CORRELATION OF ULTRASOUND AND COLLOID SCINTISCAN STUDIES OF THE NORMAL AND DISEASED LIVER

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137 patients were studied with ultrasound and scintigrams of the liver, 79 with proven diagnoses, 23 with presumptive diagnoses, and 35 with diagnoses unknown, based on autopsy, biopsy, or laparotomy. Scanning was more sensitive than ultrasound in detecting disease of the liver, yet yielded a greater percentage of false positives than ultrasounds. Ultrasound was also useful for corroborating lesions, and for evaluating consistency of lesions (cystic vs. solid). The two modalities were therefore complementary.

Since 1969 ultrasound and scintiscanning of the liver have been routinely performed at the University Hospital of San Diego County. An attempt has been made in the following manuscript to compare the diagnostic accuracy of the two modalities in predicting not only the presence or absence of liver disease but the specific type of disease.

METHODS

Medical charts were reviewed on all patients at the University Hospital of San Diego County having both ultrasound and scintiscans of the liver between June 1969 and October 1971. A total of 137 patients were studied. Some patients had more than one scan or scintiphoto of the liver. The cases were divided into three categories: (A) diagnostically proven cases (79), (B) clinically highly suggestive cases (23), and (C) cases with inadequate proof for diagnosis (35). Proof was based on autopsy findings (11), biopsy at the time of laparotomy or laparoscopy (16), closed biopsy plus appropriate clinical course (36), and laparotomy and peritonoscopy (6). Six cases of amoebic abscess were considered proven on the basis of clinical and laboratory findings and appropriate response to treatment. Four patients were considered proven by arteriography and appropriate clinical course. All but one of the scanning procedures were performed on an Anger scintillation camera using a 4,000-hole collimator. One study was performed on a Picker Nuclear rectilinear scanner. The following views were obtained: anterior, posterior, and right cross-table lateral. Views of the spleen were also taken and consisted of an anterior and left cross-table lateral. Three millicuries of ^{99m}Tc-sulfur colloid, made by a modification of the Patton method (*1*), was the only radiopharmaceutical used. Scintigraphy was initiated 10 min postinjection, and 300,000 counts were obtained on the anterior view. The time needed for this view was used in all of the projections. Size and position of the liver was determined on one anterior view using costal margin markers of known length. A second anterior study was then made for interpretation.

Ultrasound studies were performed on a commercially available Picker contact B scanner operating at a frequency of 2.25 MHz. Imaging was done at 2-cm intervals in both transverse and longitudinal directions with varying instrument gain settings as suggested by Lehman (*2*). All ultrasound studies were performed by one of two individuals. The described technique requires a knowledge of the useful gain settings of each particular instrument which must be ascertained in an empirical fashion. Therefore no numerical data relating to gain settings is relevant in this discussion of the methodology.

Original and reinterpretation scintiscan and ultrasound readings were recorded. The original readings were done with benefit of clinical data. The scintiphotography reports were dictated by a nuclear medicine trainee or a radiology resident with supervision at the time of reading by one of the four staff physicians in our nuclear medicine department. Re-

Received June 1, 1972; revision accepted Aug. 23, 1972.

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interpretations of the scans were done without the benefit of the patient's name or history by Dr. Halpern. Original and reinterpretations of the ultrasound studies were performed by Dr. Leopold with the reinterpretation again being without knowledge of the patient's name or history. All of the studies were performed within 1 week of each other and generally on the same day. All proofs were obtained within three weeks of the time of the study. The scintiphotos were interpreted as normal, locally abnormal (one or several well-defined defects were seen), or diffusely abnormal (scintiphotos with abnormal distribution of tracer in the liver and/or peripheral reticuloendothelial organ uptake but without definite local defects). The ultrasound studies were interpreted in one of three categories: (A) normal, (B) diffusely abnormal (small or coalescent echos in the liver substance), and (C) local abnormalities (well circumscribed single or multiple areas).

