Radioisotope colour scanning of the liver in the diagnosis of liver disease

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INTRODUCTION

SINCE THE INTRODUCTION of Scintillation Scanning of the liver by Stirret and his co-workers in 1953, there have been numerous reports of the uses of this new technique in investigating liver diseases. Stirret had originally used RHISA labelled with 1131 and showed that there was increased uptake over space-occupying lesions of the liver. Modern techniques involve the use of two groups of radiopharmaceuticals in both of which the lesions appear as cold areas. Stirret's original technique, using RHISA, has been given up but it is, of course, attractive in its positive rather than negative approach to the detection of liver abnormalities. However, the use of Molybdenum 99 (Sorensen 1963) is a return to this approach.

131 I Rose Bengal introduced by Friedel 1957 belongs to the group which depends on concentration and excretion by the hepatic cells. Its advantage is that the biliary excretion is monitored, and this enables detection of obstructive lesions of the biliary passages. However, the heavy concentration in the gall bladder of the agent and the rapid changes in the liver concentration make scanning difficult.

The second group of radiopharmaceuticals used in the investigation of liver conditions are the colloidal agents – 198 Au, 99m Tc – S Colloid, Albumin labelled with 1^{131} and lately Indium 113m, introduced by Goodwin in 1966.

The colloidal agents depend on the uptake by the Kupffer cells and are not excreted via the biliary passages. 99m Tc – S colloid is, perhaps, one of the best agents available today because of its favourable low energy gamma emission which enables favourable scanning and also because of its low radiation burden on the liver due to its short half-life of six hours.

In this series, 198 Au Colloid was used for scanning because of its easy availability and cheapness. The colour scanning technique first introduced by Mallard and Peachey in 1959 was used and it appears to have certain advantages over the photoscanning technique (Baum 1966). There have been several reviews of the place of liver scintillation scanning in diagnosis. Nagler, Blau and Bender reviewed 950 scans of patients with known cancer and compared the results with operation or autopsy findings. Positive scans were 83% correct and negative scans 88% correct. They had used 1^{131} Rose Bengal Gollins. Sima and Cameron (1964) found only three false positive scans among 129 abnormals they studied. Baum (1967) used the colour scanning technique in detecting hepatic metastases and concluded that the scan was more accurate than conventional tests in excluding liver metastases, only one false negative in 70 scans.

INDICATIONS FOR LIVER SCAN

1. Abdominal mass – enlarged liver.
2. Obstructive jaundice.
3. Detection of secondaries.
4. Assessing operability of primary hepatoma.
5. Cirrhosis of liver.
6. Regeneration of liver.
7. Trauma.
8. Response to therapy.
9. Amoebiasis, hydatidcysts.
10. Children-malrotation and other abnormalities of GI tract. Congenital heart disease situs inversus.

During the past nine months in which we acquired a scanner in this department, 91 patients were scanned for suspected liver diseases. The scan findings were correlated with clinical, biochemical, conventional radiological, operative and biopsy findings. In all, 55 had definite findings, at surgery, biopsy or autopsy and an attempt was made to classify the scan findings in each condition.

METHOD AND MATERIALS

Without previous preparation, each patient received 150 microcuries of Colloidal Au 198, I/V. Liver scans were done one hour after this. The scanner used had a 5-inch Th-activated Sodium iodide crystal, a coarse focusing collimator was used, placing the probe 1 cm from the skin surface. The colour calibration was adjusted so that the area of maximum activity produced a red colour on the scan. Other factors such as speed, spacing, tapping factor, and time constant were varied according to the maximum count rate. The scan speed varied from 48 to 72 cm/min. All patients were scanned in the supine position and, in addition, a lateral scan was done when indicated. After completion, the xiphisternum, costal cartilages, liver edge, spleen and other palpable masses were marked on the scan. The procedure took one hour in all. All scans were interpreted prior to the establishment of a diagnosis and a report given.

