Comparison of Scintigraphy, Sonography, and Computed Tomography in the Evaluation of Hepatic Neoplasms

JUDSON H. SNOW, JR.,[1] HARVEY M. GOLDSTEIN,[1,2] AND SIDNEY WALLACE[1]

A comparison of scintigraphy, ultrasonography, and computed tomography (CT) in 94 proven patients with clinically suspected liver disease is reported. CT proved to be the most accurate in detecting masses and assessing the complete extent of intrahepatic disease. The most reliable combination was CT and scintigraphy. The specific advantages and disadvantages of each method are discussed. The diagnostic scheme followed in the imaging evaluation of an hepatic mass in our clinical practice is discussed.

The frequency of hepatic involvement by primary and secondary neoplasia requires safe, reproducible, and accurate screening. The three imaging methods presently in clinical use for evaluation of hepatic neoplasia are scintigraphy, ultrasonography, and computed tomography (CT). Numerous reports describe the value and role of each, but to date there have been few attempts to compare their relative benefit.

Reports of overall accuracy of scintigraphy range from 68% to 90% correct diagnoses [1-3] with most near the 77% figure reported by Lunia et al. [3] in a series of 1,424 cases. However, false positive and false negative rates in excess of 15% are reported by several authors [2, 3]. Early comparative studies found scintigraphy to be a more sensitive indicator of hepatic neoplasia with an overall accuracy rate of about 70% compared with the 65% accuracy of sonography [2]. However, sonography found use in assessing the liver in cases of equivocal scintigraphy and in differentiation of solid and cystic masses first detected on scintigrams [1, 4-6]. Most investigators agree that sonography and scintigraphy are complementary [1, 2, 4, 7, 8]. Technologic advances in gray scale sonography resulted in accuracy reported as high as 90% [6, 9]. The advantages of sonography to follow the course of disease and to assess tumor response to therapy have been documented [6, 9-11]. Recently, the literature has contained conflicting reports of the efficacy of CT, which has been described as inferior, at least equal, or complementary to scintigraphy and sonography [12-16].

This report compares the three methods in the prospective clinical setting. The accuracies of the examinations both for the detection of space-occupying lesions and for the assessment of extent of disease are emphasized.

Subjects and Methods

During the first year of operation of a total body CT scanner, 410 patients were evaluated for the presence of hepatic neoplastic disease. In 94 of these cases, both gray scale ultrasonography and ^{99m}Tc scintigraphy were also performed within close temporal proximity, and the diagnosis was proven within 1 month after the three imaging studies.

In most cases, CT scans were performed with an 18 sec total body scanner only after intravenous infusion of 300 ml of 30% meglumine diatrizoate. Gray scale ultrasonography was performed on latest model commercial gray scale analog instruments. Scintigraphy was performed after an injection of 7 mCi of ^{99m}Tc sulfur colloid with a wide field of view gamma camera.

The general sequence in which the three procedures were ordered was scintigraphy, followed by sonography and CT. Prior knowledge of other test results was available in many cases since these examinations were conducted as part of the actual prospective clinical evaluation of each patient. Only the original interpretations as used in the clinical management of these patients were considered in this evaluation.

A histologic diagnosis by percutaneous biopsy, autopsy, and/or laparotomy or unequivocal subselective angiographic findings were considered conclusive proof of disease. Histologic confirmation was available in 48 cases, angiography was considered diagnostic in 22 cases, and both a tissue diagnosis and angiography were obtained in an additional 24 cases. Neoplastic involvement of the liver was proven in 52 patients; 35 of these had bilobar disease and in 17 involvement was confined to one lobe (table 1). In 42 patients, no neoplasia was demonstrated.

Results

Sensitivity is defined as the percentage of tests read as abnormal in patients with proven disease (true positive results). Specificity is the percentage of tests read as normal in patients free of disease (true negative results). Accuracy of abnormal or normal readings is defined as the percentage of those readings proven correct.

