
Emission Tomography for Assessment of Diffuse Alcoholic Liver Disease

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A method of quantitative liver tomoscintigraphy (SPECT) was compared for accuracy with planar scintigraphy (PS) in a group of patients with diffuse alcoholic liver disease. SPECT sensitivity was also compared with that of transmission computed tomography (CT), US, aminopyrine breath test (ABT) and liver chemistries (LC). One hundred and fourteen alcoholic patients with proven liver disease and 17 patients free of liver disease were included. Seven quantitative scintigraphic features and a score, including all criteria were considered. With a specificity of 95%, the sensitivity was 79% in steatosis and 97% in cirrhosis. SPECT showed a better sensitivity than PS (SPECT 89%, PS 66%), especially in patients with steatosis. In the same subsets of patients, SPECT sensitivity also compared favorably with that of transmission CT (SPECT 92%, CT 65%), ultrasonography (SPECT 88%, US 53%) and ABT (SPECT 90%, ABT 63%).

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Typical scintigraphic features of diffuse alcoholic liver disease include hepatomegaly, splenomegaly, redistribution of the colloid tracer in the spleen and the bone marrow, change in the left-to-right lobe uptake ratio and nonhomogenous liver uptake. The sensitivity of radiocolloid planar scintiscan (PS) in diffuse hepatic disease varies in a fairly wide range, from 60% to more than 90% (1-6).

Since attenuation and background problems preclude any accurate quantification, planar studies are merely qualitative. Inasmuch as SPECT overcomes some of the limitations of PS, better accuracy should be expected from routine quantitative analysis of liver and spleen SPECT studies.

The purpose of this study was to compare the sensitivity of the tomographic and the planar techniques in a group of alcoholic patients with proven liver disease. SPECT sensitivity was also compared with that of transmission computed tomography (CT), ultrasonography (US), aminopyrine breath test (ABT) and liver chemistries (LC).

MATERIALS AND METHODS

Patients

One hundred and eighty-four patients hospitalized in the Department of Internal Medicine during the last three years were included in the study (see Table 1).

Normal subjects included 70 nonalcoholic patients referred to exclude metastatic involvement of the liver from a primary neoplasm. Criteria of normality were a normal CT study at the time of inclusion together with normal liver chemistries, or normal liver chemistries and no clinical liver disease during a 6-mo follow-up period.

Abnormal subjects included 114 alcoholic patients with histological diagnosis of steatosis or cirrhosis or with portal hypertension confirmed by endoscopy. Referral for liver biopsy was the decision of the patient's physician, who was informed of the protocol of the study approved by our ethics committee. Criteria used to recommend biopsy included the extent and duration of alcohol consumption, the severity of liver blood chemistries and patient cooperation.

All exams and liver biopsy were carried out within 3 wk of admission. Forty-two patients were classified as having steatosis: 24 with pure fatty change and 18 with associated histological signs of alcoholic hepatitis or slight fibrosis but no signs of cirrhosis. Forty patients were classified as cirrhotic on histological grounds and 32 patients were included in the cirrhosis group on endoscopic grounds. Cirrhotic patients were further separated into three subgroups according to Child's classification (7).

Distribution of patients and utilization of techniques are summarized in Table 1.

SPECT Acquisition

A commercial radiocolloid (105 MBq, 5 mci) (Albures, Solco) was intravenously injected 30 min before acquisition. A single-head, large field of view camera (Apex, Elscint Co.) was fitted with a high-resolution, parallel-hole collimator. A static anterior image of 600 kcts, zoom 1.6 and matrix size 128/128 was first obtained with a lead strip marker placed on the margin of the right rib cage. Ninety projections were next acquired in elliptical step-and-shoot mode, matrix size 64 × 64.

The acquisition time of the SPECT projections was calculated from the static anterior image to obtain a maximum pixel count of about 150-200K in the SPECT anterior projection. This corresponds to about 3,000 kcts accumulated in the whole SPECT acquisition. The frame time varied from 5 to 20 sec. Whenever possible, the patient was asked to hold his arms over his head for the duration of the study. The average total examination time was about 25 min.

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TABLE 1
Patient Distribution and Utilization of Techniques

	SPECT	Bps	PS	Plq	CT	US	ABT	LC
Total	184	82	142	114	89	86	99	184
Normals	70 (67)	/	44 (41)	44 (42)	27*	/	/	70*
Abnormals	114 (103)	82	98 (65)	70 (49)	62 (40)	86 (46)	99 (62)	114 (104)
Cirrhosis [†]	72 (70)	40	63 (54)	47 (40)	36 (25)	51 (31)	61 (47)	72 (68)
Steato-fibrosis [‡]	42 (33)	42	35 (11)	23 (9)	26 (15)	35 (15)	38 (15)	42 (36)
m	24 (18)	24	21 (4)	14 (5)	13 (5)	19 (7)	20 (8)	24 (19)
Fibrosis [‡]	18 (15)	18	14 (7)	9 (4)	13 (10)	16 (8)	18 (7)	18 (17)

Bps = biopsied patients; Plq = patients with planar spleen-to-liver uptake ratios; and m = pure fatty metamorphosis.

