PRELIMINARY NOTES

Tc-99m Glucoheptonate in Detection of Lung Tumors

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Sixty-three patients aged 21–80 yr were examined. Tc-99m glucoheptonate (Tc-GH) scintigraphy was performed in 32 patients: 26 with primary lung carcinoma; six with metastases in lung, mediastinum, and pleura from carcinomas elsewhere; eight with benign pulmonary diseases; and 23 without known pulmonary disease. Tc-GH accumulated in 23 of 26 primary pulmonary carcinomas as active foci. The specificity of Tc-GH scans for neoplasm detection was higher than that of chest radiographs. The visualization of malignant tumors was much better in the late Tc-GH images (5–6 hr) than in the early (1 hr). Metastases from other carcinomas were positive in four of six patients, but they were considerably better detected in the radiographs, except in one patient with metastatic hepatocellular carcinoma. Neoplasms or their metastases in the hilar and mediastinal regions were better detected in the Tc-GH scans than in the chest radiographs. Only one of eight benign lung processes was visualized (as a weak diffuse accumulation of Tc-GH in hilar scar formation), and 23 patients without pulmonary disease had no pathological foci.

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Radionuclide tracers are used in the diagnosis of lung tumors. Ga-67 citrate (Ga-67) is the most commonly used radiotracer in tumor diagnosis. Tc-99m glucoheptonate is reported to be a superior agent in brain-tumor detection (*1*). In our laboratory we have found that Tc-GH also accumulates in lung neoplasms. Here our findings with Tc-GH imaging are compared with chest radiography in the diagnosis of lung tumor.

MATERIALS AND METHODS

Sixty-three patients, aged 21–80 yr, were studied with Tc-GH scanning and chest radiographs: 26 patients with histologically (22) or cytologically (4) proven untreated bronchogenic carcinomas; six with lung, mediastinal, or pleural metastases from histologically proven carcinomas; eight with benign lung diseases; and 23 patients without known lung disease.

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Anterior and posterior—and, if necessary, lateral—lung scans were made using a large-field-of-view Maxicamera, both at one hour and at five or six hours after intravenous administration of 15–20 mCi of Tc-GH. In two patients with bronchogenic carcinoma, the lung scans were repeated 48 hr after intravenous injection of 3 mCi of Ga-67. The scans and the chest radiographs were interpreted by two examiners independently and were characterized as negative or positive.

To verify that the uptake of Tc-GH is actually in the tumor, the scintigraphic findings were compared with chest radiographs, bronchoscopy, thoracotomy, or autopsy.

Sensitivity is defined as a percentage of tests read as abnormal in patients with proven primary lung carcinoma or lung metastases (true-positive results). Specificity is the percentage of tests read as normal in patients free of malignant lung disease (true-negative results). Accuracy of abnormal and normal readings is defined as the percentage of those readings proven correct. Positive predictive value is the probability that an ab-

TABLE 1. RESULTS OF Tc-99m GLUCOHEPTONATE (Tc-GH) SCINTIGRAMS AND CHEST RADIOGRAPHS IN MALIGNANT LUNG LESIONS

Histology	Number of patients	Tc-GH: Positive	Tc-GH: Negative	Tc-GH: Sensitivity (%)	Chest radiograph Positive	Chest radiograph Negative	Chest radiograph Sensitivity (%)
Primary lung ca. (total)	26	23	3	88	25	1	96
Squamous-cell ca.	19	17	2		18	1	
Small-cell ca.	4	4	0		4	0	
Large-cell anaplastic ca.	2	1	1		2	0	
Adenocarcinoma	1	1	0		1	0	
Metastatic to lung (total)	6	4	2	67	6	0	100
Hepatocellular ca.	1	1	0		1	0	
Adenoca. of kidney	1	1	0		1	0	
Adenoca. of thyroid gland	2	0	2		2	0	
Endometrial ca.	1	1	0		1	0	
Malignant melanoma	1	1	0		1	0	
Totals	32	27	5	84	31	1	97

TABLE 2. RESULTS OF EXAMINATION WITH Tc-99m GLUCOHEPTONATE (Tc-GH) AND CHEST RADIOGRAPHY IN PATIENTS WITH BENIGN LUNG DISEASES OR NO KNOWN LUNG DISEASE

Diagnosis	Number of patients	Tc-GH: Positive	Tc-GH: Negative	Chest radiograph Positive	Chest radiograph Negative
Benign lung diseases (total)	8	1	7	8	0
Tuberculosis	4	0	4	4	0
Hilar scar formation	1	1	0	1	0
Lung infiltration	1	0	1	1	0
Fibrosis	1	0	1	1	0
Pleuritis	1	0	1	1	0
No lung disease	23	0	23	0	23

TABLE 3. COMPARISON OF CHEST RADIOGRAPHY AND Tc-99m GLUCOHEPTONATE IMAGING (Tc-GH)

Patients and methods	Sensitivity %	Specificity %	Accuracy %	Positive predictive value %	Negative predictive value %
Patients with lung disease (40)*					
roentgenography	97	0	78	79	0
Tc-GH	84	88	85	96	58
All patients (63)*					
roentgenography	97	74	86	79	96
Tc-GH	84	97	90	96	86

* Number of patients.

normal reading is a true-positive result. Negative predictive value is the probability that a normal reading is a true-negative result.

