Scintigraphy, Ultrasound and CT Scanning of the Liver\textsuperscript{1,2}

K.J.W. TAYLOR, D. SULLIVAN, J. SIMEONE, and A.T. ROSENFIELD

Yale University School of Medicine, New Haven, Connecticut

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Isotope examination of the liver depends on the functional activity of the liver phagocytes, while ultrasound and CT scanning display the anatomical structure. Cold areas on an isotope scan may be due to impaired function or space-occupying lesions. The method is non-specific and does not differentiate between cysts, abscesses and metastases. Both ultrasound and CT scanning can differentiate space-occupying lesions with a high degree of accuracy so that both techniques can be used to improve the accuracy and specificity of the radioisotope examination. CT scanning of the liver is limited by relatively slow data acquisition and the small differences in X-ray absorption within soft tissues unless contrast agents are used. In comparison, ultrasonic data are rapidly collected and displayed and liver consistency is imaged without contrast media or ionizing radiation. Diffuse abnormalities of the liver, such as cirrhosis, cannot be detected by CT scanning but are apparent on ultrasound examination. In addition, equipment purchase and maintenance costs for ultrasound are a fraction of those for CT scanning. Experience to date at Yale indicates that ultrasound and CT scanning are complementary and supplementary to isotope examination of the liver but that ultrasound in most patients produces better resolution and enhanced tissue differentiation at considerably less cost.

Until recently, the liver has been a blind area for most radiological imaging procedures, particularly in the presence of moderate degrees of jaundice, the most common sign of liver failure. While it is difficult to assess the size and consistency of the liver clinically, it is a frequent site of inflammatory, metabolic and neoplastic disease, so that imaging techniques are required. Isotope imaging of the liver involves the intravenous administration of colloid particles labelled with a radioisotope, formerly gold and now \textsuperscript{99m}Technetium. The accuracy of this technique for the detection of proven abnormalities of the liver was reported to vary from 72 to 90\% in the initial evaluation of the method in the early 1960s [1-5]. Progressive improvements in instrumentation, from rectilinear scanners to highly sophisticated gamma cameras with increasing numbers of photo-multiplier tubes, and the introduction of \textsuperscript{99m}Tc, which is a rather ideal radiopharmaceutical, have not substantially improved the accuracy of this examination. For example, in a recent report on defects of the porta hepatis, it was noted that 58\% were due to anatomical variation while the remaining 42\% represented significant pathology [6]. This has also been our experience in attempting to interpret the \textsuperscript{99m}Tc sulphur colloid liver scan. Obviously, this differentiation between anatomical variation and significant pathology is essential for the proper clinical management of the patient.

Grey-scale ultrasonography has been used since 1973 to improve the differentiation of positive isotope scans and to further investigate equivocal scans [7,8]. This new technology results in tomographic sections through the liver, usually in the longitu-
nal plane. Since the resolution is better than 5 mm, great anatomical detail can be delineated. For comparison of the resolution currently obtained by different modalities, an ultrasound scan (Fig. 1A), a scintigram (Fig. 1B) and a CT liver scan (Fig. 1C) are shown. Ultrasound may be employed to produce a high-resolution tomogram as a complementary investigation to the isotope liver scan. The ability to accurately differentiate between solid and cystic consistencies by ultrasound is particularly valuable.

Cold areas on isotope liver scans may be due to cysts, multiple abscesses or metastatic disease. In the clinical management of the patient, this differentiation is crucial. It can be achieved in the vast majority of patients by the complementary use of ultrasound. For example, a definitely positive nuclear scan with multiple cold areas (Fig. 2) may be due to polycystic disease as revealed by ultrasound in Fig. 3, multiple abscesses (Fig. 4), or due to metastatic disease, shown by ultrasound in Fig. 5. In our experience between 1973–76, cysts, abscesses and necrotic metastases in the liver were successfully differentiated in 88% of cases.

