JOURNAL OF NUCLEAR MEDICINE 6:494-505, 1965

Evaluation of Hepatic Photoscanning With Radioactive Colloidal Gold[1]

Kee Suk Whang, M.D.,[2] Mathews B. Fish, M.D. and Myron Pollycove, M.D.

San Francisco

In 1954, Stirret and his associates (1) demonstrated space-occupying abnormalities of the liver by measurements of radioisotope distribution. Since that time, numerous reports (2-17) on hepatic scanning have appeared. ^{131}I rose bengal, ^{131}I tetraiodophenolphthalein, colloidal ^{198}Au, and ^{99}Mo have been used, and the scan image has been produced by either the imprint or the photoscan method.

These studies have shown that the hepatic scan is a useful adjunct in the clinical evaluation of liver disease. It can be used to determine the size, configuration, and position of the liver and also to demonstrate space-occupying hepatic lesions, such as primary and secondary tumors, abscesses, cysts, and arteriovenous fistulae. Scans of livers affected with diffuse pathologic processes such as hepatitis, fatty metamorphosis, and cirrhosis also frequently show characteristic abnormalities.

This paper summarizes the results of 100 consecutive photoscans of the liver in which colloidal ^{198}Au (93 scans) or ^{199}Au (7 scans) were used.

MATERIALS AND METHODS

Hepatic photoscanning was performed with a No. 1700A Nuclear-Chicago Isotope Scanner. A detector containing a 3 $\times$ 2 inch thallium activated sodium iodide crystal and a 19-hole focusing collimator were used.

Approximately 30 minutes prior to scanning, 200μC or 250μC of a suspension of radioactive colloidal gold (^{198}Au or ^{199}Au) were injected intravenously. The dose was selected according to the clinical estimate of the size of the liver, and presence or absence of ascites. The clearance of the detector was set at zero at the highest point of the anterior body surface to be scanned.

For the 0.41 MeV gamma photopeak of ^{198}Au, the analyzer was set with the base at 22.5 volts and a 10-volt window width (0.335 MeV–0.485 MeV; 0-100

[1]From the Department of Patholgy, Clinical Laboratories, San Francisco General Hospital, University of California School of Medicine, San Francisco; the Donner Laboratory and the Lawrence Radiation Laboratory, University of California, Berkeley, California.

[2]At the time this work was carried out, Dr. Whang, a fellow of the International Atomic Energy Commission, was a guest scientist at the Donner Laboratory. His present address is: Kyung-Pook National University School of Medicine, Taegu, Korea.

volts are equivalent to 0.0-15 MeV). For the 0.16 MeV gamma photo peak at ^{199}Au, the analyzer was set with the base at 27.7 volts and a 10-volt window width (0.135 MeV–0.185 MeV; 0-100 volts are equivalent to 0-0.500 MeV).

The scanning speed was set at 25 cm/min or 30 cm/min, depending upon the maximum counting rate over the liver just prior to scanning. The index of the scanner was set at 0.37 cm. During the scanning, a cloth binder was placed on the patient's abdomen to decrease respiratory movement.

Upon completion of scanning, the tip of the xiphoid process, the costal margin, the umbilicus, the palpable liver margin, and any palpable abdominal masses were marked carefully on the scan. The entire procedure usually required 45 to 75 minutes.

RESULTS

Diagnostic Accuracy of the Positive Hepatic Scans

Twenty-five of the 100 scans were interpreted as showing space-occupying lesions. Diagnoses were obtained by liver biopsy, or postmortem examination in 15 of these cases, and confirmed the presence of space-occupying lesions in 14: 13 primary and secondary neoplasms, and 1 abscess (Table 1). Postmortem examination revealed livers diffusely infiltrated by multiple tumor masses or abscesses, the largest measuring 2 to 7 cm in diameter. In one case of metastatic pulmonary carcinoma, the scan was interpreted as showing space-occupying lesions, whereas a blind needle biopsy prior to scanning revealed normal tissue.

Discrepancy Between the Palpable Inferior Liver Margin and the Inferior Margin of the Scan Image

Included in the series of patients in Table I are four in whom there was marked discrepancy between the palpable inferior liver margin of the scan image. In each of these four patients, postmortem examinations revealed massive metastatic replacement of the inferior portion of the liver, accounting for this discrepancy (Fig. 1).