Computed Tomography

CT was found to have a sensitivity of 96%, a false positive rate of neoplasia of 12%, and an accuracy of abnormal readings of 91%. The false positive diagnoses of neoplasm included a single case of an amoebic abscess and several cases of nonspecific periportal inflammation or fatty metamorphosis. In one case, focal nodular hyperplasia could not be differentiated from primary or secondary malignancy. One additional false positive case was due to reader error. The specificity of CT was 86%. False negative results of neoplasia were obtained in 4%, and the accuracy of normal readings was 95%. One false negative interpretation was probably related to the presence of metallic clips in the abdomen.

Received November 14, 1978; accepted after revision March 8, 1979.
Judson H. Snow was supported by an American Cancer Society fellowship program.
[1]Department of Diagnostic Radiology, University of Texas System Cancer Center, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77030. Address reprint requests to S. Wallace.
[2]Present address: Department of Radiology, Southwest Texas Methodist Hospital, San Antonio, Texas 78230.

0361-803X/79/1326-0915 $0.00

TABLE 1
Distribution of Histologically Proven Diagnoses

Histologic Diagnosis	No.
Neoplastic involvement:	
Primary neoplasms:	
Hepatoma	2
Cavernous hemangioma	1
Metastatic neoplasms:	
Carcinoma of the colon	23
Adenocarcinoma, unknown primary	8
Carcinoma of the breast	7
Carcinoid	2
Leiomyosarcoma	2
Malignant fibrous histiocytoma	1
Carcinoma of the gallbladder	1
Choriocarcinoma	1
Histiocytic lymphoma	1
Adrenal carcinoma	1
Undifferentiated sarcoma	1
Osteosarcoma	1
Subtotal	52
No evidence of neoplasia:	
Nonspecific periportal inflammation or fatty metamorphosis	6
Amoebic abscess	1
Focal nodular hyperplasia	1
Multiple granulomas	1
Hemosiderosis	1
Subtotal	42
Total	94

In addition, one examination of a child was inadequate for interpretation due to the paucity of abdominal fat.

Sonography

The sensitivity of sonography was determined to be 75%, with a false positive rate of 17% and an accuracy of abnormal readings of 85%. The cases of amoebic abscess and focal nodular hyperplasia were once again interpreted as neoplasm. In two cases extrinsic masses could not be distinguished from intrahepatic disease. Numerous granulomas were misinterpreted as diffuse metastases in one patient, and inhomogeneity of the hepatic echo architecture resulted in the remaining false positive results. Specificity was somewhat lower, at 50%, with false negatives in 10% of cases and an accuracy of normal readings of 81%. In one patient, an intrahepatic neoplasm could not be distinguished from extrinsic disease. Malignancy in the right lobe was not detected in one patient, and diffuse metastases were not visualized in three patients. Sonographic examinations were ruled inadequate for interpretation due to the presence of intestinal gas in 22 cases (23%). In only one case was an acceptable examination obtained after an initial attempt failed.

Scintigraphy

Scintigraphy demonstrated a sensitivity of 94%, false positive results for neoplasms were obtained in 26% of cases, and the accuracy of abnormal readings was determined to be 82%. The cases of amoebic abscess and focal nodular hyperplasia also could not be distinguished from malignancy by this method. Additional false positive results with scintigraphy were obtained in cases with dilated bile ducts, granulomas, fatty metamorphosis, and extrinsic masses. No difference in distribution of false positive results was noted between right and left lobes. The specificity of scintigraphy was determined to be 67%, with false negative results in 6% of cases and an accuracy of normal readings of 90%. False negative interpretations involved the left lobe in two cases and both lobes in one case.

Correlation of Methods

The presence or absence of neoplasia within the liver was correctly established by all three examinations in 51 of 94 cases. The correct diagnosis was made by one method alone in 12 cases. Of these 12 cases, CT alone was correct in 10, scintigraphy in one, and sonography in one. In 31 cases the correct diagnosis was made by two methods. CT with scintigraphy was the most successful combination, resulting in the correct diagnosis in 17 cases. The next most accurate combination was CT and sonography, with the correct diagnosis in nine cases. The combination of sonography and scintigraphy was least reliable, resulting in the correct diagnosis in the remaining five cases.

