The value of liver scanning

A. L. W. F. EDDLESTON
B.M., M.R.C.P.

A. P. FROST
B.Sc.

ROGER WILLIAMS
M.D., M.R.C.P.

Liver scanning was introduced in 1953 (Stirrett, Yuhl & Libby, 1953) and has been widely used in the diagnosis of liver diseases in recent years. A suitable gamma-emitting isotope is injected intravenously and concentrated within the liver. The organ is then scanned with a collimated scintillation probe and, with the Picker Magnascanner V, the machine most commonly used, the output is presented as either coloured dots on paper or as a photographic record on an X-ray type of film. In this way a picture of the spatial distribution of the isotope within the liver is produced.

$I^{131}$ Rose Bengal was one of the first substances to be used for liver scanning. It is taken up by the hepatocytes and excreted into the bile. The rate of uptake by the liver, clearance from the blood and entry into the intestine are parameters which can be measured and have been used to differentiate cirrhosis from hepatitis and intra-hepatic from extra-hepatic cholestasis (Lum et al., 1959; Garcia et al., 1959). However, when Rose Bengal is used to produce a scan the excretion may add several artefacts. The concentration of isotope within the liver changes during the scan producing an uneven picture; there is excretion into the gall bladder and bowel making delineation of the liver edge difficult and, in patients with severe hepato-cellular damage, uptake may be so poor that a satisfactory scan cannot be obtained. The excreted material accumulates in the rectum and may lead to excessive gonadal irradiation.

Because of these limitations, colloidal materials, which are taken up and retained by Kupffer cells in the liver are more satisfactory. The particle size is usually between 50 and 500 m$\mu$ so that almost all of the injected dose is extracted by the Kupffer cells. The larger particle sizes are cleared almost completely in one passage through the liver allowing the disappearance rate in the peripheral blood to be used to calculate hepatic blood flow (Vetter, Falkner & Neumayer, 1954). Three colloidal materials have been used in scanning. Aggregated albumin labelled with $I^{131}$ gives good results and has been advocated as the agent of choice (McAfee, Ause & Wagner, 1965). However, it is broken down rapidly by the Kupffer cells, and, if the thyroid uptake is blocked, the $I^{131}$ is excreted in the urine. Hence the activity in the liver declines rapidly. Colloidal radioactive gold ($Au^{198}$) is retained in the Kupffer cells and has been used for liver scanning in many centres. Its half life is 2-7 days and it emits both $\gamma$ and $\beta$ rays. Technetium ($Tc^{99m}$) is to be preferred because it has a shorter half-life (6 hr) and emits only $\gamma$ rays. We have used it for liver scanning for 18 months. The short half-life means that fresh preparations are needed each day but the isotope is easily obtained by eluting a column of $Mo^{99}$, its parent isotope, which has a half life of 67 hr. $Mo^{99}$ columns are commercially available from the Radiochemical Centre at Amersham and one 25-mCi column per week ensures continuous supplies of $Tc^{99m}$. The isotope is eluted in saline as the pertechnetate and can be transformed relatively easily, in about 1 1/2 hr, into a sulphated colloid which is ready for injection. One millicurie may be given enabling high count rates to be obtained and thus faster scanning speeds and better collimation. The radiation dose to the patient from such a quantity is small, less than that received during a conventional barium meal examination.

The position of the costal margin, the lower edge of the liver when palpable and the outline of any palpable masses are marked on the scan. In a normal scan the activity is almost all confined to the liver, although a small amount may be present in the spleen. The maximum liver activity is over the right lobe and there are no areas of markedly decreased activity within the liver. Marked variations may occur in liver shape, as described by McAfee et al. (1965) (Fig. 1). We have found that impressions on the lower edge of the liver produced by kidney or gall bladder create difficulties in interpretation.

The scan can be superimposed on an abdominal radiograph and the relation of the liver to surrounding structures can be visualized. A marked discrepancy between the upper edge of the liver and the right hemidiaphragm with displacement of the
liver downwards has been observed in the presence of a subphrenic abscess (Bodon & Holzwesser, 1964). Extrinsic masses may be seen to be compressing or indenting the liver (O’Donnell, 1963). The upper edge of the liver may be low but have a normal relationship to a low diaphragm in cases of emphysema. Fig. 2 is a scan from such a case and it can be seen that the upper edge of the liver is almost level with the xiphisternum. The lower edge of the liver may be easily palpable in these cases and the scan often helps to underline the dictum that not all palpable livers are enlarged. The liver scan can be of great help in elucidating the nature of masses in the upper abdomen. It is surprising how many times confusion arises in clinical practice. We have seen two patients with all the clinical signs of hepatomegaly where the scan was normal and where enlarged para-aortic glands were later demonstrated by lymphangiography.