Correlation of Scan Pattern and Liver Function Tests in Cirrhosis

Thirty-five cases of suspected cirrhosis were included in the series; adequate studies were obtained in 28. These patients either were proved cirrhotic by liver biopsy or had a history of chronic alcoholism, repeated hospitalization, typical physical findings, abnormal liver function tests, and characteristic clinical course.

The following liver function tests were performed: determination of serum albumin and globulin, cephalin-cholesterol flocculation, thymol turbidity, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), prothrombin time, total bilirubin (direct and indirect reacting fractions), bromsulfalein excretion, and serum alkaline phosphatase. Depending on the degree of derangement shown by liver function tests are determined by the criteria shown in Table II, cirrhotic patients were divided into four groups (Table III).

A. *Liver Function and "Mottled" Appearance on the Hepatic Scan.* "Mottling" is often found in the hepatic scans of cirrhotic patients (Fig. 2). It was evident that there was no clear correlation between severity of liver dysfunction as shown by tests and the degree of "mottling" (Table III).

B. *Liver Function and Splenic Uptake.* Splenic uptake of radiogold was observed in 16 of the 28 cirrhotic patients and was compared with the results of liver function tests (Table III and Figs. 2, 3). The splenic uptake usually increased as liver function decreased.

Eight of these patients demonstrated concomitant marrow uptake of radiogold in the sternum and vertebrae (Fig. 3). However, only 1 of 12 patients without demonstrable splenic uptake showed marrow uptake. Clinical splenomegaly did not appear to be correlated with splenic uptake.

C. *Liver Function and Enlargement of the Left Lobe.* Some degree of left lobe enlargement was present in most of the 28 cirrhotic patients (Figs. 2, 3). The four patients without apparent left lobe enlargement had only mildly abnormal hepatic function as shown by tests. The 64 patients without any clinical or laboratory evidence of cirrhosis demonstrated no enlargement of the left

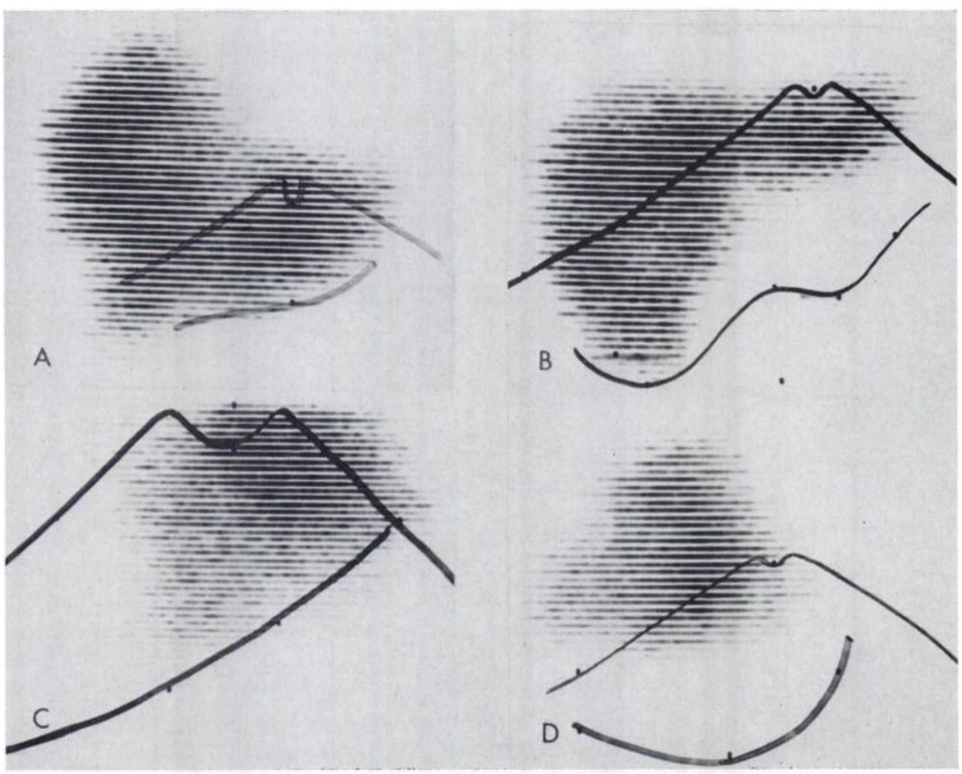

Fig. 1. Hepatic photoscans showing marked discrepancy between the palpable liver margin and the inferior margin of the scan image.