TABLE 1. PROVEN AND CLINICALLY SUGGESTIVE CASES CLASSIFIED BY DIAGNOSIS

Disease	Proven	Clinically suggestive	Total
Diffuse			
Cirrhosis	24	3	27
Fatty change	6	7	13
Hepatitis (toxic and alcoholic)	3	0	3
Hepatitis (viral)	4	0	4
Granulomatous disease	3	0	3
Bile stasis	2	0	2
Other diffuse disease (lupus, diabetes, hemosiderosis)	2	1	3
Total diffuse disease	44	11	55
Local			
Metastatic disease	16	11	27
Amoebic abscess	6	0	6
Benign liver tumor	1	0	1
Total local disease	23	11	34
Normal	13	1	14
Total	80	23	103

RESULTS

Table 1 lists the number of proven and clinically suggestive cases in each diagnostic category. There are three major categories: (A) diffuse disease, (B) local disease, and (C) normals. Thus, approximately 53% of our proven and highly suggestive cases were classified as diffuse disease, 33% represented local disease, and 13.6% were normal.

Table 2 compares the original, i.e., interpretation made with benefit of clinical information, and the reinterpretation data (without clinical knowledge). All three groups of patients (proven, clinically suggestive, and unproven) are represented in these data. Agreement was obtained in 20 patients (71%) considered "normal" by scanning; however, the reinterpretations disagreed in eight cases usually because of the suggestion of a diffuse abnormality. A similar discrepancy existed regarding "local" abnormalities with 39 of 56 patients being considered for the same category (70%). Unlike the "normal" cases, the disagreement was more evenly divided between normal and diffusely abnormal. Finally, in the cases originally described as "diffuse abnormality," 37 of 45 (82%) were reclassified the same, 6 as normal and 2 as local. In 17 cases, overlapping occurred. In these cases there was evidence for both local and diffuse disease, and for purposes of objectivity in this study it was decided that these should be classified as both. These cases are not represented as cor-

TABLE 2. COMPARISON OF THE ORIGINAL SCINTIPHOTO AND ULTRASOUND READINGS WITH THEIR RE-INTERPRETATIONS*

		Re-interpretations: Scintiphotos						Re-interpretations: Ultrasound					
		Type of disease					Disease as compared with no disease	Type of disease					Disease as compared with no disease
		N	L	D	agree	96	125	N	L	D	agree	71	109
Original interpretations	N	20	1	7	disagree	33	21	31	6	13	disagree	48	36
	L	7	39	10	partial	17		11	19	7	partial	26	
						146†	146					145	145
	D	6	2	37				8	3	21			
		Partial agreement—17						Partial agreement—26					

* All cases.

† One patient had two liver scintiscans.

Correlations are shown by matching of any two letters. Cases classified as partial agreement are not shown on diagram. These cases were classified as both diffuse and local abnormalities and all classified as "disease" in appropriate column. N = normal, L = local, D = diffuse.

TABLE 3. CORRELATION OF ORIGINAL SCINTIPHOTO AND ULTRASOUND READINGS WITH DIAGNOSIS*

	Interpretations											
	Scintiphotos						Ultrasound					
	Diagnosis			Correlation as to type of disease		Disease as compared with no disease		Diagnosis			Correlation as to type of disease		Disease as compared with no disease
	N	L	D					N	L	D			
N	2	3	8	agree	39	58	N	8	5	17	agree	38	53
L	7	18	11	disagree	34	22	L	1	12	4	disagree	30	27
				partial	7						partial	12	
					80	80						80	80
D	4	1	19				D	1	2	18			
	Partial agreement—7							Partial agreement—12					

* Proven cases.

Correlations of original interpretations and proven diagnosis showing difficulty in interpretation of specific disease state. Nuclear medicine appeared more sensitive than ultrasound but more likely to overread normal studies. Main difficulty with ultrasound was in interpretation of local defects. N = normal, L = local, D = diffuse.

relations in this table. Thus, in 96 of 146 cases (66%) there was complete agreement as to not only the presence of disease but the probable type of disease; in 17 cases (12%) there was partial agreement; and in 33 cases (22%) there was no correlation. Regarding the ability to reinterpret a liver as diseased versus nondiseased, scintiphotography readings correlated 86% of the time.