Numbers in parentheses are patients with true-positive or true-negative results.

/ No normal patients were evaluated with Bps, US or ABT.

* Normal CT and LC results were criteria of inclusion of normal patients.

[†] Cirrhosis and steato-fibrosis are subgroups of normals.

[‡] Pure fatty metamorphosis and fibrosis are subgroups of steato-fibrosis.

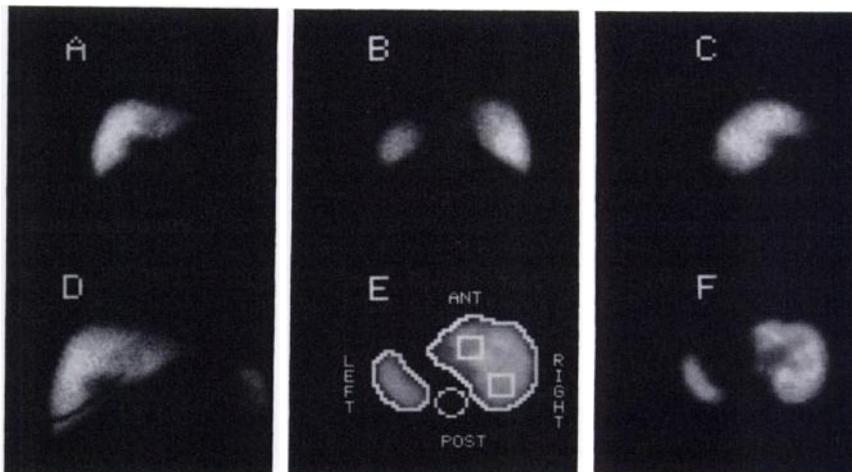
SPECT Processing

SPECT reconstruction used a Butterworth backprojection filter and attenuation correction was performed according to Chang's method, one iteration. Seven quantitative scintigraphic criteria were selected: liver and spleen volumes, spleen-to-liver volume ratio, spleen-to-liver uptake ratio, bone marrow-to-liver uptake ratio, left-to-right hepatic lobe uptake ratio and liver heterogeneity.

Computation of these parameters included the following steps:

1. A mapping image was constructed, representing the higher voxel value in all the transaxial reconstruction slices.
2. The operator roughly outlined the liver and the spleen and relocated three pre-defined regions of interest (ROIs) on this mapping image: bone marrow, left and right hepatic lobes (Fig. 1E).
3. Left-to-right hepatic lobe ratio and bone marrow-to-liver uptake ratio were also calculated on this image as the ratio of the highest pixel values in the ROIs.
4. The computer calculated an automatic outlining of the liver and the spleen on the same image inside the ROIs previously defined.
5. Voxels under a constant threshold of 25% of the higher voxel value in the liver ROI were set to zero. The same operation was performed separately for the spleen.
6. All residual counts in liver or spleen ROIs were added to give the total liver and spleen counts.
7. The same residual voxels were converted to elementary volumes and added to give the liver and spleen volumes.
8. The spleen-to-liver specific uptake ratio was calculated as the ratio of spleen and liver uptakes divided by the ratio of spleen and liver volumes. It is the ratio of the average spleen and liver uptake per unit volume.
9. Nonhomogeneity was computed from the middle transaxial slice in the liver ROI according to a method similar to that used in camera uniformity control. A local nonhomogeneity was calculated in each pixel in a centered square of 3/3 pixels. It is the ratio of the difference between higher and lower pixel values divided by the sum of these two values. Squares containing zero pixels were not retained for calcu-

FIGURE 1. Example of a patient with mild disease. (A) SPECT anterior projection. (B) SPECT posterior projection. (C) SPECT right lateral projection; (D) Conventional 600K planar anterior image with a lead strip placed on the margin of the right rib cage. (E) SPECT processing image representing the hottest pixels of all transaxial reconstruction slices. The ROIs defined on this image are: liver, spleen, liver lobes, marrow. (F) Image of a transaxial slice crossing the liver at mid-height. This patient with steatosis had a significant increase of normalized spleen volume (434, nl < 300), spleen/liver uptake (0.865, nl < 0.828) and score (1.6, nl < 0.308). Planar anterior image and SPECT projections are normal. No obvious abnormality is seen on the transaxial slice. Only quantification identifies this patient as abnormal.



lation, thereby excluding the pixels bordering the slice. Nonhomogeneity was finally expressed as the mean of nonhomogeneity values calculated in nonexcluded pixels.

