyosarcoma and one with an epithelioid sarcoma had false-negative studies; 89/105 disease sites (85%) were ^{67}Ga positive, including 100% of pleural lesions, 94% in bone, 88% in the abdomen, 85% in soft tissue, 78% in lung parenchyma and 56% of liver metastases. There was significant association between ^{67}Ga avidity and tumor grade with the exception of mesothelioma. No relationship was seen between ^{67}Ga avidity and tumor cell type, disease site or lesion size. Following therapy, ^{67}Ga correctly identified 11/12 sites of active disease in 8/9 patients. Mean pre- and post-therapy ^{67}Ga avidity scores did not differ significantly. Gallium-67 appears to have an important role in the evaluation of patients presenting with either primary or metastatic soft-tissue sarcoma.

J Nucl Med 1992; 33:1594–1599

Soft-tissue sarcomas have been shown to be ^{67}Ga avid (*1–9*) with sensitivities reported to reach 93% (*10*). Howman-Giles et al. proposed that the major role for ^{67}Ga sarcoma imaging is for the detection of local recurrences of primary lesions and for defining the presence of regional metastases (*11*). The effect of surgery, radiotherapy and chemotherapy on ^{67}Ga uptake in primary and metastatic sites has not to our knowledge been assessed.

In this study, we prospectively evaluated patients with soft-tissue sarcomas who were undergoing staging for consideration of entry into a chemotherapy protocol. Our aims were to: (a) assess the sensitivity, specificity and relative avidity of ^{67}Ga uptake at sites of primary and metastatic disease, (b) correlate the degree of ^{67}Ga avidity with cell type, anatomic disease site, tumor grade and lesion size and (c) identify the role of ^{67}Ga imaging for monitoring response to therapy.

MATERIALS AND METHODS

Patients

Patients with a diagnosis of soft-tissue sarcoma, referred to the Dana-Farber Cancer Institute for entry into the MAID* chemotherapy protocol, or, if previously treated with chemotherapy, into a single agent ifosfamide trial, comprised the population for this study (*12,13*). All individuals had recurrent, metastatic or inoperable disease.

Patient evaluations included physical examination, ^{67}Ga scintigraphy, computerized tomography (CT) scans, plain radiographs and, in selected cases, magnetic resonance imaging. Prior to commencing chemotherapy, sites of measurable disease were documented as a baseline for assessing the effects of subsequent treatment. In addition, those ^{67}Ga positive sites which were radiographically normal, i.e., had no anatomic correlate, were also recorded.

At staging there were 56 patients evaluated. The mean age was 41 (median 37, range 18–68 yr). This patient group had been extensively treated by combined modalities before our evaluation with 47 having undergone prior surgery (including 4 with metastatic disease), 17 having received radiotherapy (including 3 with metastases) and 22 having undergone prior chemotherapy. Twenty-three patients had had surgery alone and three patients had had no definitive treatment (biopsy only).

Twenty-nine patients were evaluated by ^{67}Ga imaging following therapy, of which 17 had positive baseline studies, 3 had false-negative baseline studies and 9 had no baseline ^{67}Ga study performed. In the assessment of the post-therapy patient group, a "true-negative" ^{67}Ga site was defined as one that had demonstrated at least a 50% reduction in two-dimensional tumor mass by radiographic assessment and correlated with clinical response (not necessarily implying tumor sterilization) and/or a negative, post-therapy biopsy result.

Tumor Grading

The American Joint Committee staging system was used to grade all tumors (*14*). A minimum of 50 high powered fields (hpf) were examined to determine a mitotic index (mitoses/10 hpf). All pathologic material was reviewed by the Sarcoma Pathology Group at the Brigham and Women's Hospital, Boston,

Received May 24, 1991; revision accepted Apr. 9, 1992.
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* MAID = Mesna, Adriamycin, Ifosfamide, Dacarbazine.

MA. Whenever possible, histologic differentiation was made based on the primary specimen.

Twenty-two patients underwent second biopsies as part of restaging. A median of 80 days intervened between the ^{67}Ga scan and biopsy (range 2 days to 54 mo).