It is in that disturbingly large number of patients with equivocal isotope scans that ultrasound has maximum value. Fig. 6A shows thinning of the margin of the right lobe of the liver which is probably due to an inferior extension of the liver over the anterior surface of the right kidney. A paramedian longitudinal ultrasound scan (Fig. 6B) confirms this impression and a thin tongue of liver tissue is seen anterior to the right kidney. In other patients, however, such scintigraphic appearances may represent significant pathology. In a similar isotope scan shown in Fig. 7A, a cold area is seen at the inferior edge of the right lobe on the medial aspect while ultrasound reveals a highly abnormal scan with a mass of high-level echoes throughout the liver (Fig. 7B), suggesting a chronic inflammatory process. There is also no evidence of a normal gallbladder lumen despite prolonged fasting. At surgery a small contracted gallbladder was seen without stones and the diagnosis of chronic active lupoid hepatitis was made confirming the ultrasound report.

Defects of the porta hepatitis (Fig. 8A) may be due to metastatic disease or anatomical variation. Large vessels seen, for example, in chronic congestive heart failure or right-sided failure, may produce significant porta hepatitis defects, and these large vessels are well visualized on ultrasound examination (Fig. 8B).

A formal comparison between isotope and ultrasound liver scanning was reported by Taylor and Carpenter [8] on 120 consecutive patients under active treatment for cancer and in whom definitive follow-up in terms of surgical intervention or postmortem examination was performed within three weeks of the liver investigations. Nearly half of these patients were jaundiced, producing an unusually high number of equivocal scans. Given this particularly difficult patient population, the results shown in Table 1 demonstrate the great value of ultrasound as an imaging procedure for the liver.

Ultrasound examination of the liver requires considerable expertise, and it is therefore advantageous to use the isotope liver scan as an initial screening procedure, to identify the equivocal scans and to direct the plane of ultrasound section to suspicious cold areas. A flow chart for liver imaging is shown in Fig. 9. In the presence of a normal isotope scan, we feel that ultrasound need only be undertaken if there is clinical suspicion of minimal liver involvement which might be detected by a more sensitive technique. Ultrasound can certainly confirm the presence of metastatic disease in the liver and can also be used to guide needle biopsy of the liver to the most appropriate site to obtain a positive histology. Ultrasound is also used in the small number of patients in whom there is clinical suspicion that multiple cold areas seen in
FIG. 1A. (above) Transverse ultrasonogram through upper abdomen showing the liver consistency, the right branch of the portal vein, celiac trunk and its branches originating from the aorta.

(below) Longitudinal scan through the liver 2 cm to the right of the midline showing the inferior vena cava (V) in its entire longitudinal extent, the liver substance (L) is well seen. P is the portal vein and M is the middle hepatic vein draining into the inferior vena cava.

the isotope scan could be due to non-malignant pathology such as inflammatory or polycystic disease [9].

As is apparent from Fig. 9, CT scanning of the liver has not to date attained great importance in this institution. This partly reflects the success of ultrasound in this area and is partly due to the limitations of resolution imposed upon CT scanning by biological motion. In some centers, tomographic isotope techniques are used instead of ultrasound to further investigate the cause of equivocal cold areas on the conventional scintigram.

Due to the success of CT scanning for intracranial lesions, whole body CT scanning has been approached with great enthusiasm. Since the consistency of a lesion can be determined from the specific X-ray absorption, CT scanning is a valuable means for specifying the nature of space-occupying lesions. Cysts of the liver
FIG. 1B. 99M Tc sulphur colloid radionuclide examination of normal liver. Standard, multiple views are shown. The inspiratory and expiratory views are obtained with a lead marker over the coastal margin.

FIG. 1C. Transverse computerized axial tomogram through the upper abdomen showing contour but little definition of the consistency of the organs. The liver (L) is seen, the aorta (A), the kidneys (K) and pancreas are especially well seen.
FIG. 2. 99M Tc sulphur colloid radionuclide scan showing anterior view of liver with multiple focal cold areas.