RESULTS

Tables 1, 2, and 3 present the results of our examinations. Twenty-three of the primary pulmonary cancers were detected by Tc-GH scanning as active foci. In all positive cases the visualization of tumors was much clearer in the late (5–6 hr) than in the early (1 hr) images (Fig. 1). In six cases, in which scans were also obtained 24 hr after the administration of Tc-GH, the visualization was equal to or even better than in the 5–6 hr scans. The delineation of the primary lung cancer in the Tc-GH scan was better in ten, equal in ten, and poorer in six

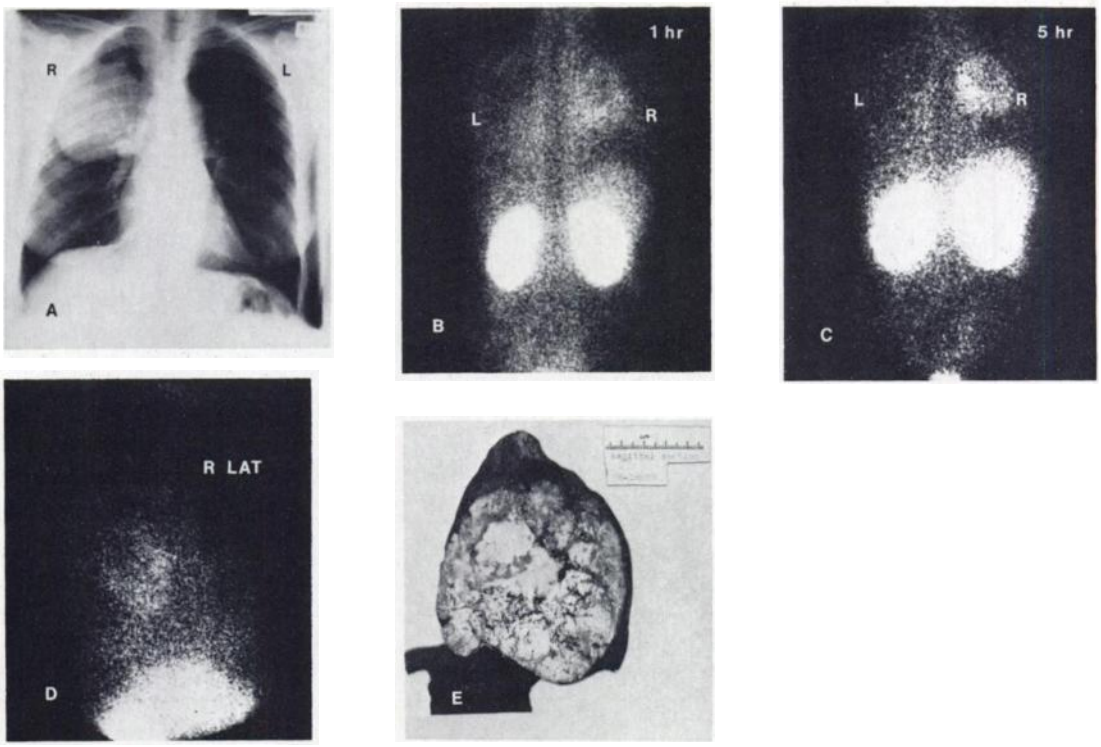

FIG. 1. Squamous-cell carcinoma of right lung. Chest radiograph (A); posterior Tc-GH scan, at 1 hr (B) and 5 hr (C) after injection. Right lateral Tc-GH scan (D), and lateral view of sliced surgical specimen (E). Note poor accumulation of Tc-GH in necrotic part of tumor (C).

patients in comparison with the chest radiographs.

Tc-GH accumulated mainly in the viable parts of two lung tumors but poorly in the necrotic tissue. One of these is shown in Fig. 1. In autopsies of three patients it was noted that a primary lung tumor or metastasis was detected more easily in the Tc-GH scans than in the chest radiographs if the growth was located in the hilar region or in the mediastinum. Also when there was atelectasis (Fig. 2) or inflammation near the tumor it was better defined in the Tc-GH scan than in the radiograph.