The data for the ultrasound studies show a greater discrepancy between the original and reinterpretation data than did scintiphotography. Thirty-one of 50 patients originally interpreted as normal were reinterpreted as "normal" (61%), 10% less reinterpretation correlation than scintiscanning. The majority of these were reinterpreted as diffuse disease. Twenty-one of 32 originally called diffuse (66%) were reinterpreted as diffuse disease. The only large discrepancy, however, concerns the like reinterpretation of local defects. Here only 19 of 37 (51%) were reinterpreted in the same way as the original impression as compared with 70% for scintiscanning. Twenty-six patients were in partial agreement with the original diagnosis. Thus, in 71 of 145 cases (49%) there was complete agreement as to both presence of disease and its type. In 26 cases (18%) there was partial agreement and in 48 (33%) there was complete lack of agreement. Regarding the presence of disease as compared with no disease, 109 of 145 (75%) were reinterpreted the same as originally.

Table 3 compares the original readings with the final proven diagnosis. Various problems have become obvious. Over-reading of normal studies occurred with both modalities. However, it was more common for nuclear medicine (11/13 as compared with 5/13) than for ultrasound. On the other hand nuclear medicine was more sensitive in diagnosing disease since only 13/80 (16%) of the scintiphotos were called normal as compared with 30/80 (38%) for ultrasound. Regarding local disease nuclear medicine correctly called 18 of 22 (82%) while falsely interpreting 18 of the 73 scans (25%) as positive for local disease.

Ultrasound interpretations of local abnormalities were 12/19 (63%) correct as compared with 5/68 (7%) false positive.

Nuclear medicine correctly interpreted only 50% of the cases of diffuse disease present (19 of 38) with 5/73 (7%) false positive as opposed to 46% (18 of 39) and 4.4% (3 of 68) for ultrasound for this entity.

The general agreement as to specific type of disease or normal study was 53% for nuclear medicine (39 of 73) and 56% for ultrasound (38 of 68). As to the presence of disease as compared with no disease, the figures were 73% accuracy for nuclear medicine and 66% for ultrasound.

Table 4 exhibits the same type of data as shown in Table 3 except that it uses as its basis the reinterpretation of the data from the scintiphoto and ultrasound studies. Over-reading of normal studies still occurred but had decreased to 8 out of 13 for nuclear medicine compared with 2 of 13 for ultrasound. Ten percent false negative (8 of 80) occurred with the scintiphotos as compared with 20 of 80 (25%) for ultrasound. Nuclear medicine correctly interpreted 18 of 23 (78%) of the scans with local defects with a false positive rate of 11% (8/75). Ultrasound correctly interpreted 14 of 23 (61%) of the local lesions with a false positive rate of 11% (9 of 79).

The increase in accuracy in the diagnosis of diffuse disease was striking for nuclear medicine with

TABLE 4. CORRELATION OF REINTERPRETATION READINGS OF SCINTIPHOTOS AND ULTRASOUND STUDIES AND PROVEN DIAGNOSIS*

Interpretations														
Scintiphotos							Ultrasound							
Diagnosis				Correlation as to type of disease		Disease as compared with no disease	Diagnosis				Correlation as to type of disease		Disease as compared with no disease	
	N	L	D	agree	52	64		N	L	D	agree	47	58	
N	5	3	5	disagree	23	16	N	11	6	14	disagree	32	22	
L	3	18	5	partial	5		L	2	14	7	partial	1		
					80	80						80	80	
D	5	2	29				D	0	3	22				
				Partial agree—5							Partial agreement—1			

* Proven cases only.

Data of Table 3 following reinterpretation. Improvement has occurred in both modalities and yet problems of overreading the normal studies (nuclear medicine) and underreading the local abnormalities (ultrasound) still exist. N = normal, L = local, D = diffuse.