Early reports of the value of liver scanning concentrated on the detection of space-occupying lesions within the liver (Bonte et al., 1962; Nagler, Bender & Blau, 1963). Any part of the liver which is devoid of Kupffer cells will be revealed on scanning as an area of diminished activity if it is large enough to be detected by the collimated scintillation probe. Two points follow from this: first that the nature of the abnormal area (abscess, neoplasm, cyst, haematomata or haemangioma) will not be apparent from the scan and second that small abnormal areas will not be detected. Although the choice of collimator, scan-speed and time-constant are important factors, it can be shown using models (Friedell, MacIntyre & Rejali, 1957; Wagner, McAfee & Mozley, 1961) that spherical defects 2–2.5 cm in diameter are the smallest lesions which can be detected in a thickness of 10 cm of surrounding isotope. If the thickness is reduced to 5 cm, defects down to 1.5 cm in diameter can be seen. How important are these figures clinically? In a post-mortem study of hepatic metastases by Ozarda & Pickren (1962), it was found that in 41% the maximum diameter of metastatic lesions was less than 2 cm. Not all these cases would have produced a normal scan as some lesions may overlap when seen in the AP projection and thus appear to act as one larger lesion. However, a significant proportion of metastatic lesions are likely to be undetectable by present-day scanning techniques. Conn & Elkington (1968) reviewing reports of liver scanning found that the presence of hepatic neoplasm, confirmed by needle biopsy, exploratory laparotomy or autopsy was associated with positive hepatic scans in 72–90% of 827 patients. They make the point that no study has been reported comparing scans taken just before death and the appearances of the liver at autopsy. Large areas of liver with low activity can be seen in Fig. 3 from a patient with
metastases. An epigastric approach to the biopsy may well have allowed a histological diagnosis of malignancy to be made and even given guidance as to the likely primary site. The nature of filling defects cannot be discerned from the scan alone, so if doubt exists further investigations must be performed before biopsy is attempted to avoid needling hydatid cysts or haemangiomata. Serial scans are useful in providing an objective assessment of the results of chemotherapy in both neoplasia and hepatic abscess, whether pyogenic or amoebic.

In recent years the value of liver scanning in patients with chronic hepato-cellular disease has been emphasized (Christie et al., 1963). In cirrhosis (Fig. 5) the findings are often characteristic. The uptake of colloid by the liver is reduced and the scan image has a patchy appearance. When the count rate over the liver is low and the scan is made at the same speed and with the same time-constant, statistical fluctuations in the count-rate can be of such magnitude that they can be seen as rapid changes in colour or density on the scan. This is the most likely cause of the patchy appearance of the scan-image in diffuse hepato-cellular disease as the peak count-rate over the liver is almost always reduced. The patchy appearance is unlikely to be a true reflection of the disordered anatomy as the areas of colour or density change are much smaller than the lower limit of the resolving power of the collimator and if the scan is repeated at a slower speed and with a longer time-constant the patchy

---

FIG. 3. Photo-dot liver scan in a patient with primary adrenal carcinoma and suspected hepatic metastases. There are many large areas of liver with low activity.

FIG. 4. Photo-dot liver scan in a patient with rectal carcinoma. There are several small areas of liver with low activity. The filling defect in the epigastric region is 3 cm in diameter.

FIG. 5. Photo-dot liver scan in a patient with primary biliary cirrhosis. The liver is enlarged and the scan image has a patchy appearance. The spleen is also enlarged and splenic activity is markedly increased, indicating a large porto-systemic collateral circulation.
appearance is no longer seen. In some cases of cirrhosis there is hepatomegaly but in others the liver size is diminished. The decrease in size may be uniform or there may be predominant atrophy of the right lobe. The activity is often perihilar in distribution.