DETAILS OF SCAN REVIEW

Hepatoma	17
Secondaries	15
Cirrhosis	9
Abscess	16
Regenerative studies	7
Obstructive jaundice	6
Normal scans	11
Polycystic disease	1
Reticulosis	1
Total done	91
Number verified PM, Biopsy, OP	55
Diagnosis wrong	4
False positive	2

RESULTS

55 of the 91 patients scanned had operations or biopsy or both in most. There were only 11 normal scans and all the rest were reported as abnormal. Diagnostic accuracy of the scan – all 11 normal scans were subsequently confirmed – clinically six and biopsy and operation five.

Of the remaining 80 cases, the diagnosis was wrong in four. As will be explained in the discussion, in all these four instances, there was indeed a space-occupying lesion at surgery but where an abscess was diagnosed in one case, a large hepatoma was found at surgery. In another instance, an abscess was detected at operation where the scan was interpreted as suggestive of hepatoma. The remaining two were cases where primary and secondary malignancy were confused. It is clear that although the scan may give clues as to the nature of the lesion, it does not warrant a pathological diagnosis. False positives were seen in two cases. One of these was a patient with cirrhosis; this will be discussed below. An accuracy of 85% in this group is similar to those reported by others (Nagler et al, Gollins et al).

Correlation with other tests

In all cases, a clinical examination, liver function tests and routine X-rays were done. Only 40% of cases with metastases had an elevated alkaline phosphatase. This contrasts sharply with recent studies (Smith & Williams 1968). The latter concluded that the alkaline phosphatase predicts a space-occupying lesion better than the scan in a study involving 296 patients. However, Baum (1967) had a similar finding (38% with raised alkaline phosphatase in liver metastases). The majority of cases detected of primary hepatomas were fairly advanced and clinically obvious but a few were detected only because of the scan. Further, cases of abdominal masses were correctly diagnosed as extra hepatic purely on the basis of the scan.

CIRRHOSIS

SCAN IN CIRRHOSIS

Total number done	9
History of alcoholism	2
Abnormal LFT	A11
Raised – enzymes (done in 5 cases)	3

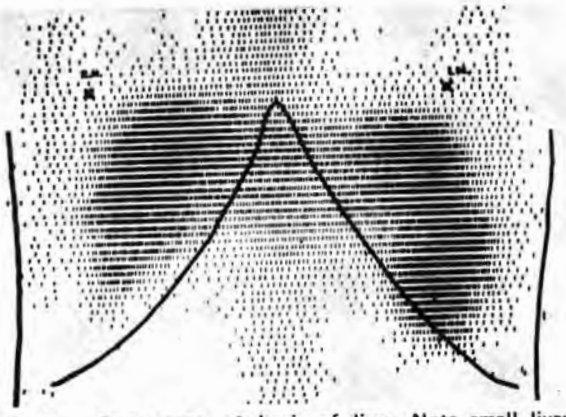

Fig. 1: Cryptogenic cirrhosis of liver. Note small liver, irregular activity over the liver, splenomegaly and marrow uptake.

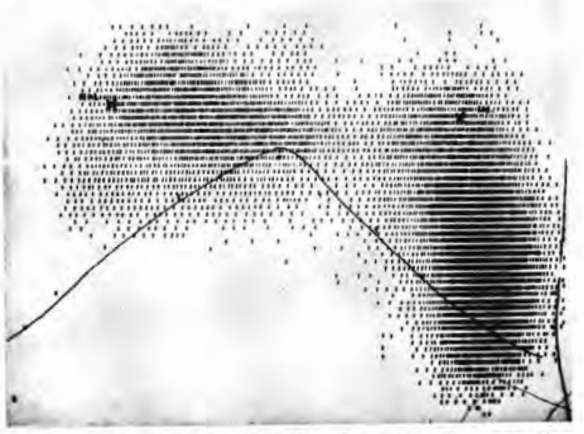

Fig. 2: Cryptogenic cirrhosis with portal hypertension. Marked reduction in liver activity.