FIG. 3. Longitudinal ultrasound scan through right lobe of the liver and right kidney. Note extensive replacement of normal anatomy by cysts of varying sizes. These appearances are indicative of polycystic disease of the liver and kidney.

may be diagnosed with extreme accuracy by both ultrasound and CT, although ultrasound is faster and more economical.
FIG. 4. Longitudinal ultrasound scan of the liver showing diffuse abnormality of the liver consistency with irregular high-level echoes which appear as white flecks (arrowed). Large cystic cavities (C) are seen disrupting the normal liver substance. Cystic cavities in a liver with evidence of inflammatory changes are most consistent with multiple abscesses. In this patient hydatid disease was diagnosed.

FIG. 5. Transverse ultrasonogram of the liver showing replacement of normal anatomy by multiple areas of very high-level echoes (arrowed) and such appearances are characteristic of metastatic disease from a carcinoma of the colon.

Although there are a number of comparisons between CT scanning and ultrasound in progress at the present time, definitive results are not yet available on the relative accuracy of the two techniques for detection of either liver abscesses or metastases. There are significant differences both in the instrumentation available at different centers and in the degree of expertise in the execution and interpretation of each technique so that any comparison between the two techniques will vary from center to center. A number of investigators have reported that contrast media are required for adequate display of liver metastases and abscesses by CT [10,11] and this
immediately renders the investigation invasive to a small degree. When CT scanning is used instead of arteriography, the administration of contrast media and the dose of ionizing radiation is trivial; but when CT scanning is used in place of ultrasound, both disadvantages exist. Figs. 10A, B, C compare the radionuclide, CT and ultrasound appearances of liver metastases. This patient suffered from the Zollinger-Ellison syndrome and had islet-cell metastases in the liver proven by biopsy at surgery three years previously. Since that time, the patient had been energetically

FIG. 6A. 99M Tc sulphur colloid radionuclide liver scan. The anterior, posterior and right lateral views of the liver show thinning of the inferior portion of the right lobe by some extrinsic structure located posteriorly.

FIG. 6B. Longitudinal ultrasound scan through the liver and right kidney showing a thin tongue of the liver (arrowed) projecting anterior to the right kidney. Thus, in comparison with Fig. 6A, the extrinsic structure located posteriorly and causing the thinning of the inferior portion of the right lobe of the liver, is the right kidney.
FIG. 7A. 99M Tc sulphur colloid radionuclide of the liver. There is decreased uptake of isotope in the medial portion of the right lobe seen on the anterior and right lateral views.

FIG. 7B. Longitudinal ultrasound scan through the right lobe of the liver showing a grossly abnormal scan with masses of high-level echoes (arrowed). Since collagen and similar interfaces appear to be the origin of ultrasound echoes, these appearances are consistent with marked fibrosis of the liver. Similar appearances were demonstrated in the spleen, and such changes in the liver and spleen are indicative of a chronic inflammatory disease. On biopsy, chronic active hepatitis was found.

treated with chemotherapy which frequently results in highly necrotic cystic tumors as seen in the ultrasound and CT scans. However, smaller solid masses can be seen which also represent metastatic disease.

With regard to diffuse abnormalities of the liver, both ultrasound and CT scanning permit detection of fatty infiltration. Fat is a natural contrast medium for CT
scanning, and this enhances the pathological change. For detection by CT scanning, there must be a difference in the mean atomic number in a given cell of the organ matrix. Fatty infiltration is one pathology which sufficiently alters the specific X-ray absorption to permit detection by CT scanning.