29 of 39 (75%) now correctly diagnosed with 7 of 75 (9%) false positive. This was an increased accuracy of 25% over the previous effort with only a 2% increase in false positives. Twenty-two of 43 readings of diffuse disease were correct for ultrasound (51%), an increase of 5%. The false positive rate was still approximately 4%. The general agreement as to specific type of disease (or normal) was now 69% (52/75) for nuclear medicine and 47 of 79 (60%) for ultrasound. As regards agreement as to disease vs no disease, the statistics were 80% for nuclear medicine and 73% for ultrasound.

Table 5 is a display of the chemical tests of liver function of the patients discussed in Table 4 and the amount of alcohol imbibed by these patients. As can be seen there are no chemical tests that predict any liver disease with 100% accuracy. Indeed, there is no battery of liver function tests that is 100% accurate for any disease process. As regards diffuse disease the BSP was abnormal in a higher percentage of cases than any other test, followed by the alkaline phosphatase and the serum proteins. The ability

TABLE 5. CHEMICAL TESTS OF LIVER FUNCTION IN PROVEN CASES*

	Diffuse disease											
	SGOT		Bili.		Alk. Phos.		Alb. Glob.		BSP		Alcohol intake	
	N	X	N	X	N	X	N	X	N	X	E	W
Cirrhosis	9	15	10	14	5	19	4	17	0	7	16	4
Fatty change	3	3	3	3	2	4	1	4	0	3	3	3
Alcoholic and toxic hepatitis	0	3	2	1	0	3	2	1	0	1	1	0
Diffuse disease												
Lupus												
Diabetes	1	0	1	0	0	1	1	0	1	0	0	1
Hemosiderosis												
Granulomatous	2	2	3	0	0	3	0	0	0	2	1	2
Bile stasis	0	3	0	3	0	3	0	1	0	0	0	2
Viral hepatitis	0	3	2	1	2	1	3	0	1	1	0	3
Total diffuse	15	29	21	22	9	34	11	23	2	14	21	15
	Local disease											
Metastatic	6	6	5	5	4	7	0	9	2	5	3	13
Amoebic abscess	2	4	4	1	2	3	0	3	3	0	3	3
Benign tumor	1	0	1	0	0	1	0	0	0	0	0	1
Total local	9	10	10	6	6	11	0	12	5	5	6	17
Normal	8	3	10	0	8	4	4	5	2	1	4	9
Totals excluding normal	24	39	31	28	15	45	11	35	7	19	27	32

* Raw data shows poor specificity for any single test and only slightly better diagnostic ability when used as "battery."

N = normal, X = abnormal, E = excessive ethanol intake, W = without ethanol intake.

TABLE 6. CORRELATIONS OF NUCLEAR MEDICINE AND ULTRASOUND DIAGNOSTIC ABILITIES

	Agreement in diagnosis			Disagreement in diagnosis			
	+S +U √ √	S U X X	Total	S U √ X	S U X √	Total	Partial agreement
Cirrhosis	12	3	15	6	2	8	1
Fatty changes	2	0	2	2	1	3	1
Alcoholic and toxic hepatitis	0	1	1	1	0	1	1
Diffuse disease	0	0	0	0	0	0	2
Granulomatous	0	0	0	3	0	3	0
Bile stasis	0	0	0	1	0	1	1
Viral hepatitis	1	1	2	1	1	2	1
Total diffuse	15	5	20	14	4	18	6
Metastatic	7	4	11	5	0	5	0
Amoebic abscess	5	0	5	0	1	1	0
Normal	5	2	7	0	6	6	0
Benign tumor	0	0	0	0	1	1	0
Total focal and normal	17	6	23	5	8	13	0
Grand total	32	11	43	31	19	12	6

S = scintiphoto, U = ultrasound, V = positive finding, X = negative finding.

to detect local disease by chemical methods was less effective and certainly none was specific. False positives were very frequent among the patients with normal liver function and reflected the sensitivity of these tests. The less sensitive tests such as the bilirubin did not show false positives while the alkaline phosphatase and the SGOT did. As would be expected, the consumption of alcohol was higher for cirrhotics than for any other class of disease. By and large, the data show that the liver battery has a very high degree of nonspecificity and that if more detailed knowledge of the patients disease status is needed, scanning or ultrasound can be more specific.