A. Correspondence between palpable margin and scan image (hepatomegaly, etiology undetermined).

B. Discrepancy between palpable margin and scan image.

C. Discrepancy between palpable margin and scan margin.

D. Discrepancy between palpable margin and scan margin.

lobe. In normal subjects there is less apparent concentration of radiogold in the left lobe than in the right lobe (Fig. 2). In contrast, hepatic scans of cirrhotic patients usually showed decreased over-all hepatic uptake and apparent concentration of radioactivity in the left lobe equal to, or even greater than that of the right lobe (Figs. 2, 3).

DISCUSSION

It is increasingly apparent that hepatic scanning has become a useful and practical aid in the diagnosis and management of various hepatic disorders. It has been shown helpful in detecting and localizing the space-occupying lesions of primary and secondary cancers (1-9, 10-12, 15, 17), hydatid cysts (11, 13), and amoebic abscesses (13, 14), as well as in evaluating the results of cancer chemotherapy and radiotherapy (7, 15). Apparent decreased uptake, "mottled" appearance, and periphilar accumulation of the activity, as well as occasional splenic visualization have been noted in the reported hepatic scans of patients with diffuse liver diseases such as cirrhosis, fatty metamorphosis, and hepatitis (5, 7-10, 16-17).

Many workers now prefer to use radioactive colloidal gold rather than the previously introduced ^{131}I rose bengal for hepatic scanning, because colloidal gold is rapidly taken up and permanently held in the Kupffer cells of the liver,

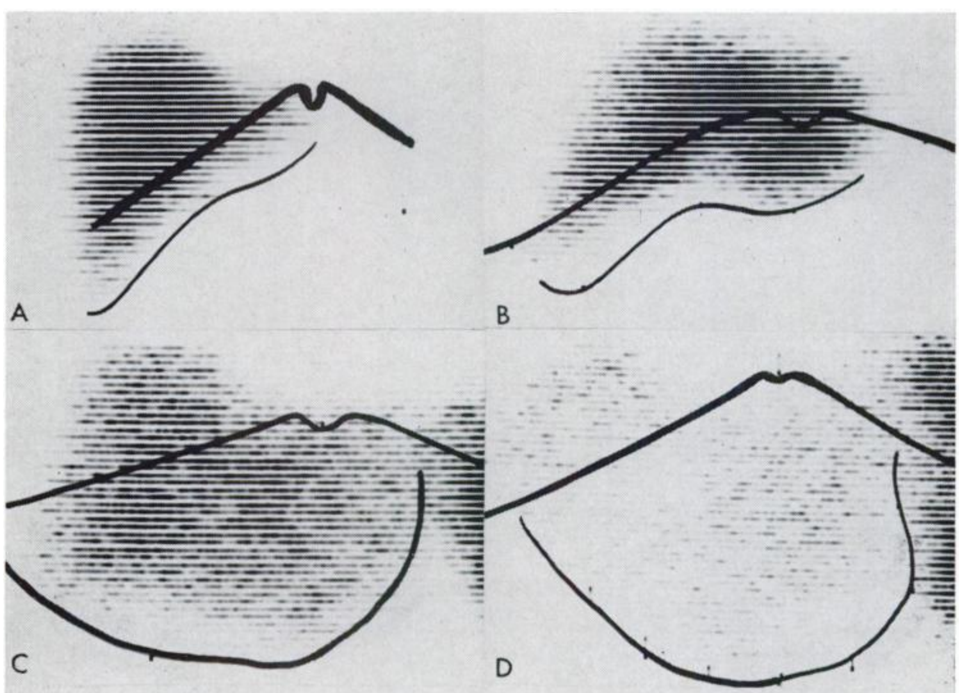

Fig. 2. "Mottled" appearance of the hepatic photoscans in cirrhosis. Note enlargement of left lobe, in B, C, and D and splenic radioactivity in C and D.

