AN EVALUATION OF ^{99m}Tc-SULFUR COLLOID LIVER SCINTISCANS AND THEIR USEFULNESS IN METASTATIC WORKUP: A REVIEW OF 1,424 STUDIES

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To determine the clinical usefulness of liver scintiscanning in detecting metastatic disease of the liver, 1,424 liver studies performed on 1,115 patients were reviewed along with their charts. Five hundred eighty-one patients had histopathological evaluation by needle biopsy of the liver, laparotomy, and/or autopsy within a mean period of 40 days of liver scan. The histopathological findings were correlated with the liver sicntiscan findings and the latter gave an overall accuracy of 77.3%.

Radioisotopic evaluation of the liver for metastases has been performed for over 20 years. Earlier workers utilized ^{131}I rose bengal, ^{99}Mo, ^{69m}ZnCl (*1–3*), etc. Later, other radiopharmaceuticals like colloidal ^{198}Au, ^{113m}In-colloid and ^{99m}Tc-sulfur colloid came into use (*4–6*). In this series, all of the 1,424 liver scintiscans were performed exclusively using 1.5–2.0 mCi of ^{99m}Tc-sulfur colloid on one of the following instruments: a 5-in. Picker dual-head scanner, a 5-in. Ohio-Nuclear dual-head scanner, or a Searle Radiographics Pho/Gamma HP. The Picker scanner was mounted with medium-energy ½-in. resolution collimators and the Ohio-Nuclear with low-energy ½-in. resolution collimators. Approximately 8% of the studies were performed on both a dual-head scanner and a gamma camera. A few selected studies were performed on a Baird-Atomic System Seventy.

MATERIALS AND METHODS

Our institution primarily handles patients with known neoplastic disease; hence, all patients undergo liver scintiscanning as part of a routine pretherapy evaluation. All the liver scans performed from July 1971 to June 1973 were reviewed. There were 1,432 studies performed on 1,123 patients. Eight patient studies were not included since they were technically unsatisfactory. The remaining 1,115 patients were diagnosed as having various malignancies. The frequency distribution of the primary disease with the subjective semiquantitative scan data are given in Table 1.

The authors reviewed all the 1,115 patient studies comprising 1,424 scans and divided them into two groups, abnormal and normal, according to the scan findings. Seventy-six suspicious scans belonging to 53 patients were included in the abnormal group. The positive or abnormal group consisted of 478 liver scans of 270 patients and the negative or normal

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TABLE 1. FREQUENCY DISTRIBUTION OF PRIMARY DISEASES OF 1,115 PATIENTS

Diagnosis	Patients (No.)	Scan pos	Neg	Susp
Lymphoma	88	11	72	5
Ca breast	92	31	56	7
Ca prostate	14	4	10	0
Ca upper GI	48	12	35	1
Ca brain	None	0	0	0
Ca colon	160	58	89	13
Ca lung	262	23	231	8
Ca pancreas	17	6	11	0
Ca thyroid	7	3	4	0
Sarcomas	31	3	27	1
Ca u. bladder	32	5	27	0
Malignant melanoma	81	22	55	4
Leukemia	9	1	8	0
Ca larynx	3	1	2	0
Ca ovary	18	7	11	0
Ca testis	24	3	20	1
Ca kidney	41	7	31	3
Miscellaneous	186	20	156	10
Total	1,115	217	845	53
Abnormal scans	217 + 53 = 270			
Normal scans	= 845			

group consisted of 946 studies of 845 patients. Table 2 gives the figures of each group with the numbers of available histopathology.

True positive. The liver scan demonstrated space-occupying disease which was confirmed on histopathological examination.

True negative. The scan failed to demonstrate definite evidence of space-occupying disease; and needle biopsy, laparotomy, arteriogram, or necropsy examination failed to document any evidence of metastatic disease.

False positive. The liver scan findings were consistent with the presence of space-occupying lesions but all other diagnostic parameters were negative.