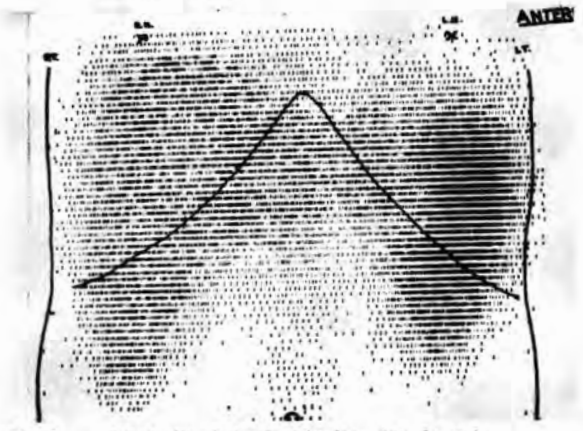

Fig. 3: Alcoholic cirrhosis. The liver is enlarged.

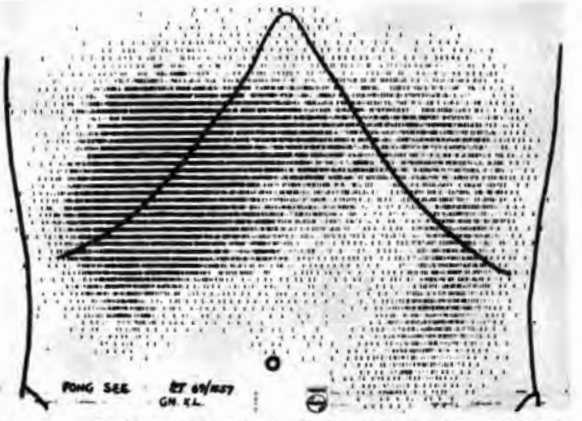

Fig. 4: Solitary cold area in cirrhotic liver. Non-malignant on biopsy. This is an example of false + ive finding in cirrhosis.

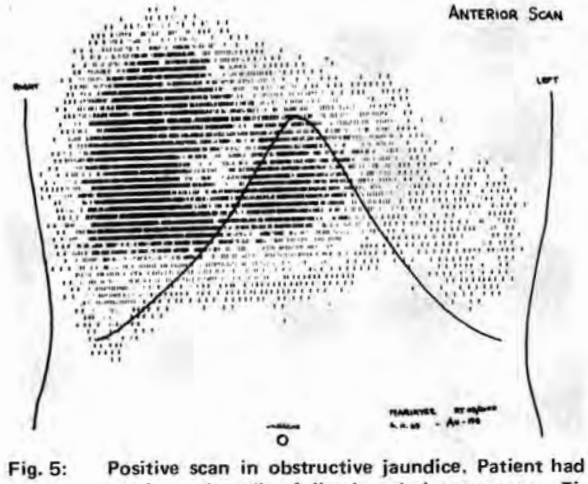

Fig. 5: Positive scan in obstructive jaundice. Patient had persistent jaundice following cholecystectomy. Final diagnosis – primary hepatoma.

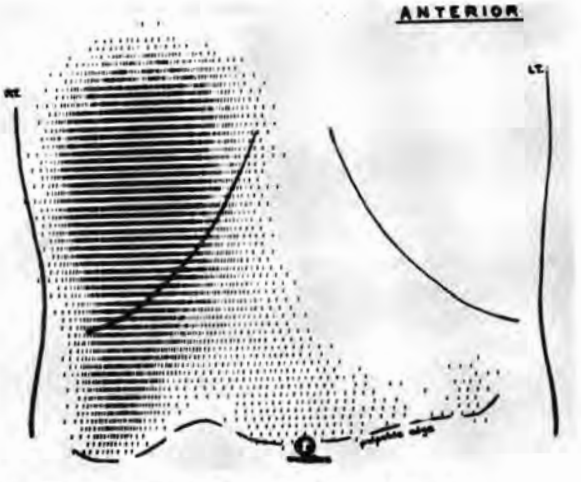

Fig. 6: Amoebic abscess of left lobe of the liver.