A. Normal scan.
B. Mild degree of "mottling."
C. Moderate degree of "mottling."
D. Marked degree of "mottling."

whereas rose bengal is rapidly excreted into the small bowel via the biliary system (18).

Recently, ^{99}Mo, which has certain advantages over colloidal ^{198}Au and ^{131}I rose bengal, has been used for hepatic scanning (17). Its use is limited at present, however, owing to the poor uptake of ^{99}Mo associated with impaired hepatocellular function and the requirement of a special generator and milking system for its production.

Use of multiple hepatic scanning views—anterior, lateral and posterior—considerably improves the detection and localization of abnormalities (13). Multiple views were not employed in this study because of limited availability of scanning time. A more rapid system of visualizing the distribution of colloidal ^{198}Au, such as the Anger Scintillation Camera (19), would be very helpful in this regard.

In our series, of hepatic scans which were interpreted as showing space-occupying lesions and in which histologic diagnosis was available, 93 per cent were correctly diagnosed by photoscannnig. These results may be compared favorably with those of Nagler's (12) large series (83% correctly diagnosed by photoscanning). A valid comparison of diagnostic accuracy or clarity of scan image could not be made between colloidal ^{198}Au and colloidal ^{199}Au, as only 7 of the 100 scans were performed with colloidal ^{199}Au. These 7 scans were comparable

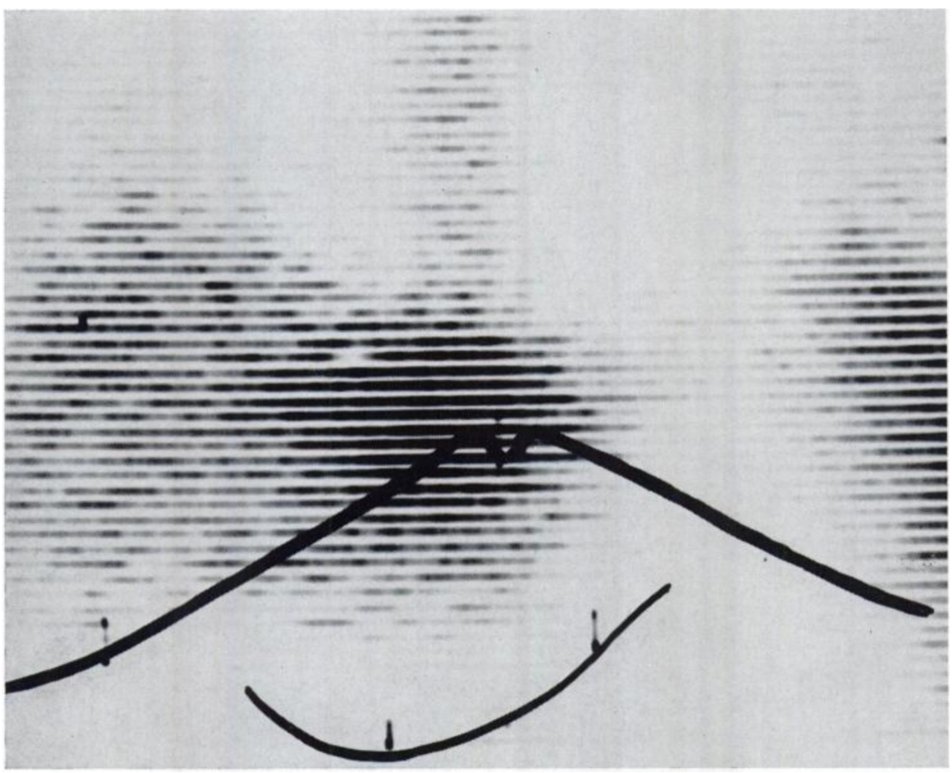

Fig. 3. Hepatic photoscan showing concomitant splenic and marrow uptake of sternum and vertebrae in cirrhosis. Compare with Figure 2C, showing splenic uptake in cirrhosis without sternal or vertebral marrow uptake. Note greater apparent concentration of colloidal gold in the left lobe than in the right lobe.