In comparison, ultrasonic display of most soft tissues usually results from interfaces involving collagen and similar rigid structures which form the fibrous skeleton
of soft tissues and which therefore have high bulk moduli. However, fatty infiltration can also be displayed by ultrasound because fat has markedly different acoustic properties than other tissues. The scattering at such interfaces is related to the square root of the bulk moduli which for supporting tissues such as collagen differ by a factor of 10,000 from those of the surrounding tissues [12]. Thus, any pathology resulting in increased deposition of collagen or replacement of the normal collagen framework, will be demonstrated by the ultrasound technique. Ultrasonic visualization is especially successful for diseases resulting in intrahepatic fibrosis. Such pathologic changes occur during the development of cirrhosis and as a reaction in inflammatory states. Cirrhosis presents characteristic ultrasound and scintigraphic appearances but cannot be diagnosed by CT scanning. Fig. 11A shows the typical nuclear scan features of cirrhosis—small liver, enlarged spleen and shift of colloid to the spleen and bone marrow. A transverse ultrasonogram is shown in Fig. 11B. There are extremely high-level echoes emanating from the liver substance indicating an abnormal degree of intrahepatic fibrosis, and the attenuation within the liver is increased. These changes indicate fibrosis and are consistent with cirrhosis. Other manifestations of cirrhosis can also be demonstrated by ultrasound, including an enlarged and tortuous portal vein associated with portal hypertension and congestive splenomegaly secondary to portal hypertension.

Ascites can be demonstrated by both CT and ultrasound with similar success, as in Figs. 12A and 12B. In both scans, there is a low-density or low-reflective interval between the liver tissue and the anterior abdominal wall. In addition, there is a further fluid-filled space lying anterior to the hilus of the left kidney. Ultrasound scan reveals that there are high-level echoes surrounding this fluid collection, and this we
FIG. 10A. 99M Tc sulphur colloid radionuclide scan of the liver. Anterior view displayed on Polaroid film by triple-lens technique, showing a large irregular cold area with small, satellite focal lesions.

FIG. 10B. Longitudinal ultrasound scan through the right lobe of the liver showing large echo-free areas which are necrotic metastases (M). More posteriorly, small homogeneous tumors are seen (T) and these solid tumors, which replace the normal anatomy, are the most characteristic appearances of metastatic disease to the liver.

FIG. 10C. Computerized axial tomography through the liver showing multiple low-density areas (arrowed) consistent with metastatic disease.
FIG. 11A. 99M Tc sulphur colloid radionuclide scan of the liver. The anterior view of the liver-spleen scan shows changes secondary to cirrhosis including shift of colloid to the spleen, which is enlarged, poor liver uptake of isotope and marked uptake of isotope in the bone marrow. A definite cold area is seen in the region of the porta hepatis.

FIG. 11B. Transverse ultrasonogram through the liver. The liver consistency (L) is highly abnormal since the liver returns dense, white echoes which are characteristic of diffuse intrahepatic fibrosis, most often due to cirrhosis. In addition, there is increased attenuation of the ultrasound beam. Medially and anteriorly a dilated gallbladder (G) is seen, and this was the cause of the cold area seen on the nuclear scan.

interpret as a rim of collagen forming a capsule for either a pseudocyst or an abscess. Thus, in this patient both techniques provide similar information, but the demonstration of collagen interfaces forming a thick capsule narrows the differential diagnosis. Ultrasound also permits the diagnosis of cirrhosis to be made from this scan.

Ultrasound and CT scanning appear equally successful for imaging the biliary tree. Distension of the gallbladder is easily demonstrated by either technique (Figs. 13A and C). Though displayed in different planes, (Figs. 13A,B,C), both show a Courvoisier gallbladder and a pancreatic tumor (Figs. 13A,B and D). In addition, the ultrasound scan reveals dilatation of the biliary canaliculi with superior resolution. Figs. 14A,B,C show the radionuclide, CT and ultrasound appearances of dilated
canaliculi in a patient with jaundice due to extrahepatic obstruction. The ability to demonstrate these structures using the grey-scale ultrasound technique was first reported by Taylor and Carpenter in 1974 [7] and has been shown to be a highly successful application for the ultrasound technique. In 150 patients followed-up to date, dilated biliary canaliculi have been demonstrated with an accuracy of 97% in patients with extrahepatic obstruction. Similar success has been achieved with the CT scanning method by Sagel at the Mallinckrodt Institute who reported an accuracy of 92% in a series of 72 patients (personal communication).