SCAN FINDINGS

	Non-Alcoholic	Alcoholic
Size of liver	Small 4 Enlarged 1	Enlarged 2
Left lobe	Enlarged 4	Normal
Spleen enlarged	6 cases	2 cases
Diffuse changes including mottling	7 cases	2 cases
Marrow uptake	5 cases	2 cases
Cold areas	None	1 case

There were nine cases of cirrhosis; 3 cases showed an enlarged liver in the scan, one showed a normal liver, and the remainder all had grossly reduced liver outlines. The size of the liver was related to the history of alcoholism. In all three, the liver was not palpable clinically. (McAfee et al 1965 – liver enlargement in the majority of their cirrhotics).

There was splenomegaly in eight cases, and in all the nine cases, a patchy activity in the scan was noted. There appeared to be no correlation between the liver function tests and severity of these findings. Focal change, suggestive of a space-occupying lesion, was seen and reported in one case which at operation was not confirmed.

PRIMARY HEPATOMA

SCAN IN PRIMARY HEPATOMA

Total number done	17 cases
Number with hepatomegaly	17 cases
Number with abnormal liver function tests	14 cases
Scan Findings	
Liver enlargement	15 cases
Liver edge does not correspond to scan margin	8 cases
Cold lesions	All 17 cases
Diffuse changes	7 cases
Splenomegaly	3 cases

All the 17 cases scanned showed gross hepatomegaly. Often the enlargement involved the unaffected part of the liver. A striking finding was the disparity between the liver scan edge and the palpable liver edge. It is quite clear that hepatic metastases can produce a scan appearance of large SOL exactly like a hepatoma. One case was missed at peritoneoscopy, and here the scan showed a large cold zone occupying the posterior part of the liver, only seen in the lateral view. 90% of hepatomas at operation proved to have co-existent cirrhosis. However, it was not easy to detect the diffuse changes seen in cirrhosis in the scan – this might be one means of distinguishing hepatomas from other SOL of the liver, like abscesses. Splenomegaly was seen in only three of these 17 scans. One of the cases with splenomegaly, and diffuse changes suggestive of cirrhosis in the presence of a large SOL was reported as a hepatoma on this reasoning but it turned out to be an abscess at surgery.

AMOEBIC ABSCESS

SCAN IN AMOEBIC ABSCESS OF LIVER

Total number of cases scanned		16
Hepatomegaly		12
Cold Areas:	Solitary	10
	Multiple	1
	Involving whole lobe	2
Diffuse changes		1
Normal scan		1
Hilar cold area		1

Sixteen cases of amoebic abscesses were scanned. Definite cold areas corresponding to the lesions were identified in ten of them. All ten were confirmed at surgery. In one case, there were two abscesses in the scan although only one was identified at surgery. It is possible the cold area is merely an area of necrosis or fatty change. There was marked hepatomegaly in all ten, and involved both lobes. A normal scan was seen in two cases clinically diagnosed and treated as amoebic hepatitis. Diffuse changes in the liver scan, such as in cirrhosis, was seen in only one case. The unaffected areas of the liver showed very uniform appearance in the scan. This makes us feel that the disease occurs in an essentially normal liver and is a localised suppurative process. Further studies are being carried out to test this theory.

The majority of cases had an alcoholic history. Normal scans were seen in two cases and hepatomegaly without focal change in two others; these four cases might constitute the group of so-called amoebic hepatitis. However, small focal lesions less than 2 cms. in diameter could be missed in the scan. Multiple views might have helped to locate them.

The problem of cold areas in the hilar region in liver scans of patients with obstructive jaundice has been well described by Morris, McRae et al (1965). In six cases of obstructive jaundice scanned, the diagnosis was fairly clear from the scan appearances. In three of the cases, there were extensive cold areas near the hilar area also extending into the rest of the lobe. All three were found at surgery to be primary hepatoma involving the hilar region and bile ducts. In one case, there were minimal changes in the hilar area associated with diffuse changes over the rest of the liver. This case was diagnosed correctly as diffuse