TABLE I

SCAN FINDINGS AND ANATOMICAL DIAGNOSES IN PATIENTS WITH SCANS SHOWING SPACE-OCCUPYING LESIONS

Age	*Sex*	*Clinical Diagnosis*	*Scan Findings*	*Histologic Diagnosis of Liver*	*Obtained by:*
58	F	Primary Hepatoma	Multiple space-occupying lesions in most of the right lobe.	Hepatoma	Postmortem Examination
33	M	Primary Hepatoma	A space-occupying lesion in the right lobe.	Hepatoma	Postmortem Examination
63	F	Primary Hepatoma	Large space-occupying lesions in the inferior margin and superior portion of the right lobe.	Hepatoma	Postmortem Examination
62	M	Pyogenic Hepatic Abscess	Multiple space-occupying lesions in the right and left lobes.	Pyogenic Abscess	Postmortem Examination
72	M	Pulmonary Carcinoma	Large space-occupying lesions in the right lobe.	Normal	Needle Biopsy (prescan)
71	M	Colonic Carcinoma	Several space-occupying lesions in the right lobe.	Metastatic Adenocarcinoma	Postmortem Examination
83	M	Pancreatic Carcinoma	Large, confluent, space-occupying lesions in the right lower half of the right lobe.	Metastatic Anaplastic Carcinoma	Needle Biopsy
70	M	Pulmonary Carcinoma	Space-occupying lesions throughout the liver.	Metastatic Undifferentiated Carcinoma	Needle Biopsy
64	M	Colonic Carcinoma	A large space-occupying lesion in the left lobe.	Metastatic Adenocarcinoma	Needle Biopsy
75	M	Gastric Carcinoma	A marked discrepancy between the palpable inferior liver margin and the interior margin of the scan image. A space-occupying lesion in the right lobe.	Metastatic Adenocarcinoma	Postmortem Examination

TABLE I—*Continued*

Age	*Sex*	*Clinical Diagnosis*	*Scan Findings*	*Histologic Diagnosis of Liver*	*Obtained by:*
60	F	Colonic Carcinoma	Multiple small space-occupying lesions throughout the liver.	Metastatic Adenocarcinoma	Postmortem Examination
69	M	Rectal Carcinoma	A marked discrepancy between the palpable inferior liver margin and the inferior margin of the scan image. Several large space-occupying lesions in the right lobe. A mild splenic uptake.	1 Undifferentiated small cell carcinoma; Portal fibrosis	Postmortem Examination
71	M	Rectal Carcinoma	A marked discrepancy between the palpable inferior liver margin and the inferior margin of the scan image. Poor visualization of the right lobe.	Metastatic Adenocarcinoma	Postmortem Examination
70	M	Colonic Carcinoma	A marked discrepancy between the palpable inferior liver margin and the inferior margin of the scan image. A space-occupying lesion in the right lobe.	Metastatic Adenocarcinoma	Postmortem Examination
73	M	Colonic Carcinoma	A large space-occupying lesion in the left lobe and multiple space-occupying lesions in the right lobe.	Metastatic Adenocarcinoma	Needle Biopsy

to hepatic scans performed with colloidal ^{198}Au, though theoretically the considerably lower gamma energies of ^{199}Au (160 KeV, 210 KeV, 50 KeV) should permit better delineation of isotope distribution than ^{198}Au (410 KeV). The one patient whose scan indicated space-occupying lesions but whose needle biopsy revealed normal tissue, was known to have pulmonary carcinoma and was suspected of having metastasis to the liver. (This needle biopsy had been performed prior to scanning.) Difficulty in diagnosing metastasis by blind needle biopsy of the liver has been well documented (20-22).

Marked discrepancy between the palpable inferior liver margin and the inferior margin of the scan image occurred in four cases; all demonstrated massive carcinomatous involvement of the lower portion of the liver at postmortem examination, illustrating the importance and usefulness of the superposition of organ and abdominal mass landmarks on the scan.