Gallium-67 Imaging

Seventy-two hours after injection of 296–370 MBq (8–10 mCi) of ^{67}Ga, multiple static images of the body were obtained on either of the two large field of view (LFOV) gamma cameras using two (93 and 184 keV) or three (addition of 296 keV) photopeaks with 20% centered energy windows. Views were obtained for 500,000 counts/image with the exception of: (a) approximately 300,000 count views (paired for time) of each axilla with arms abducted, (b) lateral neck views (paired for time), which contained approximately 300,000 counts and (c) anterior femoral views which were imaged for the time needed to acquire the anterior, 500,000 count pelvic view. Additional views of any suspicious site were also obtained (i.e., lateral, oblique, or delayed images, particularly in the abdomen when bowel excretion created an interpretative problem).

Gallium-67 images were interpreted with full knowledge of clinical, radiographic and CT findings and, when necessary, the results of a directed physical examination. SPECT imaging was performed in only a small number of patients, hence the utility of this modality was not analyzed.

Gallium-67 Avidity Scores

Gallium-67 tumor avidity was graded visually according to a relative uptake scale, where 0 was equal to background ^{67}Ga activity, 1 = uptake greater than background but less than that in the sternum, 2 = uptake equal to sternal activity, 3 = uptake greater than that of the sternum but less than liver activity and 4 = avidity greater than that of the liver.

Statistical Analysis

An average lesion avidity was calculated for each patient based on the degree of uptake in ^{67}Ga positive sites. The average avidity score for each ^{67}Ga positive patient was then used to calculate a mean avidity score for each histologic classification (Tables 1 and 2). The nonparametric Kruskal-Wallis analysis of variance test was used in the comparison of average avidities for each histologic group (*15*). In examining the association between ^{67}Ga tumor avidity scores and tumor grade (Table 3), the Mehta-Patel (*16*) network implementation of Fisher's exact test was used to test for the significance of this association.

Data Analysis

Results of the ^{67}Ga studies were analyzed in relation to anatomic metastatic site, tumor cell type, tumor grade and lesion size (except in cases of mesothelioma and bone metastases where lesion size could not be accurately measured). In addition, for those patients who underwent ^{67}Ga studies following therapy, the significance of ^{67}Ga positive and ^{67}Ga negative disease sites was assessed.

RESULTS

At initial evaluation, 52 of 56 patients (93%) had positive ^{67}Ga studies (Table 1). Four patients had false-negative studies: 1/12 patients with leiomyosarcoma, 2/4 with liposarcoma, and 1 patient with an epithelioid sarcoma.

Three patients with widespread disease, manifested as both multiple pulmonary and abdominal masses, were, for purposes of assessing ^{67}Ga lesion sensitivity and avidity, coded as harboring a maximum of five tumor sites. Of the 105 sites of known active disease, 89 (85%) were ^{67}Ga positive (Tables 1 and 2). Gallium-67 was highly sensitive for detecting lesions in the chest wall and pleura (100%), bone (94%), abdomen (88%), and soft tissue (85%), however, only 78% of parenchymal lung lesions and 56% of liver metastases were detected (Table 2).

The mean ^{67}Ga tumor avidity by patient ranged from 2.8 for fibrosarcomas and mesotheliomas to 4.0 for angiosarcomas and malignant fibrous histiocytomas. The Kruskal-Wallis "analysis of variance" test was not signifi-

TABLE 1
Gallium Avidity as Related to Histology at Initial Evaluation

Histology	Patients Ga+/Total	Sites Ga+/Total	Sites (%)	Mean patient avidity*
Leiomyosarcoma	11/12	28/33	85	3.3
Mesothelioma	8/8	10/10	100	2.8
Malignant schwannoma	7/7	8/10†	80	2.9
Rhabdomyosarcoma	6/6	11/11†	100	3.0
Fibrosarcoma	4/4	4/4	100	2.8
Endometrial stromal	3/3	5/8‡	63	3.8
Angiosarcoma	2/2	3/3	100	4.0
Liposarcoma	2/4	2/5	40	3.0
Synovial	2/2	4/5	80	3.3
MFH§	2/2	4/4	100	4.0
Other	5/6	10/12	83	2.9
Totals	52/56 (93%)	89/105	85	3.1

* Mean of average individual patient lesion avidity scores.
† Additional site of anatomical abnormality that was ^{67}Ga negative proven not to be tumor.
‡ Three ^{67}Ga negative lung lesions in a single patient.
§ Malignant fibrous histiocytoma.