Table 6 correlates the reinterpretation findings of nuclear medicine and ultrasound as to type of disease (proven cases only). Here the data were divided into agreement or disagreement and each of these further subdivided into (A) how the agreements correlated with the actual pathology and (B) in the case of disagreement which modality was right and which wrong. Some cases of partial agreement are listed to the right of the table. Thus, as regards diffuse disease, 20 of 38 cases were in agreement (53%) and of those 75% were in correct agreement while 25% correlated wrongly with the known pathology. Of the 18 in disagreement (add to this those in partial agreement), the scan was correct in the majority of cases. When dealing with local disease, 16 cases were in agreement of which 12 were correctly in agreement (75%). Disagreement was present in seven of which five were correctly diagnosed by the scan. In the case of normals, 7 of 13 were positively correlated and 5 of those 7 were correctly correlated (72%). Of the six normals that did not correlate, all six were correctly diagnosed as normal by ultrasound. Taking all of the cases as a whole, 32 of 43 were in correct agreement (75%), 31 were in disagreement, and 6 in partial agreement. Of those in disagreement 19 of 31 were correctly diagnosed by nuclear medicine (61%).

Correlations of the two modalities in the clinically suggestive cases and in those cases in which the clinical data were inadequate for diagnosis, show that 45% of the clinically suggestive cases correlated positively as to type of disease and 60% positively as to the presence or absence of disease. In the "inadequate for diagnosis" cases, 34% agree positively as to type and 55% as to the presence or absence of disease.

Finally, an attempt was made to determine if either modality was having difficulties in its interpretation in any specific portion of the liver. Dramatic findings were noted in certain cases. Lesions in the dome of the right lobe of the liver, that were large and very obvious by scanning were sometimes missed by ultrasound and it seemed that the modality had trouble in resolving this area. Conversely, the scan technique miscalled lesions in the left lobe that were easily seen to be due to anatomical variations by ultrasound. The statistics show, however, that of 18 local lesions involving the right lobe, scintiphos missed only 4 while the ultrasound missed 10. This problem diminishes as one approaches the left lobe or the porta hepatis with the nuclear medicine technique having three false negatives and the ultrasound five false negatives in this area. As regards false positives, once again the scintiphotography tended

to have a greater percentage of false positives than ultrasound.

DISCUSSION

The first study comparing ultrasound and nuclear medicine evaluation of the liver was performed by Bogin and Upyrev (*3*). The results of their studies would not be totally comparable to our own because of the difference in instrumentation and radiopharmaceutical used. Their study used a rectilinear scanner of Hungarian origin (type MV-7101) and ^{198}Au-colloid as the isotope used. The ultrasound device was a UEZ-4 with "the experimental scanning transmitter on a frequency of 1.76 megacycles. This permitted examination of the liver tissue to a depth of 18–20 cm in a cross section." Forty patients were studied, 18 with known carcinoma, 13 with cirrhosis of varying etiologies, 6 with "chronic disease of the cholagogic system," 2 with cysts not involving the liver, and 1 with a duodenal ulcer. In 36 of the 40 patients there was good correlation between scanning techniques and ultrasound. Four cases show noncorrelation. One of these patients was shown to have metastases and the scan found this while the ultrasound showed a picture more compatible with cirrhosis. A second patient had a normal liver scan, but the ultrasound showed abnormalities in the right lobe of the liver which on operation were shown to be connective tissue in origin. The remaining two patients were not described in detail. Twenty of the 40 patients had biopsy, laparotomy, and autopsy data. Of these 20 patients, 18 were correctly and coincidentally diagnosed by the two modalities while 2 were incorrectly diagnosed. The authors' conclusions were, in effect, that the two modalities complemented each other.