The hepatic scan in cirrhosis frequently has a "mottled" appearance that may represent the diffuse fibrotic and regenerative changes of cirrhosis. Our data show that the hepatic scans of 8 of the 28 patients with cirrhosis were not associated with this "mottled" appearance and, indeed, no significant correlation was found between the degree of abnormality of the liver function tests and the degree of "mottling." Fifty-seven percent of the cirrhotic group showed evidence of splenic uptake; the degree of uptake was roughly correlated with the degree of abnormality shown by liver function tests. Half of the patients with splenic uptake showed concomitant marrow uptake. Marrow uptake was seldom observed in the absence of splenic uptake. These observations may be explained on the basis of increased uptake of colloidal particles in the spleen and bone

TABLE II

CRITERIA ON CLASSIFICATION OF LIVER FUNCTION TESTS

Liver Function Tests	*Classification*			
	Normal	*Abnormal*		
		Mild	*Moderate*	*Marked*
Bilirubin (mg/100 ml)	0.1–1.1	1.2–4.0	4.1–7.0	> 7.0
Bromsulfalein Retention (%)	0–8	9–15	16–25	> 25
Serum Alkaline Phosphatase (unit)	0.5–3.0	3.1–5.0	5.1–6.5	> 6.5
Cephalin-Cholesterol Flocculation	0-++	+++	++++	++++
Thymol Turbidity (unit)	0–5	6–8	9–12	> 12
Serum Albumin (gm/100 ml)	3.5	3.5–3.1	3.0–2.6	< 2.6
Serum Globulin (gm/100 ml)	3.5	3.5–3.9	4.0–4.4	> 4.4
Prothrombin Time (%)	100–75	74–45	44–25	< 25
SGOT (unit)	8–40	41–80	81–125	>125
SGPT (unit)	5–30	31–70	71–115	>115

TABLE III

CLINICAL AND SCAN FINDINGS IN PATIENTS WITH CIRRHOSIS

Classification by Liver Function Test	*Patient*	*Age*	*Sex*	*Clinical Findings*		*Scan Findings**			
				Hepatomegaly cm below costal margin	*Splenomegaly cm below costal margin*	*Left Lobe Enlargement*	*Mottling*	*Splenic Uptake*	*Marrow Uptake*
Normal	16	52	M	16	0	present	+	0	0
	17	57	F	6	4	present	+	+	0
Mild	18	44	M	8	0	present	++	0	0
	19	61	F	8	0	0	++	+	0
	20	62	M	8	0	present	0	+	+
	21	55	F	2	2	present	+	+++	0
	22	59	M	0	0	0	0	0	0
	23	58	M	0	0	present	0	0	0
	24	49	M	2	4	present	+	++	+
	25	80	F	8	2	present	+	0	0
	26	50	M	10	0	present	+	0	0
	27	62	M	10	0	0	0	0	0
	28	65	M	6	0	0	0	+	0

TABLE III—Continued

CLINICAL AND SCAN FINDINGS IN PATIENTS WITH CIRRHOSIS

Classification by Liver Function Test	*Patient*	*Age*	*Sex*	*Clinical Findings*		*Scan Findings**			
				Hepatomegaly cm below costal margin	*Splenomegaly cm below costal margin*	*Left Lobe Enlargement*	*Mottling*	*Splenic*	*Marrow*
Moderate	29	49	F	10	2	present	+	+	+
	30	51	M	8	0	present	+	++	0
	31	54	M	0	0	present	0	0	0
	32	39	M	10	0	present	+	0	0
	33	52	F	20	0	present	0	+++	++
	34	58	M	4	2	present	+	+++	++
	35	50	M	10	0	present	+	0	+
	36	51	F	10	4	present	++	+++	0
Marked	37	63	M	10	2	present	+++	+++	0
	38	35	F	6	4	present	+	+	0
	39	61	F	6	4	present	+	0	0
	40	57	M	6	0	present	+	+	+
	41	39	M	8	0	present	+	+++	+++
	42	65	M	6	6	present	+	0	0
	43	41	M	10	2	present	0	+++	+++

*Mild degree +
Moderate degree ++
Marked degree +++

marrow occurring as a result of the decreased competitive uptake by the reticuloendothelial system in the liver. When hepatic function is normal, approximately ten times as much radioactive colloidal gold is required for adequate visualization of the marrow (23). The decreased hepatic uptake possibly may be a consequence of a decrease and/or shunting of hepatic blood flow in addition to increased phagocytosis in the spleen and bone marrow (24, 25).