All processing steps following definition of the ROIs were completely automatic. The entire processing time was less than 1 min.

SPECT Quantification

The normal upper limit of each parameter was fixed at the 95 percentile of the distribution of normal subjects since most distributions were not gaussian. Therefore the specificity of any parameter equals 0.95. Its sensitivity in study patients was calculated accordingly. An overall quantitative abnormality score taking into account the weight of each abnormal parameter was also calculated for each patient. This score was obtained by adding the number of standard deviations beyond the normal limit for each parameter. The normal upper limit of the score was set in the same way to include 95% of normals, yielding a specificity of 0.95.

Planar Studies

Besides the conventional anterior static image of 600 kcts, additional planar images in other views were obtained by reframing three consecutive projection images.

Results were independently reviewed by two experienced nuclear physicians unaware of the final diagnosis. They were asked to qualitatively evaluate five parameters (liver and spleen volume, spleen-to-liver and marrow-to-liver relative uptake, liver homogeneity) and to classify the results as normal or abnormal. In order to evaluate interobserver reproducibility, the data were first independently examined by both observers. Conflicting results were next reviewed in concert and the common interpretation was then compared with the final diagnosis.

The maximum spleen-to-liver uptake ratio in a posterior view (8) was calculated in some patients. This parameter was not included in planar study evaluation but was considered for comparison with the SPECT spleen-to-liver uptake ratio.

Nonhomogeneity obtained from calculation was compared for validity with visual assessment of the conventional planar anterior view.

Computed Transmission Tomography

Hepatic scanning was performed on a Philips Tomoscan 350 CT scanner without injection. All the patients underwent examination with contiguous 9-mm-thick sections at 120 keV and 200 mA, with a 4.8-sec acquisition time. Images were reconstructed using a 256/256 pixels matrix.

Images were reviewed retrospectively by an experienced radiologist with no clinical information about the patients. CT diagnosis was based on the usual criteria: volume of the liver and the spleen, Hounsfield Unit (H.U.) density value of the liver, heterogeneity and presence of ascites. From these criteria, results were classified as normal or abnormal.

Ultrasonography

Sonographic evaluation of the liver was obtained using a Toshiba ultrasound tomographic apparatus (Sonolayer-V model SSA-100 A) with a 3.75 MHz phased array sector probe.

US data was reviewed retrospectively from the protocols given at the time of the study. It was not possible to obtain subsequent sonography results recorded independently of the radiologist's clinical information. US diagnosis was based on classical criteria:

liver echogenicity, liver and spleen size and contour and presence of ascites. Results were accordingly classified as normal or not.

Aminopyrine Breath Test

The specific activity of exhaled ^{14}C -dioxide aminopyrine was measured 2 hr after oral administration of a standard activity of 37 kBq and expressed as the percentage of the ingested ^{14}C after correction for body weight (9). Values less than 4.3% were considered as abnormal according to the normal range of our laboratory.

Liver Chemistries

Liver chemistries were obtained either at admission or within the following few days. They were considered abnormal if serum bilirubin, gamma-glutamyltransferase (GGT) or aminotransferases (ASAT and ALAT) were above the normal range of our laboratory.

Statistical Analysis

Comparison between SPECT and the other methods were assessed in subgroups of patients referred for both procedures. Nonparametric statistical analysis used MacNemar's test for paired observations, including Yates' correction for continuity. Nominal p values ranging from 0.05 to 0.10, though not significant, are given for full information.

RESULTS

SPECT: Normal Patients

The liver volume normalized to body surface area calculated in the 70 normal subjects (mean \pm 1 s.d.) was 1323 \pm 284 cc. Normalized spleen volume was 203 \pm 60 cc.

The normal upper limits (percentile 95) of the most important SPECT parameters were as follows: normalized liver volume 1770 cc, normalized spleen volume 300 cc, spleen-to-liver uptake ratio 0.828 and marrow-to-liver uptake ratio 0.183. The normal upper limit of the planar spleen-to-liver uptake ratio was 0.759 and the upper limit of the score was 0.308.

SPECT: Study Patients

The sensitivity of each SPECT criteria is summarized in Figure 2. The spleen-to-liver specific uptake ratio had the highest sensitivity for steatosis as well as cirrhosis. There was no liver heterogeneity in steatosis and this criteria was present in only half the cirrhotic patients. Moreover, analysis of individual results indicates that liver nonhomogeneity was never present as a single abnormal parameter.