The second study comparing ultrasound and nuclear medicine techniques in the diagnosis of liver disease was performed by McCarthy, et al (*4*). The ultrasound scanner used was a modified Diasonograph NE4100 type with a frequency of 1.5 MHz and a swept gain rate of 1.8 dBcm-1. Isotope scanning was performed with a 3-in. rectilinear scanner (homemade) using a collimator with an 8-cm focal length. The isotope used was ^{99m}Tc-sulfur colloid (Patton method). Two millicuries of the radiopharmaceutical was used. Ninety-three patients were classified as having a variety of liver problems. Twenty-three patients were classified as normal with 13 proven as normal and the other 10 listed as probable. The nuclear medicine technique correctly diagnosed 13 of the 23 to be normal (56%) which is considerably better than our 5/13 or 39%. The majority of their ten incorrect studies were incorrectly classified as diffuse disease (seven) and three were called localized. This is similar to our own findings in which 5 of the 13 patients were called diffuse and 3 local. The ultrasound technique correctly diagnosed 19 of the 23 patients as normal (82.6%) and the other 4 were called diffuse. This correlates well with our findings of 11 of the 13 patients (85%) correctly called normal. In studies of the patients with cirrhosis of the liver, 14 of 21 (66.6%) were correctly diagnosed by the nuclear medicine technique, slightly less than in our study. Unexplainable is the fact that by the ultrasound technique, 18 of their 21 patients were correctly diagnosed as having diffuse disease (86%). This is compared to a 51% correct finding by our own ultrasound studies. It was not possible to say whether all the patients with diffuse disease diagnosed by both modalities correlated with each other since the data were not presented in such a way that this was interpretable. Regarding the patients with tumors, 12 of 15 (80%) were correctly diagnosed as having focal disease by nuclear medicine technique. This correlates quite well with the 78% finding in our own series. In 14 of the 15 cases, they were able to correctly diagnose at least a liver abnormality by the nuclear medicine technique where a focal defect existed. Again, this correlates well with our data. The ultrasonic technique is capable of correctly diagnosing local disease in only 7 of 15 lesions (47%) by the British investigators as opposed to 61% in our study. They did, however, correctly diagnose the liver as abnormal in 13 of 15 patients using this modality (87%). Once again this is close agreement with our own data.

Our data strongly suggest that if both modalities consider a liver abnormal, one may assume with a high degree of accuracy that this is the case. Occasionally, as in the case of a borderline normal, poor correlation will be obtained. The reason for this appears to be the high degree of sensitivity of the scanning techniques which causes more false positives to be diagnosed. As regards the site of the missed lesions, the ultrasound technique appears to have problems in diagnosing focal lesions in the superior portion of the right lobe of the liver. The reason for this is obscure. However, it is the opinion of the authors that the etiology may be due to overlapping by the lung in this particular area. Problems were encountered regarding false negative lesions in the left lobe of the liver on scintiscanning. The probable reason for this is the hesitancy of the investigator to call lesions in an area where the anatomy is so often variable. It is here that ultrasound can be of great benefit since the normal anatomy is so well outlined by this technique. Therefore, even if the ultrasound study showed no evidence of disease in that area, the nuclear medicine physician can with

a high degree of certainty have an answer to his problem of whether the defect in question could be due to normal anatomic relationships. Ultrasound can also determine if a lesion is solid or cystic, a point of major importance in the differential diagnosis of a local defect in a febrile patient.

Finally, it should be noted that the instruments now in use by both ultrasound and nuclear medicine are not optimal and that major changes in both are currently taking place. This is especially true in ultrasound, a fact that may continue to increase the value of this technique.

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Tibor Doby

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Analysis of Pancreas Scintiphotos (Letter to the Editor). Accepted 10/19/72.
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James B. Hatchette