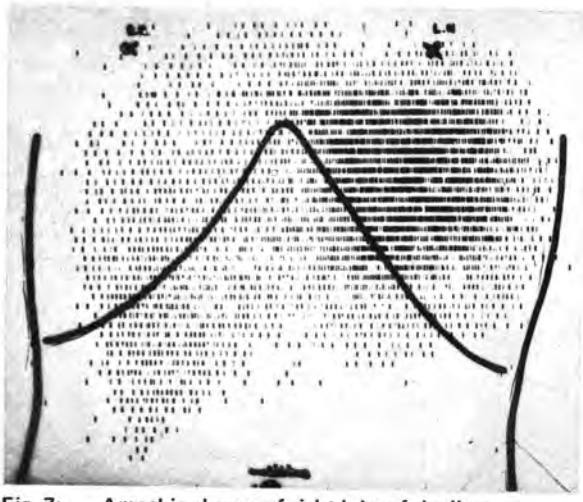

Fig. 7: Amoebic abscess of right lobe of the liver.

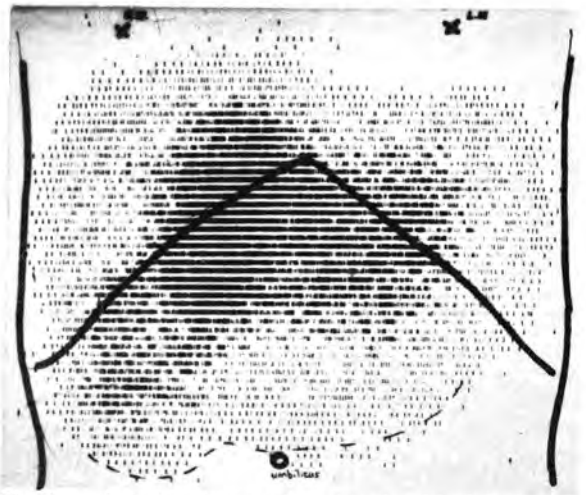

Fig. 8: Amoebic abscess situated in the right lobe laterally. Scan suggests diffuse involvement of the liver as well. This is usual.

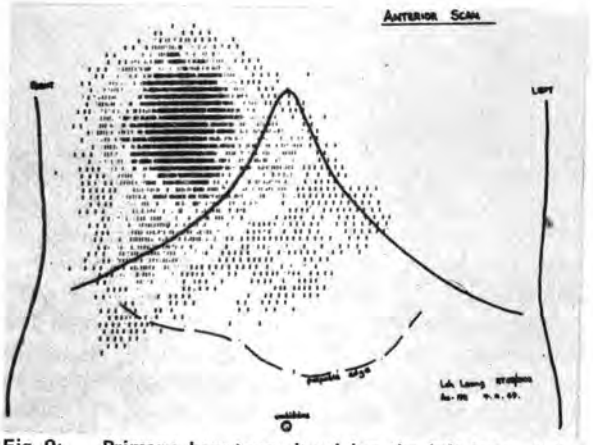

Fig. 9: Primary hepatoma involving the left lobe of the liver. Note disparity between scan edge and palpable edge of the liver.

Fig. 10. Primary hepatoma involving the right lobe of the liver.

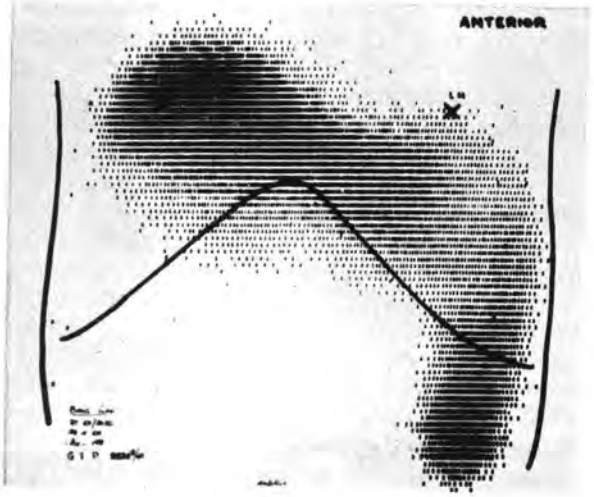

Fig. 11: Primary hepatoma involving the right lobe of the liver arising in a cirrhotic liver. Note splenomegaly. This is a common association.