The score including all criteria gave an overall sensitivity of 90% (79% in steatosis and 97% in cirrhosis). While some patients with severe disease may have had a low score, all patients with a high score had a disease stage beyond simple fatty change (Fig. 3).

Comparison of SPECT and Planar Techniques

Ninety-eight alcoholic patients and 44 normal subjects were evaluated with both planar and SPECT radionuclide techniques. When reading the planar images, the two observers disagreed on at least one criteria in 56% of the alcoholic and 26% of the normal patients. SPECT had a

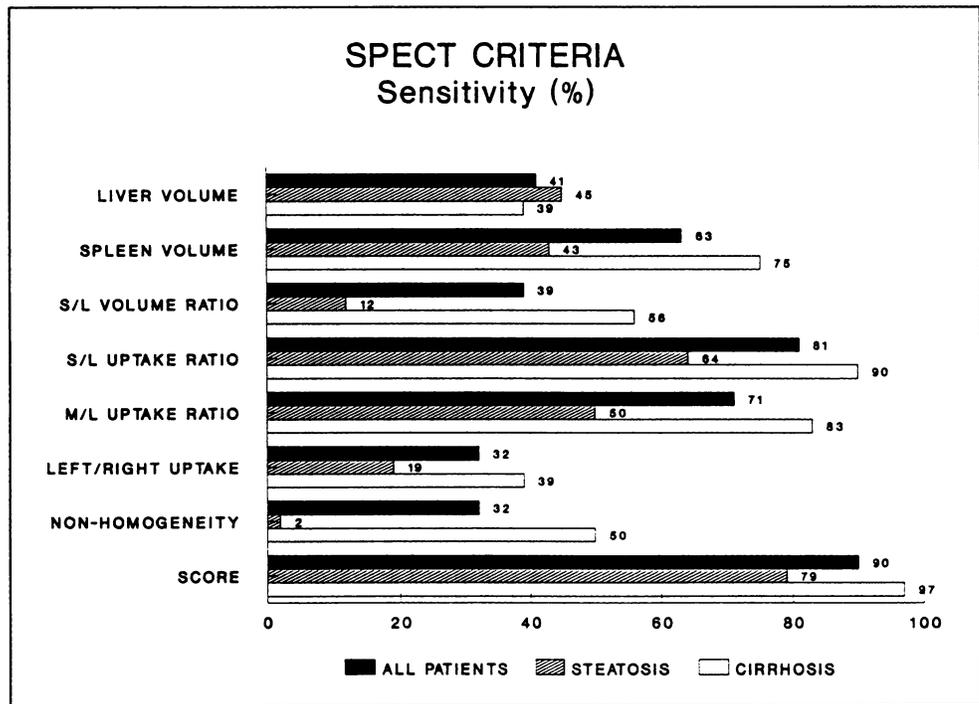


FIGURE 2. Sensitivity of the seven SPECT criteria. Percentage of each positive criterion and global score in all abnormal patients and in subgroups with steatosis and cirrhosis. Specificity of each SPECT criterion and score was set at 0.95.

significantly higher sensitivity than PS in patients with steatosis as well as in cirrhotic patients (Fig. 4A). According to the final diagnosis, SPECT provided the correct response in 89% of the abnormal patients versus 66% for conventional scintiscan ($p < 0.001$). SPECT had higher sensitivity in patients with steatosis (SPECT 74%, PS 31%, $p < 0.001$) as well as in cirrhotic patients (SPECT 97%, PS 86%, $p < 0.05$). In the 21 patients with simple fatty

change, SPECT sensitivity was 15/21 versus 4/21 for planar studies ($p < 0.005$).

Figure 1 shows an example of one of these patients with a false-negative planar study and an abnormal SPECT score.

In the subgroup of patients in which the spleen-to-liver uptake ratio was calculated from the planar posterior view, the SPECT index was significantly higher than the planar index (Fig. 4B).

Nonhomogeneity calculated on the SPECT middle slice was slightly less sensitive, though not significantly, than its visual assessment on the conventional anterior view in steatosis patients (SPECT 2%, PS 12%) and in cirrhosis patients (SPECT 50%, PS 60%).