One of the squamous-cell carcinomas not seen in the Tc-GH scan was diagnosed by bronchoscopic biopsy; it was too small to be detected in the radiograph. The other squamous-cell carcinoma not detected in the Tc-GH image was also missed in the Ga-67 scan. It was about 1 cm in diameter in the radiograph. A larger squamous-cell carcinoma, however, was visualized better by Ga-67 than by Tc-GH. A large-cell anaplastic carcinoma not visualized by Tc-GH was about 1.5 cm in diameter; clinically it was progressing very slowly.

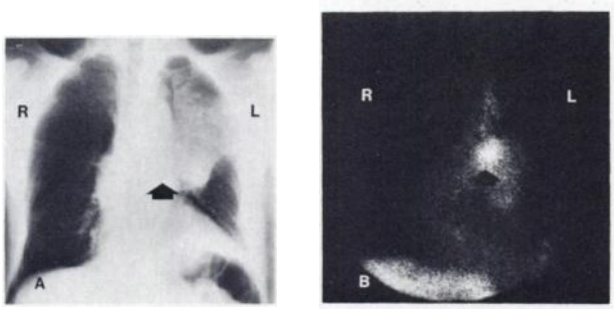

FIG. 2. Squamous-cell carcinoma of left lung, with atelectasis. Chest radiograph (A) and Tc-GH scan 5 hr after injection (B). Tc-GH indicates primary tumor (arrow) and metastases much better than the radiograph.

The metastases were considerably better detected in the radiographs than in the Tc-GH images, in which they were seen as diffusely increased activity without clear foci except in the case of metastases from liver cancer. The latter showed as clear foci, and the primary liver carcinoma also accumulated Tc-GH greater than normal liver (Fig. 3). Primary carcinomas of the kidney or thyroid gland, and their metastases, were rather poorly visualized by Tc-GH.

Only one of the eight benign lung processes was seen as a weak diffuse accumulation of Tc-GH in the hilar scar formation (Fig. 4). The uptake of Tc-GH in the benign process was not gradual and progressive, as in the malignant tumors. Moreover, we have noted that Tc-GH does not accumulate in benign cysts or abscesses in the liver or spleen. The mammary glands of some women accumulated Tc-GH, which made the interpretation of the images somewhat more difficult in women.

Chest radiographs were found to have a sensitivity of 96% for primary carcinoma of the lung, 100% for pulmonary metastases, and 97% for all pulmonary malignancies (Tables 1 and 3). The sensitivity of Tc-GH was 88% for primary lung carcinoma, 67% for pulmonary

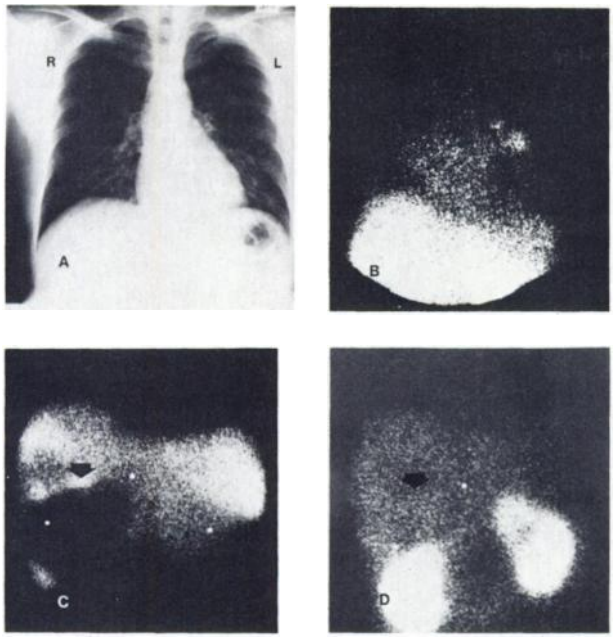

FIG. 3. Pulmonary metastases from a hepatocellular carcinoma. Chest radiograph (A), 5-hr Tc-GH scan of lungs (B), Tc-99m tin colloid scan of liver (C), primary tumor and Tc-GH scan of liver (D). Pulmonary metastases accumulate Tc-GH greater than primary tumor.

metastases, and 84% for all pulmonary malignancies. Tc-GH proved to be superior in specificity, accuracy, and positive predictive value both in those patients with lung disease and in the entire group. The negative predictive value was determined to be 58% with the Tc-GH scan and zero with radiographs in patients with proven lung disease, but the corresponding values were 86% and 96% in the entire group studied.

Every positive Tc-GH scan of patients with proven primary lung carcinoma was compared with chest radiography, bronchoscopy, thoracotomy, or autopsy (Table 4). Tc-GH images showed good correlation with all other observations, which confirms that Tc-GH really concentrates in tumors of the lung. The other tumors were also histologically proven and their pulmonary metastases were typical in chest radiographs showing progressive growth.