Gallstones can also be demonstrated by both methods, and do not have to be radio-opaque. Eighty percent of gallstones are of mixed composition and have high
X-ray absorptions, whereas pigment stones appear as “holes” within the gallbladder lumen. In our experience to date, we find both techniques rather poor at visualizing intraductal stones due to the tomographic nature of the method.

In view of the similarity and the success of these techniques in the investigation of the liver, it is interesting to compare and contrast the current value of scintigraphy, ultrasound and CT scanning of the liver and to attempt to predict the future improvements in instrumentation and the possible impact on imaging techniques. This is summarized in Table 2.

The scanning time has important implications in relation to the degradation of resolution due to biological motion [13]. Respiratory movements certainly limit the
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FIG. 13C. Longitudinal ultrasonogram through the liver showing a Courvoisier gallbladder (G) and dilated bile ducts are very well displayed (arrowed).

FIG. 13D. Longitudinal ultrasonogram 2 cm to the right of the midline showing the inferior vena cava (V) posteriorly while a grossly dilated common bile duct (BD) is well demonstrated immediately anterior to the inferior vena cava. The common bile duct can be traced into a large homogeneous mass with irregular contours, and this is consistent with a carcinoma of the head of the pancreas (P). Dilatation of the intrahepatic biliary ducts (arrowed) is well demonstrated.

resolution obtainable by isotopic techniques although gating and motion corrector devices improve this to some extent. Using the ultrasonic technique, it is possible to generate up to 4,000 data lines per second which permits the possibility of real-time imaging, discussed below. CT scanning at present varies from 5 to 200 seconds per section.

Although technical improvements can substantially reduce this scan time, this can only be achieved at a considerable cost, both financially and in ionizing radiation exposure. Comparing the radiation dose for each modality, a conventional isotope scan results in about 2 rads per examination and a CT scan currently gives some 2
FIG. 14A. 99M Tc sulphur colloid radionuclide examination of the liver showing linear defects of isotope activity radiating towards the porta hepatis. This pattern is characteristic of biliary distention.

FIG. 14B. Computerized axial tomogram through the liver in a patient with obstructive jaundice showing dilated ducts (arrowed) characteristic of extrahepatic biliary obstruction.

FIG. 14C. Transverse ultrasonogram through the liver showing marked dilatation of the biliary vessels (arrowed) in the same patient as shown in Figs. 14A and B.
rads per slice. Since there is virtually no scatter between adjacent slices, the exposure for any particular volume of tissue is not substantially more than that of a single tomogram. However, if fast scanning is to be achieved with present detectors while maintaining the same photon flux, doses of up to 30 rads per slice must be considered in the extreme.

The resolution of current isotope imaging is approximately 2 cm in vivo although tomographic techniques may improve this, while the development of a radiopharmaceutical specific for tumor uptake would substantially improve this resolution. Current resolution of ultrasonic equipment is certainly better than 2 cm and depends upon the degree of focusing and the frequency employed, both of these dependent upon the depth of tissue to be examined. At present, the best resolution in the liver is approximately 3 to 5 mm, although dynamic focusing with an annular array should improve the resolution to 1 mm throughout the entire scan. In comparison with this, the resolution currently available by CT scanners depends upon the inherent tissue contrast, the patient dose that is deemed acceptable, and present computer technology.

Imaging of the liver by radioisotope methods depends upon phagocytic function and this may be impaired by radiotherapy, producing spurious cold areas. The physical processes on which CT and ultrasound scanning of the liver depends have already been discussed. It should be noted, however, that the differences in mechanical properties between the collagen and the surrounding soft tissues are great, so that any pathology involving deposition of collagen will be easily visualized by ultrasound in the reflective mode. In contrast, rather small differences of X-ray absorption occur between different soft tissues necessitating the frequent use of contrast media to image soft tissues. However, when one is mainly interested in the contours of soft tissues, as in radiotherapy planning, CT scanning is ideal.