Splenic uptake is often increased in the presence of cirrhosis and may exceed liver uptake while in some cases significant activity is present in the reticulo-endothelial cells in the bone marrow. The reduced hepatic activity and increased splenic and bone marrow activity is probably due to decreased hepatic blood flow and reduced hepatic clearance of colloid from the blood allowing more time for uptake by reticulo-endothelial cells elsewhere. The number and nature of reticulo-endothelial cells within the liver and spleen may also be altered in cirrhosis. If effective hepatic blood flow is reduced by the presence of collateral porto-systemic channels, whether they are intra- or extra-hepatic, splenic uptake would be expected to be particularly high and the degree of splenic activity does in fact correlate well with the degree of abnormality of the ammonia tolerance test (Castell & Johnson, 1966), a known index of collateral circulation. Although it is possible on the above criteria to make a fairly definite diagnosis of cirrhosis from the liver scan, both bilharzia (Mustafa et al., 1966) and sarcoidosis (McAfee et al., 1965) have been noted as producing a high splenic uptake and we have seen a case of Gaucher's disease where liver activity was reduced and splenic activity was equal to liver activity. The hepatic extraction ratio was markedly reduced in this case, although collateral channels were not present, and it is possible that the Kupffer cells, which were affected by the abnormal storage process, functioned poorly. Recently we have shown that the ratio of splenic to hepatic activity correlates well with the ratio of splenic to hepatic blood-flow in patients who have no porto-systemic anastomoses (Eddleston et al., 1969).

A problem in the interpretation of the liver scan in cirrhosis is the presence, in several cases, of large filling defects, not due to a hepatoma. We have seen two cases recently which illustrate this point:

O.S. was a West Indian man with biopsy changes of an active cirrhosis. One of his early liver scans is shown in Fig. 6. A large central filling defect can be seen together with changes typical of cirrhosis; patchy appearance; atrophic right lobe; perihilar distribution of activity and intense splenic activity. The scan was repeated after 1 month and was unchanged. Arteriogram showed no evidence of hepatoma or metastasis and when the scan was repeated 6 months later, the filling defect had virtually disappeared (Fig. 7). Four months later he died and no evidence of metastatic deposits or hepatoma could be found at autopsy.

E.B. was a patient with alcoholic cirrhosis who was admitted with ascites. Her liver scan on admission (Fig. 8) showed hepatomegaly with a patchy appearance over the liver and intense splenic activity over the enlarged spleen. There was a large area of

FIG. 6. Photo-dot liver scan in a patient (O.S.) with active cirrhosis. The liver is reduced in size and there is atrophy of the right lobe, the appearance is patchy, there is perihilar distribution of activity and intense splenic uptake. A large central filling defect was thought to be a hepatoma.

FIG. 7. Photo-dot liver scan in the same patient as Fig. 6 taken 6 months later. The central filling defect is much smaller.
Fig. 8. Photo-dot liver scan in a patient (E.B.) with alcoholic cirrhosis. The liver is enlarged and the scan image is patchy. There is intense activity over the enlarged spleen. The filling defect in the upper part of the right lobe of the liver is suggestive of a space-occupying lesion, but no evidence of this could be found at post-mortem examination.

Fig. 9. Photo-dot liver scan in a patient with Budd-Chiari syndrome. Most areas of the liver show diminished activity except for an area near the midline which may represent uptake by the caudate lobe. Splenic activity is increased.
reduced activity in the upper part of the right lobe of the liver. Biopsy showed no evidence of a hepatoma. The scan was repeated 2 and 5 months later and the filling defect showed some decrease in size. The patient died 8 months after admission and no evidence of hepatoma or other lesion which could be responsible for the filling defect was found at post-mortem examination.

The problem of localized filling defects in liver scans in cirrhosis has not been stressed in the literature although McAfee et al. (1965) mention that autoradiographs of the liver, in some cases of advanced cirrhosis, have shown ‘anatomical’ filling defects, or areas of non-function from localized scarring or infarction, and Johnson & Sweeney (1967) have reported a small series of patients with false positive hepatic scans all of whom had cirrhosis.

In the Budd–Chiari syndrome (Fig. 9) the liver scan is strikingly abnormal and can be diagnostic. Most areas of the liver show diminished activity, except for an area near the midline which may represent uptake by the caudate lobe as it has been demonstrated that the veins draining this lobe are not involved until late in the disease (Hales & Scatllif, 1966). Indeed some cases of this syndrome have been reported where massive hypertrophy of the caudate lobe has occurred. Splenic uptake is again increased, probably because of the impaired liver blood flow.

The applications of hepatic scanning which are useful in clinical medicine may be summarized as follows. It is a valuable method of investigating the nature of upper abdominal masses. It can detect filling defects whether they are neoplasms, cysts, abscesses, haematomas or haemangiomias, although false positive results may be obtained in cirrhosis, and can be used to select a suitable site for liver biopsy. It may confirm the diagnosis of cirrhosis, where biopsy may not always be possible. It is often diagnostic in Budd–Chiari syndrome and it is a useful objective assessment of progress in cases of neoplasm or abscess.

Acknowledgment

We wish to thank the British Empire Cancer Campaign for the generous grant which was used to purchase the Picker Magnascanner V.

References