In the hepatic scan of the normal liver, the radioactivity of the left lobe is less than that of the right lobe. The great majority of the cirrhotic group, however, showed varying degrees of left lobe enlargement associated with equal or even greater apparent concentration of colloidal gold in the left lobe than in the right lobe. This appearance may be the result of decreased uptake by the impaired right lobe relative to the left lobe. Normally, the colloidal particles are almost completely removed from the blood by the Kupffer cells, leaving the hepatic venous blood free of colloidal particles. In cirrhotic patients, however, measurement of hepatic arterial and venous blood demonstrates that extraction of colloidal chromic phosphate is decreased to as low as 46 per cent (24). The capacity of the hepatic reticuloendothelial cell is normally very much greater (approximately 2500 times) than that required to remove the amount of colloidal material used for the scanning procedure, approximately 100 μg (26). A marked increase, rather than a decrease, of Kupffer cells has been observed in cirrhosis (27). Thus, the decreased hepatic uptake of radiogold observed in cirrhosis is probably the result of shunting and decreased blood flow: sinusoidal reticuloendothelial cells are bypassed with resultant decreased extraction, rather than decreased Kupffer cell function. Similarly, the relative increase of left lobe radioactivity seen in cirrhosis may reflect a corresponding relative increase of blood supply and extraction by the enlarged, possibly regenerative left lobe (28).

SUMMARY

A series of 100 consecutive photoscans of the liver with radioactive colloidal gold were reviewed and evaluated.

1. Of 15 hepatic scans showing space-occupying lesions for which anatomical diagnoses were available, 14 were confirmed histologically.

2. Marked discrepancy between the palpable inferior liver margin and the inferior margin of the scan image occurred in 4 cases; postmortem examination revealed massive metastatic replacement of the inferior portion of the liver, emphasizing the importance of the careful marking of organ and abdominal masses on the scan.

3. In 28 patients with cirrhosis, the study revealed no distinct correlation between the degree of abnormality shown by the liver function tests and the degree of "mottling." Splenic uptake was roughly correlated with the results of liver function tests. Marrow uptake was demonstrable in half of the patients with visible splenic uptake but was rarely observed in the absence of visible splenic uptake.

REFERENCES

1. Stirrett, L. A., Yuhl, E. T., and Cassen, B.: Clinical Applications of Hepatic Radioactivity Surveys. *Amer. J. Gastroenterol.* 21:310, 1954.

2. Friedell, H. L., MacIntyre, W. J., and Rejali, A. M.: A Method for the Visuali-

zation of the Configuration and Structure of the Liver. Part A. Preliminary Clinical Investigations. *Amer. J. Roentgenol.* 77:455, 1957.

3. Bender, M. A. and Blau, M.: A Versatile, High-Contrast Photoscanner for the Localization of Human Tumors with Radioisotopes. *Internat. J. Appl. Rad. and Isotopes.* 4: 154, 1959.

4. Bender, M. A. and Blau, M.: Detection of Liver Tumors with I^{131} Rose Bengal in *Medical Radioisotope Scanning.* Int. Atomic Energy Agency, Vienna, 83-87, 1959.

5. Donato, L. Becchini, M. F., and Panichi, S.: Liver Scanning with Colloidal Radiogold in *Medical Radioisotope Scanning.* Int. Atomic Energy Agency, Vienna, 87-105, 1959.

6. Fee, D. A. and Fedoruk, S. O.: Clinical Value of Liver Photoscanning. *New England J. Med.* 262:123, 1960.

7. Wagner, H. N., Jr., McAfee, J. G., and Mozley, J. M.: Diagnosis of Liver Disease by Radioisotope Scanning. *Arch. Intern. Med.* 107:324, 1961.

8. Bonte, F. J., Krohmer, J. S., Elmendorf, E., Presley, N. L. and Andrews, G. J.: Scintillation Scanning of the Liver. II. Clinical Applications. *Amer. J. Roentgenol.* 88:275, 1962.