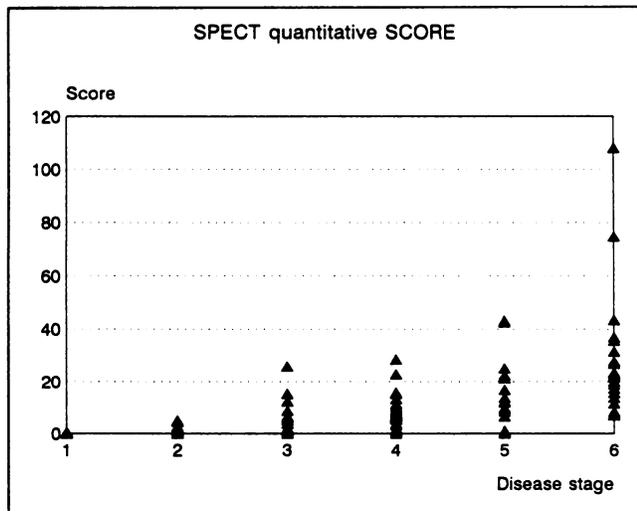


FIGURE 3. Relation of the SPECT score with the stage of disease. N = normals, M = pure steatosis, F = steatosis + fibrosis/hepatitis and A-B-C cirrhosis = Child's classification A, B or C. All patients with a score higher than nine have a disease stage more severe than pure fatty change.

Comparison of SPECT and Other Methods

SPECT sensitivity was significantly better than CT in the entire group of alcoholic patients that underwent both studies and in the subgroup of cirrhotic patients. A similar trend was seen in the subgroup with steatosis although the difference was not statistically significant (Fig. 4C).

SPECT sensitivity was significantly higher than US in the subgroup of patients with steatosis as well as in the subgroup with cirrhosis (Fig. 4D).

The sensitivity of ABT was significantly less than SPECT in the subgroup with steatosis and in the cirrhotic subgroup (Fig. 4E).

The sensitivities of SPECT and LC lie in the same range (Fig. 4F).

The specificity of methods other than scintigraphy was not evaluated since abnormal data and especially abnor-

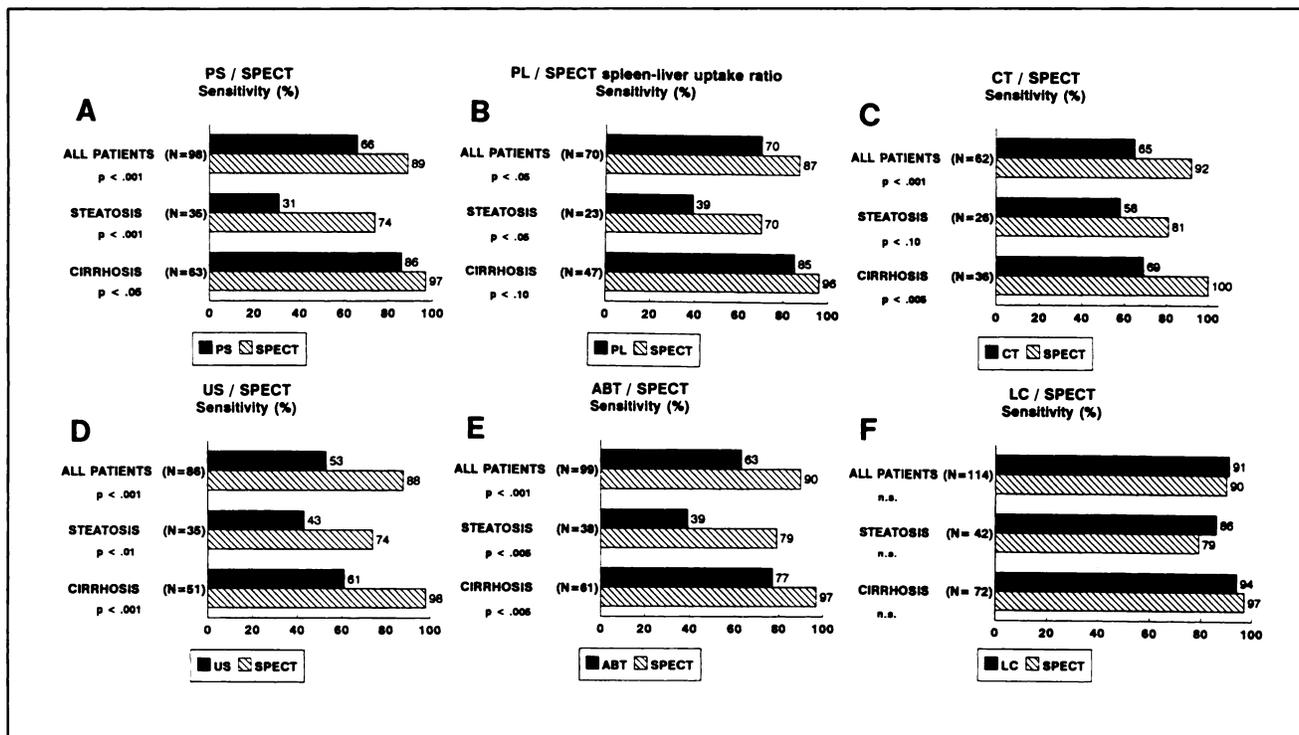


FIGURE 4. Compared sensitivity (percent). SPECT specificity = 0.95. (A) SPECT (score) and PS (planar scintiscan); (B) SPECT spleen/liver uptake and planar uptake (only uptake ratio is considered in this comparison); (C) SPECT (score) and CT; (D) SPECT (score) and US; (E) SPECT (score) and ABT; and (F) SPECT (score) and LC (liver chemistries). N = number of patients included in each comparison.

mal liver chemistries were criteria for patient exclusion in the normal group.