TABLE 2
Gallium Sensitivity Related to 105 Disease Sites at Initial Evaluation

Histology	Liver	Lung	Soft Tissue	Abdomen/ Pelvis	Bone	Pleura/ Chest wall
Leiomyosarcoma	5/8	9/10	1/1	9/10	4/4	—
Mesothelioma	—	—	—	2/2	—	8/8
Schwannoma	—	2/2	3/3	2/3	1/2	—
Rhabdomyosarcoma	—	—	7/7	1/1	2/2	1/1
Fibrosarcoma	—	—	1/1	2/2	—	1/1
Endometrial stromal	—	1/4	—	4/4	—	—
Angiosarcoma	—	—	1/1	—	1/1	1/1
Liposarcoma	—	—	1/3	0/1	—	1/1
Synovial	—	2/3	—	—	2/2	—
MFH	—	3/3	—	—	1/1	—
Other	0/1	1/1	3/4	1/1	5/5	—
Total	5/9	18/23	17/20	21/24	16/17	12/12
Percentage	56	78	85	88	94	100

MFH = malignant fibrous histiocytoma.

cant. For all cell types, mean patient tumor avidity pretherapy was 3.1 (median 3.3).

At the time of our initial ^{67}Ga evaluation, 35 patients evidenced either residual or recurrent primary tumor. With respect to sites, 32/35 primary lesions (91%) were ^{67}Ga positive and 57/70 (81%) of metastatic foci were detected. The difference between ^{67}Ga sensitivity for detecting primary versus metastatic lesions was not statistically significant using the Z-test for differences between proportions.

By excluding the eight patients with mesothelioma, there was a positive association between tumor grade and ^{67}Ga avidity; five of six (83%) low grade tumors evidenced a ^{67}Ga avidity of 0–2 and 30/40 (75%) high grade tumors demonstrated an avidity of 3 or 4 (Table 3). By using the Fisher's exact test (*14*), the association between tumor grade and avidity was found to be highly significant ($p = 0.009$). This relationship was not seen with mesothelioma patients.

Gallium-67 image results were also analyzed to determine if detectability was related to lesion size. Lesion size both in terms of volume and maximum diameter was obtained. There were 70 sites where accurate lesion size was available. However, there were many sites where size could not be accurately determined; multiple bone and mesothelioma sites had to be excluded for this reason. No meaningful association between size and ^{67}Ga avidity was evident (Table 4).

Five of 56 patients (9%) had sites of active disease identified only by ^{67}Ga imaging (Table 5, Figs. 1 and 2). Three patients with ^{67}Ga negative sites of radiographically apparent "active" disease were shown by biopsy to have benign process.

Gallium-67 imaging results for detecting lesions in the 29 patients evaluated after additional courses of chemotherapy are shown in Table 6. When only the 17 patients with positive ^{67}Ga baseline studies were considered, ^{67}Ga correctly identified 8/9 patients (89%) with active tumor and 11/12 sites (92% sensitivity) of residual disease. Gallium-67 imaging was shown to be false-negative in only one instance, a patient with an angiosarcoma. Eighteen of 18 sites in the remaining 8 patients were correctly identified as true-negative with no false-positive findings encountered (specificity of 100%).

The mean ^{67}Ga avidity of disease sites before therapy was 3.1 ($n = 52$). Similarly, the mean ^{67}Ga lesion avidity following therapy was 2.8 ($n = 8$).

TABLE 3
Association of ^{67}Ga Tumor Avidity Scores and Tumor Grade*

	^{67}Ga avidity				
Tumor grade	0	1	2	3	4
High	1	3	6	8	22
Intermediate	1	0	0	0	2
Low	2	2	1	1	0

* Excludes eight patients with mesothelioma.