The potential for real-time scanning largely depends upon the scanning rate, although some information may be obtained by dynamic imaging of the liver during the uptake of radioactive colloids. Using ultrasound scanning, data acquisition is sufficiently rapid to produce 30–40 frames per second so that the real-time imaging of
rapidly moving structures may be achieved [14]. The rather small differences in contrast between various soft tissues in terms of their X-ray absorption effectively precludes real-time scanning by CT without administering huge and totally unacceptable exposures to ionizing radiation using current technology.

The accuracy of these various techniques is still under active evaluation. There is no doubt that the accuracy of isotope examination could be improved, either using the tomographic equipment or by the development of a tumor-specific radiopharmaceutical. The accuracy of ultrasound is in excess of 90% depending upon the pathology. Improved instrumentation and experience in the method should cause a substantial improvement in this accuracy rate. The accuracy of CT scanning of the liver is still being assessed and no large series have yet been recorded. Certainly, inability to recognize varying degrees of cirrhosis is a major disadvantage for the CT technique in the liver.

Since the introduction of CT scanning techniques, the quantitative estimation of specific X-ray absorption numbers has been an important advance towards making a tissue diagnosis. Computation of the X-ray absorption allows cystic consistencies or hematomas to be recognized from other space-occupying lesions with different absorptive properties. In the differential diagnosis of renal masses, it allows confident recognition of cysts from homogeneous tumors. In contrast, isotope examination of the liver using radioactive colloid is completely nonspecific as demonstrated in Fig. 2. The use of another isotope such as $^{67}$Gallium does not improve differentiation between abscesses or tumors. Considerable differential diagnosis can be achieved by ultrasound techniques based purely on the echo amplitude and their spatial distribution. The attenuation through cystic or tumor areas can be assessed from the size of the distal echoes. However, there is much more information in the ultrasound beam than can be analyzed or displayed by present technology. Attenuation could be quantified similarly to CT scanning and could provide more specific information to differentiate between various tissues. Initial investigations and quantitative analyses of the amplitude of the returned echoes have revealed significant differences between normal and pathological states [15,16,17]. More data exists in a returned ultrasound beam in terms of the velocity of propagation, tissue attenuation, phase information, frequency analysis and its angular dependence. This interaction between the tissue and the ultrasound beam, properly analyzed, should give sufficient information to identify a number of different soft tissues. Such analysis will, of course, be expensive and detract from one major advantage of the ultrasound technique, that capital cost is approximately one-tenth that of a CT scanner. This vast differential in capital cost renders simple ultrasound scanners suitable for initial diagnosis and screening at the community hospital level.

In conclusion, CT scanning and ultrasound scanning of the liver result in a similar display of space-occupying masses but with present technology, resolution by ultrasound is better than that obtained on CT scanning. Ultrasound scanning is also capable of displaying a number of pathologies characterized by deposition or replacement of fibrous tissue. Considerable experience is required in the method to obtain maximal accuracy but the lack of ionizing radiation and low cost of the instrumentation should encourage further use of the ultrasound technique in the imaging of the liver. Although the isotope technique can be used to rapidly screen the whole of the liver, both the equivocal results and the need to differentially diagnose the nature of space-occupying lesions require further investigations which can be carried out by ultrasound or by CT scanning.
ADDENDUM

The CT scans shown in this paper were obtained on a first-generation CT scanner, which requires four minutes for data acquisition. In second and third-generation equipment the data acquisition time has been reduced to less than 5 seconds with considerable improvement in resolution due to less biological motion. Tissue discrimination, however, is still limited by the small differences which exist in the X-ray absorption of soft tissues.

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K.J.W. Taylor, M.D., Ph.D.
D. Sullivan, M.D.
J. Simeone, M.D.
A.T. Rosenfield, M.D.

Department of Diagnostic Radiology
Yale University School of Medicine
333 Cedar Street
New Haven, Connecticut 06510