DISCUSSION

Since the early sixties, conventional planar liver scintigraphy has proven to be a valuable clinical tool to evaluate diffuse hepatic disease, especially cirrhosis. Although SPECT has been widely used in the detection of focal lesions, little attempt has been made to apply this technique in diffuse liver disease (6,10-13). Yet, evaluation of diffuse diseases takes better advantage of the functional nature of the scintigraphic technique.

We have tested a method of quantitative SPECT as a potential improvement of planar liver imaging in a group of severe alcoholic patients selected for liver biopsy on clinical grounds. Histology or portal hypertension was the gold standard for SPECT sensitivity evaluation, as well as for comparative evaluation with planar imaging and other methods. Normal values were calculated from a group of patients presumably free of any liver disease. The specificity fixed accordingly therefore refers to normal patients and not to patients without alcoholic liver disease but with other hepatic or general diseases.

When we compare planar and tomographic scintigraphy, SPECT shows a higher accuracy than PS. Furthermore, there is no interobserver variation since the calculated score is virtually operator-independent. The large

variability in the visual evaluation of diffuse liver disease in abnormal patients confirms another study comparing subjective assessment by several observers (14). The difference in sensitivity between PS and SPECT is especially meaningful in patients with steatosis, suggesting a particular advantage of SPECT over PS in patients with low-stage disease. Besides the anterior view, which is a standard planar acquisition, all other views are reframed from SPECT projection images yielding acceptable quality for reframed planar images, as can be seen in Figure 1, which shows standard and reframed anterior images in the same patient. While the lower resolution of the reframed images certainly involves loss of information in focal disease, it is of much less importance in diffuse liver disease. As a matter of fact, evaluation of most scintiscan features of liver disease, such as relative spleen or marrow uptake, left-to-right lobe uptake or liver and spleen volumes do not need to have a high resolution. Eventually, the only scintiscan criterion demanding a high resolution is liver inhomogeneity. This criterion can be assessed on the standard anterior view.

Among all SPECT criteria, an increase in the relative splenic uptake is the most common feature in fatty liver disease as well as in cirrhosis. Extra-hepatic colloid redistribution may be particularly sensitive in liver disease of alcoholic origin (15). Although it has been said that this criteria is rather uncommon as a single abnormal feature

(3), in our patients it is more sensitive than any combination of other criteria. It was most often associated with other scintiscan abnormalities but was the only abnormal feature in seven patients.

The SPECT spleen-to-liver uptake ratio is more accurate than the planar ratio measured in posterior view, although most of the abnormal values identified by SPECT are also recognized by the planar index. This is in agreement with another study showing a good correlation between planar and SPECT ratios (16). However, a slight increase in the relative splenic uptake is best assessed by the SPECT technique (12,13,17). Indeed, due to limitations of the planar technique, the apparent liver uptake assessed by visual inspection or by the spleen-to-liver planar uptake ratio may remain normal. This may be due to an increase in liver size and thus an increase of the total liver uptake; whereas the liver uptake per unit volume actually decreases.

A reliable estimation of liver volume from planar scintiscan is very difficult (16). SPECT allows a three-dimensional assessment of the problem with good correspondence between measured and true volumes, at least in phantom studies. Our results in phantoms are quite comparable to those of other studies using similar methods (11-13,18). We used the same method as Kodama but with a slightly different threshold value, giving in our experience a better agreement with phantom measurements.

The left-to-right hepatic lobe uptake ratio does not appear to be a very good criterion in this series, but we used a different method than that applied more successfully by Schreiner et al. in cirrhotic patients (19).

Nonhomogeneity calculated on the SPECT middle slice was not compared with its visual assessment on the same image. Although this SPECT criterion does not perform better than its visual assessment of the conventional static anterior view, we used calculations to get a SPECT processing independent of the operator and a final result independent of subjective evaluation. Our results suggest there is room for improvement of this criterion evaluation. Anyway, whether assessed from planar or SPECT images, nonhomogeneity was seldom present in patients with steatosis. In the cirrhosis group, nonhomogeneity criterion was useless because when present it was always associated with other obvious scintiscan abnormalities.