TABLE 4
Gallium-67 Detectability of 70 Tumor Sites as Related to Lesion Size

Lesion size*	True-Positive	False-Negative
>10	11	1
5–10	16	4
2–5	13	3
<2	17	5

* Maximum diameter in centimeters.

TABLE 5
Disease Sites Identified only by ^{67}Ga Imaging

Patient no.	Disease site	Previous RX	CT/X-ray
1	Bone-Shoulder	RT	"Fibrosis"
2	Soft tissue-Abdomen	RT	Normal
3	Soft tissue-Retroperitoneum	SG	"Fibrosis"
4	Soft tissue-Abdomen	RT, SG, CH	"Bowel edema"
5	Bone-Peripheral	None	X-rays normal

RT = radiation therapy, SG = surgery and CH = chemotherapy.

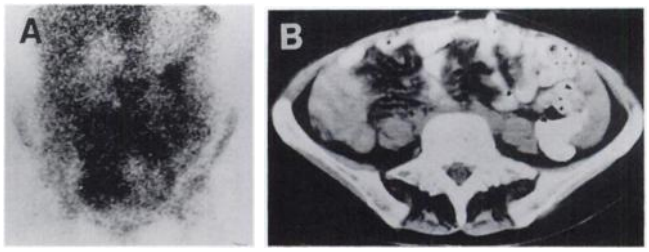

FIGURE 2. (A) Persistent and extensive abdominal radiogallium activity indicated active metastatic uterine leiomyosarcoma in a patient post-surgery and radiotherapy. (B) The CT scan of the patient seen in (A) was interpreted as being within normal limits.

DISCUSSION

Reported series of ^{67}Ga imaging in patients with sarcoma are derived from studies performed at staging. Although some cell types (liposarcomas, synovial sarcomas and rhabdomyosarcomas) have been shown to demonstrate a relatively reduced avidity for ^{67}Ga (*2,4,7*), most histologic subtypes of sarcoma appear to be quite ^{67}Ga avid (*1–11*). Our results in a heterogeneous patient population (extensive tumor involvement, most with active metastatic disease and many having received prior chemotherapy and/or radiotherapy) confirm a high sensitivity (85%) for detecting disease sites.

It should be emphasized that these ^{67}Ga results were obtained using an optimized planar imaging technique. This included appropriate oblique, delayed and "thresholded" or high count density views (1 million counts) of areas of specific clinical relevance. It is probable that a less critical technique, for example, blinded interpretations of anterior and posterior total body sweep images, would have resulted in poorer results.

Although ^{67}Ga is a "nonspecific" tumor marker, in our series there were only two false-positive sites. One patient had a localized infection in the soft tissues of the neck, which in light of clinical information was interpreted correctly at the time of the ^{67}Ga study. The second patient had an unexplained site of focal ^{67}Ga uptake in the abdomen, which has been assumed to be false-positive uptake in the bowel.

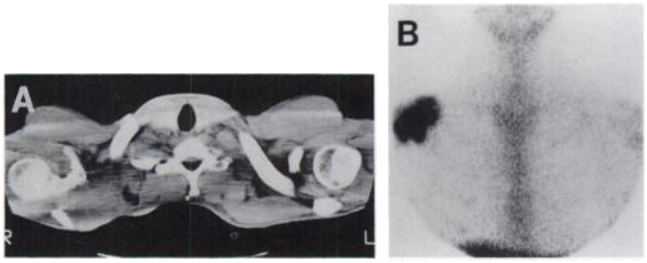

FIGURE 1. (A) The post-radiation therapy CT scan of a patient with synovial cell sarcoma of the right shoulder. The asymmetry, increased on the right, was felt to be consistent with changes due to radiation. (B) The concomittant anterior ^{67}Ga scan of the chest shows intense abnormal uptake in the right shoulder consistent with residual active tumor.