The ability of each method to determine the extent of disease within the liver was also examined. Only those cases in which the extent of disease was established by autopsy, biopsies of several areas, or unequivocal angiography were included in this analysis. Of those 35 patients with neoplastic involvement of both lobes of the liver, an incorrect diagnosis of unilobar disease was made in 25% of cases with CT, in 24% of cases with sonography, and in 39% of the cases with scintigraphy. It should be noted that in 33% of the cases included in this smaller series, sonography could not be interpreted due to abdominal gas. In addition, false positive results indicating bilobar disease were obtained by both scintigraphy and sonography in 12% of the 17 patients known to have neoplasm confined to one lobe of the liver. CT scans correctly identified unilobar neoplasia in all cases.

Discussion

Comparison of the three screening methods demonstrated that CT was the best single examination to determine both the presence and extent of space-occupying lesions within the liver (table 2). CT scanning proved to be superior in specificity, sensitivity, and accurate diagnoses. Prior knowledge of previously performed imaging procedures may have resulted in an improved bias position to CT, but CT consistently resulted in the lowest rate of false positive and negative diagnoses. In our series, CT scanning was also the procedure of choice to define and differentiate extra- from intrahepatic masses. Inherent limitations were a paucity of abdominal fat and artifacts due to intraabdominal clips. Sonography was less sensitive and specific, with some difficulty encountered in interpreting an inhomogeneous sonographic architecture when no focal lesions were present. However, the major difficulty en-

TABLE 2

Comparison of Screening Methods

Performance Standards	Examination/Results (%)		
	CT	Sonography	Scintigraphy
Sensitivity	96	75	94
False positive interpretations	12	17	26
Accuracy of abnormal interpretations	91	85	82
Specificity	86	50	67
False negative interpretations	4	10	6
Accuracy of normal readings	95	81	90

countered was interference by abdominal gas, present in 23% of the cases. Scintigraphy proved to be a very sensitive but relatively nonspecific screening test due to limitations in differentiating diffuse parenchymal abnormalities, anatomic variants, and extrinsic masses from hepatic tumors.

An intrahepatic space-occupying lesion was correctly diagnosed or excluded in 51 of 94 cases by each of the three methods. Otherwise, the most accurate combination of screening tests was CT and scintigraphy (both correct in 17 cases) followed by CT and sonography (both correct in nine cases). CT alone was correct in 10 cases. The combination of scintigraphy and sonography was least desirable, being responsible for the correct diagnosis in only five cases.

For the purpose of determining a surgical or medical therapeutic regimen for our patient population, the definitions of specificity, false positive, etc. were based both on the detection of malignancy and on the differentiation of malignancy from benign pathologic processes. Despite the high sensitivity of the screening methods to hepatic lesions, with each of the three methods a relatively large number of scans erroneously indicated the presence of only unilobar disease. The significance of this information in those cases in which a hepatic lobectomy is contemplated emphasizes the necessity of angiography. The nonspecificity of the various methods, even in combination, is demonstrated by the cases of focal nodular hyperplasia, cavernous hemangioma, and amoebic abscess which could be differentiated from malignant neoplasms only angiographically and ultimately histologically.

The results obtained in this study differ from those reported by Grossman et al. [13]. In their series of 35 patients with all forms of liver disease, sonography was rated as the most accurate with the best combination being sonography and radionuclide imaging. CT was the least accurate. However, only one-half of the cases had contrast enhancement, wide window settings were used, and the equipment was not comparable since CT scan time was 2.7 min. This illustrates the difficulty of obtaining data in such comparative studies when technology changes so rapidly. A retrospective comparison of radionuclide scans and CT by MacCarty et al. [14] reports more false positives with scintigraphy (16% vs. 4%), and suggests that the two studies are complementary. The results published by Scherer et al. [15] were similar to ours. CT was reported to have a sensitivity of 89%, a specificity of 90%, and a false negative rate of 4%.