While the spleen-to-liver uptake ratio is the single most useful criterion, other criteria contribute to increase sensitivity. For example, although not sensitive in the entire group of patients, the left-to-right hepatic lobe uptake ratio was abnormal in five patients with a normal spleen uptake ratio. Two cirrhotic patients had an increase in spleen volume and a normal spleen uptake ratio. In two patients, the only abnormality was an increase in liver volume. In two other patients, an abnormal score was reached by adding the contribution of several criteria.

Among the abnormal patients, certain criteria, espe-

cially increased spleen volume and bone marrow uptake, are indicative of cirrhosis. Such finding confirms other studies using conventional scintiscan (20). However, they are not specific enough to ascertain the severity of disease as they may be present in uncomplicated steatosis. In the same way, the correlation of the quantitative score with disease severity is rather weak. Some cirrhotic patients in Child class A or B may have minor scintigraphic abnormalities and low score values (Fig. 3). On the other hand, it is noteworthy that all patients with a score higher than 9.0 have a disease stage more severe than simple fatty change, the only stage that is completely reversible (21).

To illustrate the value of the quantification score, we have performed receiver operator characteristic analysis of the score and the seven SPECT criteria, respectively in steatosis and cirrhosis patients (Fig. 5A-B).

Our data show the superiority of SPECT over PS, as well as over CT or US, in detecting steatosis and cirrhosis in alcoholic patients. A number of other comparative evaluations previously showed better sensitivity of spleen-liver scintigraphy compared to that of transmission tomography in the diagnosis of cirrhotic disease, generally with a slightly lower specificity (2,5,6). In the less advanced disease stage of fatty change, scintigraphy is also better than CT, although scintigraphic abnormalities are less frequent and less important than in cirrhotic patients (1,5,12). Reviewing cumulative data comparing scintiscan and CT, McClees reports an average sensitivity of 87% and a specificity of 76% for the radionuclide technique versus a sensitivity of 38% and a specificity of 93% for CT imaging (22).

While the reported specificity of US in diffuse liver disease is generally good, its sensitivity is quite variably estimated: ranging from 49% to 95% in cirrhosis and 60% to 94% in steatosis (23-30). Such discrepancies might be explained by differences in patient selection or by technical factors, since US is a largely operator-dependent technique. The two studies besides this one comparing RS and US in the same group of patients also found a better sensitivity in the former (5,31). Therefore, the current tendency of screening patients for alcoholic liver disease with US is not based on a firm background in terms of comparative accuracy with other methods and especially RS.

The sensitivity of aminopyrine breath test appears somewhat lower than previously reported in alcoholic liver disease, especially in patients with cirrhosis (9,32). Again this might be related to differences in patient selection, since ABT is more a test of the severity than of the presence of the disease (33).

The sensitivity of liver chemistries is in the same range as that of SPECT. Some patients may have normal LC with an abnormal SPECT study or vice versa. It must be emphasized that the threshold of LC was set at a very narrow limit, because chemistries were considered abnormal if any test exceeded the normal laboratory range.

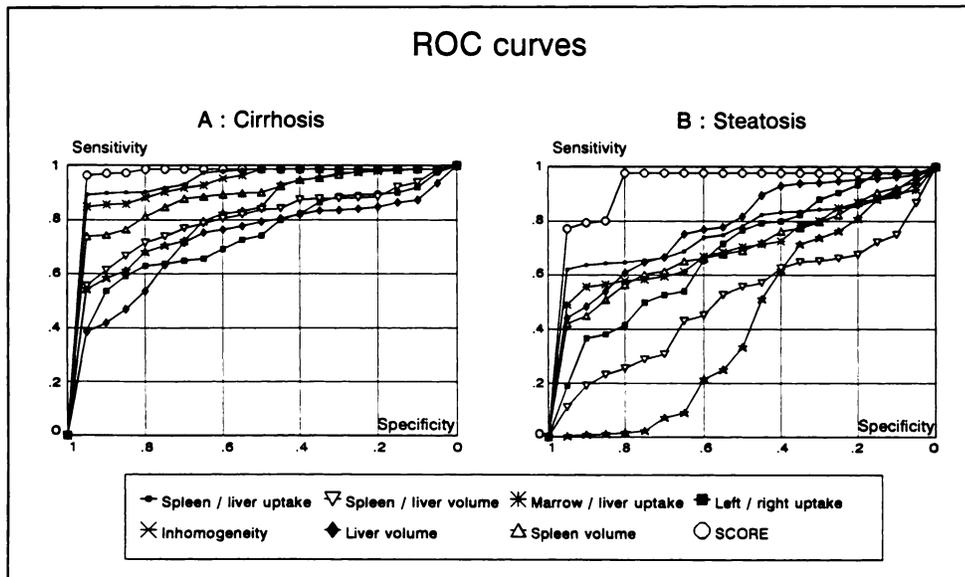


FIGURE 5. ROC curves of SPECT criteria and quantitative score. (A) Steatosis and (B) cirrhosis.