OBSTRUCTIVE JAUNDICE

DETAILS OF PATIENTS SCANNED FOR OBSTRUCTIVE JAUNDICE

		Case					
Total number done	6 cases	1	2	3	4	5	6
Clinical features	Hepatomegaly	–	–	–	+	+	+
	Splenomegaly	–	–	–	–	–	–
	Duration of jaundice	2M	2Wk	1M	2M	1M	3M
Scan features	Hepatomegaly	+	+	+	+	+	+
	Solitary cold area	–	–	+	+	+	+
	Multiple cold areas	+	–	–	–	–	–
	Splenic uptake	–	–	–	–	–	–
	Hilar cold area	+	+	+	–	–	–
	Diffuse changes	–	+	–	–	–	–
Final diagnosis	Secondaries in liver	+	–	–	–	–	–
	Primary hepatoma	–	–	+	+	+	–
	Diffuse hepatitis	–	+	–	–	–	–*

*Case 6: diagnosis not known even after laparatomy

hepatic disease – hepatitis – and was confirmed. In one patient, the operation finding did not reveal a cause for the obstructive jaundice. The scan revealed a prominent cold area near the hilum extending into the centre of the liver. This has now been confirmed to be a carcinoma on follow-up.

HEPATIC METASTASES

As already mentioned, 15 patients were correctly diagnosed on scan appearances as having metastases. The diagnosis were often made in the presence of normal liver function tests, and in a few, in the absence of liver enlargement. Scan findings were usually quite characteristic with multiple cold areas in the liver; however, cases of multicentric hepatoma gave the same picture. Also, large cold areas in the liver similar to findings in hepatoma were seen in secondaries in one case.

DISCUSSION

It is obvious there is much to be achieved in diagnostic accuracy in scintillation scanning of the liver. The scan is fairly reliable in diagnosing the presence or absence of space-occupying lesions of the liver, in detecting the size and shape of the liver, in diagnosing displacement of the liver, and in detecting diffuse hepatic diseases. However, it does not give a pathological diagnosis. Krael, Jones et al have compared scintillation scanning of the liver with hepatic arteriography and have concluded that both methods can detect space-occupying lesions of the liver but the angiographic technique is able to distinguish malignant tumours from cysts and demonstrate lesions less than 2 cms.

Both procedures can give false positives and the value of each is enhanced by doing both. A space-occupying lesion less than 2 cms. is unlikely to give rise to much by way of symptoms and in clinical practice, by the time a patient has symptoms, space-occupying lesions, such as hepatomas, are easily demonstrable on the scan. As far as conventional tests, such as alkaline phosphatase, to detect space-occupying lesions are concerned, it must be pointed out that these are not comparable. It has never been proved that hepatic metastases, for example, produce excessive alkaline phosphatase. In some reports, the alkaline phosphatase has been shown to be elevated early but in this series, 40% of metastases occurred in the presence of an elevated alkaline phosphatase.

It is interesting to consider the findings in cirrhosis. Much of the patchy activity and false positives seen are due to poor statistics as a result of low activity in the liver. Klion, Nagler, Bender et al have shown that false positive scans are common. The Kupffer cells, which are responsible for the uptake of colloidal agents that are used, actually increased instead of being decreased in cirrhosis. Further, the actual amount of colloid used is 2500 times less than

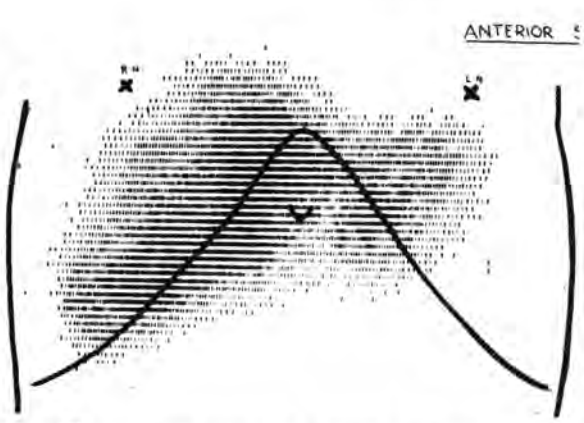

Fig. 12: Scan of a patient with primary hepatoma.