TABLE 4. AGREEMENT BETWEEN Tc-99m GLUCOHEPTONATE UPTAKE AND OTHER STUDIES IN PRIMARY LUNG CARCINOMA

Studies	Number of patients
Chest radiography and bronchoscopy	11
Chest radiography, bronchoscopy, and thoracotomy	2
Chest radiography, bronchoscopy, and autopsy	3
Chest radiography and thoracotomy	1
Chest radiography and autopsy	2
Chest radiography and needle biopsy	4
Total	23

DISCUSSION

Our findings show that Tc-GH accumulates visibly in primary lung carcinomas above 2 cm in diameter. As far as we know this observation has not been described before. In the detection of primary lung tumors there was no discrepancy between Tc-GH images and the findings made by chest radiography, bronchoscopy, thoracotomy, or autopsy. This justifies the suggestion that Tc-GH really accumulates in tumors of the lung.

Neoplasms or their metastases in the hilar and mediastinal regions seem to be better detected in Tc-GH scans than in chest radiographs, and this finding agrees well with earlier observations with Ga-67 (*2,3*) and Se-75 selenomethionine (*4*). The tumor was better delineated by Tc-GH than by chest radiograph if there was atelectasis or inflammation near the tumor.

The specificity of the Tc-GH scan was higher than that of chest radiography in tumor detection. Only one of our benign lung processes accumulated Tc-GH diffusely, and some of our unpublished observations suggest that Tc-GH accumulates in malignant processes of liver but not in cysts or abscesses. In brain studies, however, we note that although Tc-GH progressively concentrates in tumors, it is also taken up by circulatory lesions, though not in the same manner (*5*).

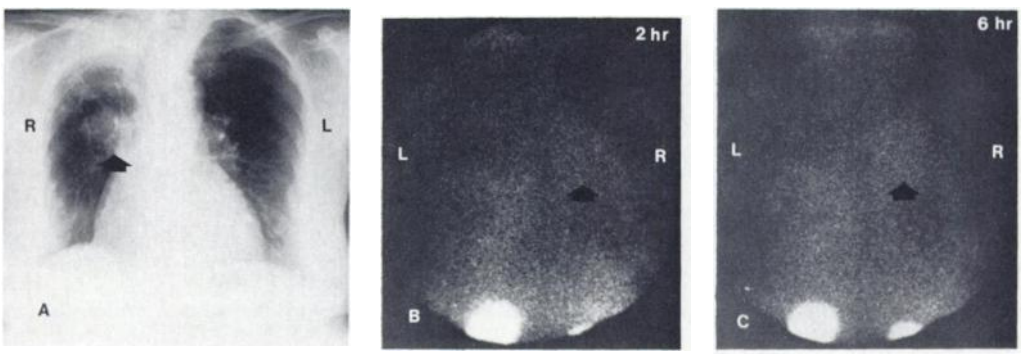

FIG. 4. Chest radiograph (A). Tumorlike scar formation is seen in right hilus after resection of right lobe because of bronchial cyst (arrow). Posterior Tc-GH scans, at 2 hr (B) and 6 hr (C) after injection. Weak diffuse accumulation of Tc-GH occurs in scar formation (arrows).

Because of the blood background, the time interval from the administration of Tc-GH to the scanning should be long enough—presumably at least 5 hr and perhaps up to 24 hr.

The number of patients in our study was too small to make certain whether Tc-GH accumulates in different ways in different types of lung tumor. However, because different primary tumors and their pulmonary metastases concentrate this radionuclide in different amounts, we dare to offer a cautious conclusion that the type of tumor may be important in the accumulation of Tc-GH in neoplastic tissue. Perhaps Tc-GH is taken up like a glucose analog by an active transport mechanism to be used as substrate for energy by the metabolically active tumor tissue. This was suggested also by Léveillé et al. (*5*) in their brain tumor study. This claim is supported by our observation that Tc-GH accumulates much better in the viable components of tumors than in the necrotic parts. Tc-GH probably accumulates somewhat in the necrotic tissue, as it does in myocardial necrosis (*6*), but the mechanism of accumulation must be different. The exact mechanism of Tc-GH uptake in different parts of lung tumors remains for further study.

The sensitivity of chest radiographs was 96% for primary carcinoma of the lung, which supports the common practice of using radiography as the preferred screening method. Tc-GH had a sensitivity of 88%. The sensitivity of Ga-67 is reported to be of about the same order: 84% (*7*) or 90% (*8*). Because Ga-67 scanning has not been our routine method, we have not yet made a comparison of Tc-GH with Ga-67. We think, however, that it is important to make such a comparison to learn whether it is possible to replace some of the Ga-67 studies by this cheaper and more practical Tc-labeled substance. Open questions also concern the effect of radiation therapy on the Tc-GH images and whether it is possible to follow the effectiveness of therapy with Tc-GH. In all, it seems necessary to make further tumor examinations with Tc-GH and perhaps with other metabolically active Tc-labeled substances to find the most suitable tumor-scanning agents.

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