Therefore, LC has a high sensitivity but probably a low specificity.

CONCLUSION

Quantitative SPECT liver scintigraphy seems to be a valuable noninvasive test indicated for patients with intermediate probability of diffuse alcoholic liver disease. When comparing different imaging procedures in the same group of patients, SPECT yields the higher sensitivity in such patients, whether at the stage of simple steatosis or cirrhosis. The clearly lower sensitivity of either CT or US procedures confirms elsewhere reported comparative studies. Inasmuch as SPECT with quantification has a better sensitivity than PS, the former should be recommended in alcoholic patients selected on clinical grounds before consideration for liver biopsy. Histological confirmation would then be indicated in patients with a low or intermediate pathological score. On the other hand, high pathological scores will be considered for full study, including ABT and search for portal hypertension, since most of these patients will show some degree of irreversible hepatic damage.

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EDITORIAL

Diagnostic Imaging of the Liver

Diagnostic imaging of the liver may be undertaken for the identification of focal neoplastic disease or diffuse hepatic functional disorders. Anatomy-based hepatic imaging in patients with known or suspected liver cancer constitutes the vast majority of liver studies today. Evaluation for diffuse functional diseases is not commonly undertaken because unless these disorders are advanced they do not produce alterations in gross hepatic morphology (size and shape) to permit detection with anatomic imaging studies.

DIFFUSE LIVER DISEASE

In this issue of *JNM* (1), Delcourt and colleagues report that in patients with alcohol-related diffuse liver abnormalities, quantitative tomoscintigraphy (SPECT) correlates well with liver histology and therefore provides clinically useful diagnostic information. This study establishes the need to further develop functional hepatic imaging and demonstrates that despite limited anatomic resolution (for example, in comparison to CT) it can be effective for such diagnostic evaluation.

Diffuse hepatic disorders that produce an alteration in hepatic function must be investigated with markers tar-

geted to specific hepatic cells and therefore assess specific cellular activity. In their report, Delcourt and colleagues show that hepatic reticuloendothelial (RE) function is reduced in patients with alcoholic liver disease. As a result, there is decreased hepatic sequestration of the radiocolloid and a relative increase in splenic uptake. It is of interest that in addition to hepatic fibrosis and cirrhosis, even diffuse fatty-change, the earliest and only reversible manifestation of alcoholic liver disease, produces such a colloid shift. Not surprisingly, the functional tomoscintigraphic liver examination (SPECT) was superior to anatomy-based imaging studies (CT and US). These conclusions would not have been different even if the CT examination was performed on state-of-the-art equipment or if the US comparison was undertaken on real-time images.

An important inference that can be made from these results is that information on tomographic images is superior to projection images. As a result, one may speculate that with its superior anatomic resolution, functional MRI with hepatocyte-specific or RE cell-specific contrast agents (2) may be even more effective for the evaluation of diffuse liver diseases. Indeed such cell-specific contrast agents are already undergoing clinical trials. Additional investigations will be required to determine if functional imaging studies can be useful in a setting of nondiffuse functional disorder (for

example, focal fatty-change) or in other diffuse liver diseases such as hepatitis (alteration in hepatocellular function). Furthermore, a most basic issue also remains unresolved, which is whether functional imaging studies can accurately portray the earliest manifestations of diffuse liver disease and hence replace the need for a liver biopsy.

FOCAL LIVER DISEASE

Due to inferior display of gross liver anatomy, it is unlikely that conventional scintigraphic functional imaging studies will be useful in oncologic patients for the diagnosis of focal liver cancer (primary or metastatic). In these patients, lesion detection and lesion tissue characterization are two equally important concurrent diagnostic goals. The importance of the latter objective has been highlighted by recent recognition of a high (>20%) prevalence of benign liver tumors in adults (3). Hence benign liver tumors (hemangiomas, focal nodular hyperplasia) can occur in patients with a history of cancer or benign and malignant liver tumors may coexist.

Contrast-enhanced CT is presently the examination of choice for survey or screening examination of the liver for neoplasms (4). Precise implementation of techniques (5) for contrast administration and CT scanning is critical for optimal liver examination. Although contrast-enhanced CT misses approximately 50% of individ-

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