In the mesothelioma patient population, ^{67}Ga was a useful adjunct to CT scanning. Four of seven patients with pleural disease had undergone prior decortication surgery followed by radiotherapy (two patients) or chemotherapy (two patients); considerable scarring was present and the CT scans were difficult to interpret with respect to the potential for persistent tumor. Gallium-67 imaging allowed identification of those individuals with active malignant disease.

With respect to ^{67}Ga sensitivity by site, previous reports have suggested a poor sensitivity in bone (*1*). In our series, however, 94% of bone lesions (most of which were metastatic) were identified. Our findings agree with the results of more recent studies (*9*).

Although there are reports that ^{67}Ga is less sensitive in identifying sites of abdominal sarcoma (*2,10*), in our series, 88% of known abdominal tumor sites were identified by combining clinical and radiographic correlation with delayed views at 5–10 days post-Ga-67 administration. The primary anatomic region associated with difficulty in using ^{67}Ga imaging for identifying metastatic sarcomatous involvement appears to be in the liver where only five of nine sites (56%) were detected. Two of these foci showed reduced uptake relative to adjacent liver, noted as photopenic sites; only three of nine hepatic lesions showed increased ^{67}Ga uptake.

In this series, the apparent difference between ^{67}Ga sensitivity for detecting primary versus metastatic sites of active tumor was related mainly to this difficulty in defining foci of increased tracer uptake within liver, an organ which normally sequesters radiogallium (Table 2). When the nine hepatic sites were excluded from analysis, a similar sensitivity for detecting metastases (0.93) versus primary lesions (0.91) was noted. Indeed, CT imaging is the preferred modality for defining intrahepatic sites of sarcoma and thus this potential deficit in ^{67}Ga sensitivity should not compromise its role in evaluating patients with soft-tissue sarcomas.

Although parenchymal lesions of the lung (most of which were greater than 1 cm in diameter in this series) were detected in 78% of our cases, multiple, small (1–2 mm) lesions seen only with CT scanning were negative on

TABLE 6
Gallium-67 Results for Detecting Lesions in 29 Patients After Chemotherapy

Histology	# Patients	Patients with residual disease	Results by site†			Mean ^{67}Ga avidity*
			TP	TN	FN	
Leiomyosarcoma	4	4	6	3	—	3
Fibrosarcoma	4	2	2	2	—	1.5
Angiosarcoma	2	1	1	1	1	3
Rhabdomyosarcoma	2	1	1	2	—	3
Endometrial Stromal	2	0	—	7	—	—
Liposarcoma	1	1	1	—	—	4
Other	2	0	—	3	—	—
Patients without baseline ^{67}Ga						
Hemangiopericytoma	1	1	1	—	3	1
Leiomyosarcoma	3	0	—	3	—	—
Liposarcoma	3	0	—	3	—	—
MFH‡	1	0	—	1	—	—
Mesothelioma	1	0	—	1	—	—
Excluded (FN baseline)	3	0				
Totals	29	10	12	26	4	2.8

* Mean = mean of the average, individual patient avidity scores.
† TP = true-positive, i.e., ^{67}Ga positive/disease positive; TN = true-negative, i.e., ^{67}Ga negative/disease negative; and FN = false-negative, i.e., ^{67}Ga negative/disease positive.
‡ MFH = malignant fibrous histiocytoma.

^{67}Ga studies. Our results, however, indicate that the size of the lesion had no relationship to ^{67}Ga detectability. For example, a 9 × 10 cm lesion in the soft tissue was ^{67}Ga negative, whereas a 3 × 3 mm lesion in the abdomen was ^{67}Ga avid. That very small pulmonary lesions in particular appear unlikely to be ^{67}Ga positive may relate to factors other than size; indeed, a threshold effect cannot be excluded.

With the exception of mesotheliomas, tumor grade was an important factor in predicting ^{67}Ga avidity. Two of eight patients with low-grade sarcomas (an epithelioid and liposarcoma) were ^{67}Ga negative.

A single ^{67}Ga negative patient with liposarcoma was staged as having high grade disease based on a small biopsy proven focus of high-grade tumor. When the mass was more completely sampled, it was found to be composed almost entirely of low-grade tumor. The only other patient with a negative study had an intermediate grade leiomyosarcoma.