9. Crespo, G. G., MacIntyre, W. J., and Christie, J. H.: A Comparison of I^{131} Rose Bengal and Colloidal Au^{198} in Liver Scanning. *Amer. J. Roentgenol.* 88:296, 1962.

10. Feldman, F., Rubenfeld, S. and Collica, C.: The Radioactive (I^{131}) Rose Bengal Hepatoscan. *Radiology.* 79:457, 1962.

11. Adams, R., Hindawi, A. Y., and Qassab, Kh.: Localization of Hydatid Liver Cysts with Colloidal Radiogold. IAEA Scanning Program in Iraq. *J. Nuclear Med.* 3:315, 1962.

12. Nagler, W., Bender, M. A. and Blau, M.: Radioisotope Photoscanning of the liver. *Gastroenterology.* 44:36, 1963.

13. Czerniak, P., Lubin, E., Djaldetti, M. and deVries, A.: Scintillographic Follow-Up of Amoebic Abscesses and Hydatid Cysts of the Liver. *J. Nuclear Med.* 4:35, 1963.

14. Ibrahim, M. S. and Abdel-Wahab, M. F.: Detection of Amoebic Liver Abscess by Isotope Scanning. *Brit. Med. J.* No. 5341: 1325, May 18, 1963.

15. Ackerman, N. B. and McFee, A. S.: Radioisotope Liver Scanning in Children as a Diagnostic Aid to the Surgeon. *Surg., Gynec., Obstet.* 117:41, 1963.

16. Christie, J. H., MacIntyre, W. J., Crespo, G. G. and Koch-Weser, D.: Radioisotope Scanning in Hepatic Cirrhosis. *Radiology.* 81:455, 1963.

17. Sorensen, L. B. and Archambault, M.: Visualization of the Liver by Scanning with Mo^{99} (Molybdate) as Tracer. *J. Lab. Clin. Med.* 62:330, 1963.

18. Kriss, J.: Radioisotope Scanning in Medical Diagnosis. *Ann. Rev. Med.* 14:381, 1963.

19. Anger, H. O.: Gamma-ray and Positron Scintillation Camera. *Nucleonics.* 21:56, 1963.

20. Bowden, L. and Kravitz, S.: Needle Biopsy of the Liver, a Diagnostic Aid in the Treatment of Cancer. *Cancer.* 6:1010, 1953.

21. Ward, J., Schiff, L., Young, P., and Gall, E. A.: Needle Biopsy of the Liver. IX. Further Experiences with Malignant Neoplasm. *Gastroenterology.* 27:300, 1954.

22. Fenster, L. F. and Klastskin, G.: Manifestations of Metastatic Tumors of the Liver. A Study of Eighty-One Patients Subjected to Needle Biopsy. *Amer. J. Med.* 31:238, 1961.

23. Edwards, C. L., Andrews, G. A., Sitterson, B. W., and Kniseley, R. M.: Clinical Bone Marrow Scanning with Radioisotopes. *Blood.* 23:741, 1964.

24. Rankin, J. G., Playoust, M. R., and Beal, R. W.: Significance of Alterations in Extraction and Distribution of Colloidal Chromic Phosphate in Patients with Liver Disease. *J. Lab. Clin. Med.* 58:920, 1961.

25. Meulengracht, E. and Gormsen, M.: Blood and Bone Marrow in Infective Subacute and Chronic Atrophy of Liver. *Blood.* 3:1416, 1948.

26. Dobson, E. L. and Jones, H. B.: The Behavior of Intravenously Injected Particulate Material: Its Rate of Disappearance from the Blood Stream as a Measure of Liver Blood Flow. *Acta. Med. Scand.* 144: Supplement 273, 1952.

27. Leevy, C. M., Tenhove, W., and Howard, M. M.: Kupffer Cell Proliferation in Fatty Liver and Cirrhosis of the Alcoholic. (Abstract 31) *J.A.M.A.* 184:207, 1963.

28. Leong, G. F., Pessotti, R. L. and Brauer, R. W.: Liver Function in Regenerating Rat Liver. $CrPO_4$ Colloid Uptake and Bile Flow. *Amer. J. Physiol.* 197:880, 1959.