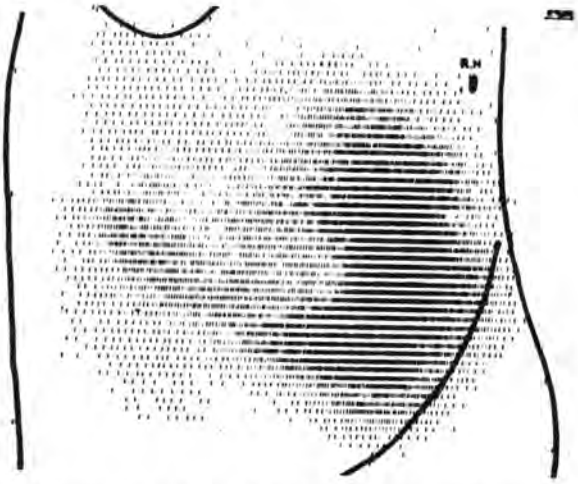

Fig. 13: Lateral view in the above patient clearly localises the growth posteriorly and superiorly – importance of lateral views.

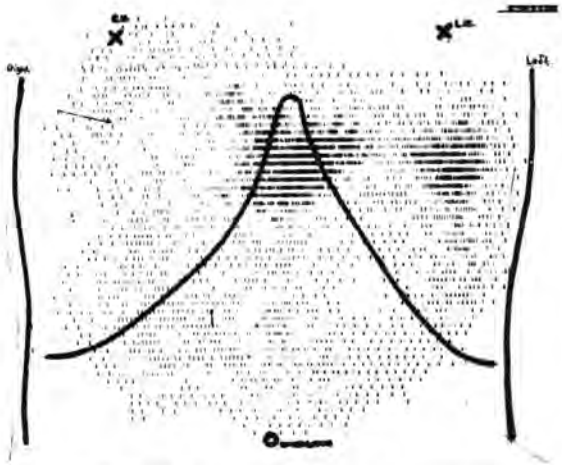

Fig. 14: Secondaries in the liver from a nasopharyngeal carcinoma. Note picture of multiple cold areas.

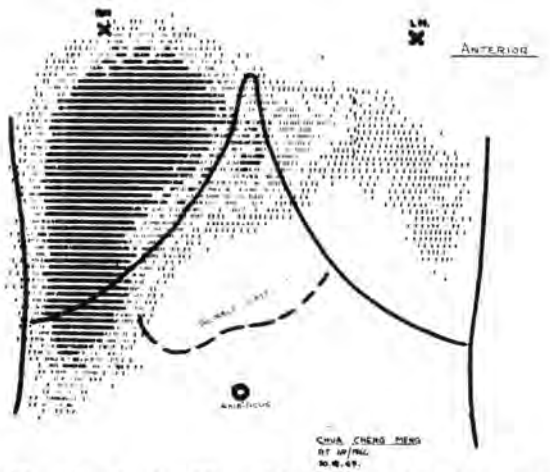

Fig. 15: Scan in the differential diagnosis of an abdominal mass. Lesion here is a carcinoma of the stomach and the scan clearly shows that it is extra-hepatic.

the liver's capacity. So it is quite clear that the poor hepatic uptake in cirrhosis is due to other factors such as blood supply. This explains the absence of a clear correlation between liver function tests and the scan appearance.

Better counting statistics, using newer radiopharmaceuticals, better instrumentation, use of blood pool studies, etc., may lead to a clearer evaluation of the problem of cirrhosis. It is difficult to ignore a positive scan in a cirrhotic in view of the incidence of primary hepatoma in relation to cirrhotic livers.

CONCLUSION

1. 91 Liver scans done in the department were reviewed.
2. All except 11 showed abnormalities.
3. A diagnostic accuracy of over 85% was obtained.
4. The scan in the investigation of hepatoma, cirrhosis, abscesses, secondaries in the liver, and in obstructive jaundice was shown to be helpful. The scan often supplied information not available by any other conventional investigations.
5. A general review of the developments in scintil-

lation scanning of the liver and some of the pitfalls of the method is discussed.

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