Tumor grade may explain why liposarcomas tend to be ^{67}Ga negative, since these tumors are often comprised of large areas that microscopically evidence a low mitotic rate. We cannot explain why mesotheliomas appear to differ from other sarcomas in this regard.

When considering only those sites that were ^{67}Ga positive on the baseline studies, ^{67}Ga avidity in active tumor sites following chemotherapy was not significantly altered. The ^{67}Ga scan was able to correctly identify 11/12 sites (92%) of residual disease. Eighteen of 18 sites (100%) were also true-negative. Thus, a ^{67}Ga positive site that reverts to negative is indicative of a favorable response to therapy. We must again underscore that the high sensitivity and specificity associated with this study reflect a critical attention to technical detail, delayed imaging and full knowledge of the clinical and radiologic status of the patient at the time of the radionuclide study.

Gallium-67 imaging appears to have an important adjunctive role in the evaluation of patients with soft-tissue sarcomas, particularly in identifying foci unsuspected clinically or radiographically. In particular, it is able to indicate foci of active tumor within residual, post-treatment masses. Uptake is closely associated with tumor grade and, with the exception of liposarcomas and very small pulmonary and intrahepatic metastases, appears unrelated to cell type, lesion size of anatomic location.

ACKNOWLEDGMENTS

The authors wish to thank Laurie Pugsley, Linda Springs and Mary Beth Reynolds for their assistance in the preparation of this manuscript.

REFERENCES

1. Lepanto PB, Rosenstock J, Littman P, Alavi A, Donaldson M, Kuhl DE. Gallium-67 scans in children with solid tumors. *AJR* 1976;126:179–186.
2. Bitran JD, Bekerman C, Golomb HM, Simon MA. Scintigraphic evaluation of sarcomata in children and adults by Ga-67 citrate. *Cancer* 1978; 42:1760–1765.

3. Kirchner PT, Simon MA. The clinical value of bone and gallium scintigraphy for soft tissue sarcomas of the extremities. *J Bone Joint Surg* 1984; 66:319–327.
4. Finn HA, Simon MA, Martin WB, Darakjian H. Scintigraphy with gallium-67 citrate in staging of soft tissue sarcomas of the extremity. *J Bone Joint Surg* 1987;69:886–891.
5. Berkerman C, Hoffer PB, Bitran JD. The role of gallium-67 in the clinical evaluation of cancer. *Semin Nucl Med* 1984;14:296–323.
6. Wentz von K-U, Irngartinger A, Georgi P, Van Kaick A, Kleckow M, Vollhaber HH. Malignant pleural mesothelioma-accuracy of Ga-67 scintigraphy vs. computed tomography. *ROFO* 1986;145:61–66.
7. Sorek M, Rom WN, Goldsmith SJ. Gallium-67 citrate in the staging of diffuse pleural mesothelioma. [Abstract]. *J Nucl Med* 1978;19:692–693.
8. Armas ER, Goldsmith SJ. Gallium scanning in peritoneal mesothelioma. *AJR* 1985;144:563–565.
9. Ramanna L, Waxman A, Binney G, Waxman S, Mirra J, Rosen G. Thallium-201 scintigraphy in bone sarcoma: comparison with gallium-67 and technetium-MDP in the evaluation of chemotherapeutic response. *J Nucl Med* 1990;31:567–572.
10. Kaufman JH, Cedermark BJ, Parthasarathy KL, Didolkar MS, Bakshi SP. The value of Ga-67 scintigraphy in soft tissue sarcoma and chondrosarcoma. *Radiology* 1977;123:131–134.
11. Howman-Giles R, Stevens M, Bergin M. Role of gallium-67 in management of paediatric solid tumours. *Aust Ped J* 1982;18:120–125.
12. Elias A, Ryan L, Sulkes A, Collins J, Aisner J, Antman KH. Response to mesna, doxorubicin, ifosfamide, and dacarbazine in 108 patients with metastatic or unresectable sarcoma and no prior chemotherapy. *J Clin Oncol* 1989;7:1208–1216.
13. Antman KH, Ryan L, Elias A, Sherman D, Grier HE. Response to ifosfamide and mesna: 124 previously treated patients with metastic or unresectable sarcoma. *J Clin Oncol* 1989;7:126–131.
14. Russell WO, Cohen J, Enzinger F, et al. A clinical and pathological staging system for soft tissue sarcomas. *Cancer* 1977;40:1562–1570.
15. Zar JH. *Biostatistical Analysis*, 2nd edition. Englewood Cliffs, NJ: Prentice Hall; 1984:176–179.
16. Mehta CR, Patel NR. A network algorithm for the exact treatment of Fisher's exact test in RxC contingency tables. *J Am Stat Assn* 1983;78: 427–434.