False negative. The liver scan did not reveal any evidence of space-occupying disease but the presence of disease was confirmed at laparotomy and/or by histopathological means.

Table 3 compares levels of scan accuracy with histopathological findings in 581 patients. There were

TABLE 2. CLINICAL SUBDIVISION OF SCAN DATA

Clinical interpretation	Scans (No.)	Patients (No)	Histopath available
Normal	946	845	376
Abnormal	478	270	205
Total	1,424	1,115	581

183 abnormal patient studies, 152 of which had histopathological confirmation of disease in the liver, giving a true-positive figure of 83%. Histopathological examination of the liver did not reveal metastatic disease in 31 patients who had abnormal liver scans and they were categorized in the false-positive group (17%). Of the 398 patients with normal scans, 297 did not show the presence of disease in the liver by other diagnostic means, and comprised the true-negative group (74.6%). In the remaining 101 patients who had normal scans, histopathological examination revealed evidence of metastatic disease in the liver, giving a false-negative figure of 25.4%.

An overall scan accuracy of 77.3% was obtained in this study, and similar figures have been reported in the series of other authors (*7–13*) as listed in Table 4. The incidence of a 25.4% false-negative figure in our series, though acceptable, is worrisome. To ascertain the possible cause for error in this category, the authors analyzed all the 101 false-negative patient studies and their charts. Of the 101 patients in this group, 99 underwent laparotomy and/or autopsy 8–144 days following liver scan. In 40 patients, metastatic lesions in the liver were less than 2.5 cm in their greatest diameter (0.2–2.5 cm); in 59 patients lesions greater than 2.5 cm were found. The remaining two patients in this false-negative group had only needle biopsy of the liver; hence, the size of the lesions could not be ascertained (Table 5).

Some of these false-negative scans might be accounted for by interval progression or occurrence of disease between the time of scan and that of histopathological examination. However, other factors play a part. The authors feel that the instrumentation available to nuclear medicine does not provide sufficient detecting capability for in vivo diagnosis of "cold" lesions less than 2.0 cm in diam. Computer analysis of the liver scintiscan data is claimed to be better than semiquantitative evaluation (*14*).

In practice, multiple factors influence resolution capability of the instrument, especially when evaluating an organ like the liver. The important factors are: (A) the size of the organ with the possible occurrence of deep-seated lesions surrounded by thick normal liver tissue, (B) the motion of the liver during respiration which may obscure the delineation of the lesion (*6,15*), (C) concomitant pathology such as interference from ascites; and (D) the instrumentation manipulative errors.

Thirty-one patients comprised the 17% false-positive rate in this study. Four patients had extrinsic pathological findings in the region of the liver, producing abnormalities compatible with space-occupying lesions; 17 patients were receiving multiple

TABLE 3. SCAN ACCURACY OF 581 PATIENTS WITH HISTOPATHOLOGICAL CONFIRMATION

Scan findings	Patients (No.)	True positive	%	False positive	%
abnormal	183	152	83.0	31	17.0
		True negative		False negative	
normal	398	297	74.6	101	25.4
		Accurate dx.		Inaccurate dx.	
Total	581	449	77.3	132	22.7

TABLE 4. REPORTED ACCURACY OF LIVER SCINTISCANNING IN METASTATIC EVALUATION

Ref No.	Group	Patients (No.)	Accuracy (%)	Radiopharmaceutical	Year
7	Nagler	548	84.0	^{131}I-rose bengal	1963
8	Gollin	129	77.0	^{198}Au colloid	1964
9	Ferrier	155	84.0	^{198}Au colloid	1968
10	Ariel	196	85.2	^{131}I RB and ^{198}Au colloid	1969
11	Covington	387	81.6	^{198}Au colloid and ^{131}I RB	1970
12	Castagna	109	74.3	^{131}IHSA	1972
13	Dupriest	56	75.4	^{99m}Tc S-C	1973
	This study	581	77.3	^{99m}Tc S-C	1974