Our results suggest that the most accurate screening plan would consist of scintigraphy followed, as clinically indicated, by CT. However, the large volume of cases at our institution as well as cost considerations have dictated a different sequence of diagnostic procedures. Scintigraphy is performed as the initial examination and is often used to follow the course of disease because it is very sensitive, the least expensive, and can be performed on the largest number of patients daily. Sonography is often used to confirm isotopic findings and to resolve problem cases whenever possible. Because of its greater expense and limited patient capacity, CT is reserved for those situations when conflicting reports between scintigraphy and sonography occur. In this series of cases, the combination of scintigraphy and sonography would have resulted in the correct diagnosis in 84 cases, while a CT scan performed alone would have indicated the correct diagnosis in 87 cases. Hepatic angiography is indicated if results of the imaging examinations remain inconsistent or inconclusive. In addition, angiography is critical prior to contemplation of partial hepatic resection or major chemotherapy regimens.

ACKNOWLEDGMENTS

We thank Janet Schell and Shirley Anne Davis for editorial and secretarial assistance in preparing this manuscript.

REFERENCES

1. Garrett W, Kossoff G, Uren R, Carpenter D: Grey scale ultrasonic investigation of focal defects on ^{99m}Tc sulphur colloid liver scanning. *Radiology* 119:425–428, 1976
2. Lomonaco A, Kline P, Halpern S, Leopold G: Nuclear medicine and ultrasound: correlation in diagnosis of disease in liver and biliary tract. *Semin Nucl Med* 5:307–324, 1975
3. Lunia S, Parthasarathy K, Bakshi S, Bender M: An evaluation of ^{99m}Tc sulphur colloid liver scintiscans and their usefulness in metastatic workup: a review of 1424 studies. *JNM* 16:62–65, 1974
4. Carlsen E: Liver, gallbladder and spleen. *Radiol Clin North Am* 13:543–556, 1975
5. Leyton B, Halpern S, Leopold G, Hagen S: Correlation of ultrasound and colloid scintiscan studies of normal and diseased liver. *JNM* 14:24–33, 1973
6. Taylor K, Carpenter D, Hill C, McCready V: Grey scale ultrasound imaging. *Radiology* 119:415–423, 1976
7. Carlsen E, Grames G, Jansen C: The combined use of radionuclide imaging and ultrasound grey scale imaging in focal liver disease, in *Recent Advances in Nuclear Medicine: Proceedings of the First World Congress of Nuclear Medicine*, Tokyo and Kyoto, September 1974, pp 472–473
8. Green B, Bree RL, Goldstein HM, Stanley C: Grey scale ultrasound evaluation of hepatic neoplasms: patterns and correlations. *Radiology* 124:203–208, 1977
9. Gilley E, Taylor K: Ultrasound monitoring of hepatic metastases during chemotherapy: preliminary communication. *Br Med J* 1:371–373, 1975
10. Taylor K, Carpenter D, McCready V: Grey scale echography

in the diagnosis of intrahepatic disease. *JCU* 1:284–287, 1973
11. Taylor K, Carpenter D, McCready V: A clinical evaluation of grey scale ultrasonography. *Br J Radiol* 49:244–252, 1976
12. Alfidi R, Haaga J, Havrilla R, Pepe R, Cook S: Computed tomography of the liver. *AJR* 127:69–74, 1976
13. Grossman Z, Wistow B, Bryan P, Dinn W, McAfee J, Kieffer S: Radionuclide imaging, computed tomography and gray scale ultrasonography of the liver: a comparative study. *JNM* 18:327–333, 1977
14. MacCarty R, Heinz W, Stephens D, Sheedy P, Hattery R: Retrospective comparison of radionuclide scans and computed tomography of the liver and pancreas. *AJR* 129:23–28, 1977
15. Scherer U, Rothe R, Eisenburg J, Schildberg FW, Meister P, Lissner J: Diagnostic accuracy of computed tomography in circumscript liver disease. *AJR* 130:711–714, 1978
16. Levitt R, Sagel S, Stanley R, Jost R: Accuracy of computed tomography of the liver and biliary tract. *Radiology* 124: 123–128, 1977