SELF-STUDY TEST

Gastrointestinal Nuclear Medicine

Questions are taken from the *Nuclear Medicine Self-Study Program I*, published by The Society of Nuclear Medicine

DIRECTIONS

The following items consist of a heading followed by numbered options related to that heading. Select those options you think are true and those that you think are false. Answers may be found on page 1668.

True statements concerning the lactulose-H_2 breath test for detecting bacterial overgrowth within the small intestine include which of the following?

1. Up to 30% of patients with bacterial overgrowth do not have bacterial flora capable of producing H_2 from metabolism of the standard 10-gm lactose load.
2. H_2 may result from normal host tissue metabolism.
3. Fasting H_2 breath levels occur after cigarette smoking.
4. Fasting H_2 breath levels may result from small intestinal bacterial overgrowth.
5. Patients who have no rise in H_2 level (> 20 ppm H_2) above baseline after administration of 10 g of lactulose should be retested with 30 g of lactulose.

True statements concerning cholecystokinin (CCK) cholescintigraphy include which of the following?

6. It is an appropriate screening test for patients with upper abdominal pain of uncertain origin.
7. It can be used to identify patients with sphincter of Oddi dyskinesia.
8. Use of CCK increases the sensitivity of hepatobiliary imaging for detecting mechanical cystic duct obstruction.
9. Rapid bolus injection of CCK increases the positive predictive value of CCK cholescintigraphy for diagnosing biliary dyskinesia.

True statements concerning cholecystokinin (CCK) include which of the following?

10. It is produced by the duodenal mucosa.
11. All commercial forms of CCK retain physiologic activity by reproducing the complete 33 amino acid polypeptide chain length.
12. It decreases hepatic bile secretion.

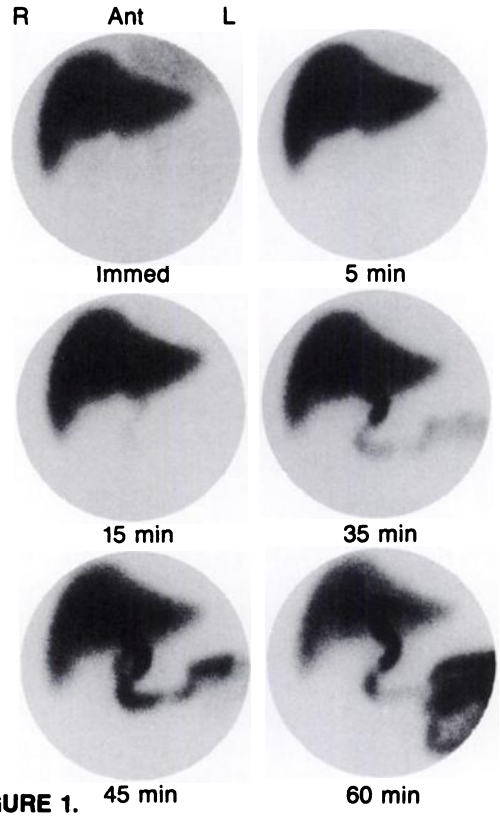

FIGURE 1.

A 51-yr-old man, five days post-coronary artery bypass surgery, develops fever, nausea, and abdominal pain. You are shown this patient's ^{99m}Tc lidofenin hepatobiliary study (Fig. 1).

Which of the following could explain the findings in these images?

(continued on page 1668)