TABLE 5. RESULTS OF ANALYSES OF 101 FALSE-NEGATIVE AND 31 FALSE-POSITIVE STUDIES

A		B	
False-negative studies		False-positive studies	
Size of lesions	Patients (No.)	Abnormality due to following factors	Patients (No.)
Less than 2.5 cm	40	Extrahepatic path	4
More than 2.5 cm	59	Marked hepatic dysfunction	17
Not ascertained	2	Severe obstructive jaundice	2
Total	101	Not ascertained	8
		Total	31

TABLE 6. OVERALL CORRELATION OF LIVER SCINTISCANNING WITH HISTOPATHOLOGY ACCORDING TO PRIMARY SITE OF DISEASE IN 581 PATIENTS

Primary site	Patients (No.)	Scan pos	Scan neg	Bx.	Lap.	Autop.	Correct dx (No.)	Correct dx (%)	Incorrect dx (No.)	Incorrect dx (%)
Lymphoma	61	13	48	37	14	29	48	78.7	13	21.3
Ca breast	44	17	27	8	30	19	34	77.3	10	22.7
Ca prostate	8	4	4	2	2	4	6	75.0	2	25.0
Ca u.g.i.	37	8	29	10	32	18	26	70.3	11	29.7
Ca brain	0	0	0	0	0	0	0	0	0	0
Ca colon	118	52	66	17	93	41	100	84.7	18	15.3
Ca lung	98	12	86	6	13	85	76	77.6	22	22.4
Ca pancreas	16	6	10	2	12	12	13	81.3	3	18.7
Ca thyroid	5	1	4	3	3	2	2	40.0	3	60.0
Sarcomas	13	5	8	1	9	5	11	84.6	2	15.4
Ca u bladder	17	5	12	1	8	10	9	53.0	8	47.0
Malignant melanoma	32	15	17	5	8	24	21	65.6	11	34.4
Leukemia	8	3	5	1	1	7	6	75.0	2	25.0
Ca larynx	0	0	0	0	0	0	0	0	0	0
Ca ovary	16	7	9	5	11	6	14	87.5	2	12.5
Ca testis	12	4	8	2	7	6	11	91.7	1	8.3
Ca kidney	16	5	11	3	5	13	11	68.8	5	31.2
Miscellaneous	80	18	62	24	52	21	61	76.3	19.3	22.7

chemotherapeutic agents who had overt signs of toxicity with abnormal liver chemistries (although no histopathological evidence of metastatic disease was found, the possibility of parenchymal damage with involvement of the reticuloendothelial system contributing to the abnormal findings could not be ruled out); and two patients had severe obstructive jaundice due to carcinoma of the head of the pancreas with resultant dilated hepatic biliary ducts which might explain abnormal scan findings. In the remaining eight patients, no explanation of the scan abnormalities could be ascertained (Table 5).

Comparing the histopathology with liver enzymes (SGOT, LDH, alkaline phosphatase), it was found that in the absence of any bony metastases, the alkaline phosphatase level correlated best. They did not, however, correlate well with the extent of the disease.

The authors evaluated the liver scintiscan accuracy in each of 17 different types of malignancies (Table 6). Correlation was excellent (84–91%) in carcinoma of the testis, ovary, colon, and in sarcomas; good (75–81%) in carcinoma of the pancreas, lung, breast, prostate, and in lymphomas and leukemias; fair in carcinoma of the upper GI tract, and in malignant melanoma; and equivocal in carcinoma of the urinary bladder and in thyroid carcinoma.

CONCLUSION

We believe that liver scintiscanning is an excellent noninvasive diagnostic tool for evaluation of metastatic disease. However, to our surprise, the level of diagnostic accuracy has not changed to any extent despite the availability of newer radiopharmaceuticals, the recent advances in instrument capability, and the use of multiple views.

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