

Usefulness of Scintillation Camera and ^{131}I -Rose Bengal in Evaluating Liver and Gallbladder Functions

Kanji TORIZUKA*, Ken HAMAMOTO*, Masahiro FUJII*, Toru MORI*
 Rikushi MORITA*, Takao MUKAI*, Tadako KOUSAKA*
 Kenichi ITOH**, Jun NAKAGAWA** and Chisato MINAGUCHI**

Introduction

Liver scanning with ^{131}I -labeled rose bengal has been considered to afford us anatomic as well as physiological information about the liver. Since Taplin and associates (1) introduced ^{131}I -labeled rose bengal for testing liver and biliary tract function by an external scintillation counting method, some attempts have been made to evaluate the sensitivity and reliability of radioisotope hepatic photoscanning (2, 3, 4).

The scintillation camera, invented several years ago by Anger (5), uniquely provides the opportunity to demonstrate in vivo the dynamics of certain biological processes. The scintillation camera has some advantages over conventional mechanical line scanning in that the entire area of interest is examined during the scanning period and one can take a series of pictures in very rapid sequence. Moreover, the multichannel analyzer makes possible the quantitative evaluation of photographs taken with the scintillation camera.

The purpose of this paper is to describe the results of dynamic studies of liver and gallbladder function using a scintillation camera[†] with a 1600 channel analyzer^{††}, and to discuss its usefulness in evaluating diseases of the liver and gallbladder.

Materials and Methods

The subjects of this study were six normal persons, four patients with acute hepatitis, nineteen patients with chronic hepatitis, seven patients with liver cirrhosis, three patients with extrahepatic obstructive jaundice, three patients with space-occupying lesions of the liver and four patients with gallbladder disorders. Patients having no history or evidence of impaired liver function were selected as controls, and for each patient a definitive diagnosis was made by biochemical tests of liver function, liver biopsy or laparotomy.

The location and size of the liver were determined by physical examination, and the patient was positioned so as to place the liver, inferior cardiac blood pool, and intrahepatic area of the abdomen in the field of view of the crystal. One hundred μCi of ^{131}I -rose bengal^{†††} was injected intravenously in all subjects in the fasting state, and the camera was activated. Exposures were made at three-minute intervals for a period of one and a half hours, and the distribution of radioactivity in the liver was accumulated by the 1600 channel analyzer for every five minutes, and was printed out by the high speed printer, successively. From the chronological change of sum of radioactivity in the adjacent 10×3 matrices in the center area of the liver which was printed out from the 1600 channel analyzer, the time lapse before maximum liver uptake of ^{131}I -rose bengal

* The Central Clinical Radioisotope Division

** The Second Division of Internal Medicine
 Kyoto University School of Medicine, Kyoto,
 Japan.

受付: 1970年12月25日

別刷請求先: 京都市左京区聖護院川原町

京大病院 中央放射線部

鳥塚莞爾 (〒 606)

† PHO/GAMMA III, Nuclear Chicago Co.,
 Ill., U. S. A.

†† CDS-1600, Nuclear Chicago Co., Ill., U.S.A.

††† Abbott Laboratories, Ill., U. S. A.

was determined. The time at which ¹³¹I-rose bengal began to appear in the gallbladder or intestine was determined on the serial scintiphotos.

By the use of a ratemeter and recorder connected with a scintillation camera, the chronological changes of all radioactivity below the detector were recorded, as shown in the left part of Fig. 1. At the same time, a scintillation detector with 2" x 2" NaI crystal was placed on the head of the patients, and the rate of decline in blood radioactivity was monitored. If the dynamics of the intravascular ¹³¹I-rose bengal in the liver is considered to be similar to the changes of radioactivity over the head, the difference between the hepatic isotope uptake curve and the isotope concentration curve on the head indicates the extra-vascular hepatic uptake. The chronological changes of the extravascular hepatic uptake were plotted on semilogarithmic paper. As shown in the right part of Fig. 1, this curve reached a plateau 90 minutes after the injection of ¹³¹I-rose bengal. The slope

of the line obtained by subtracting this curve from the plateau line is considered to indicate the uptake rate of ¹³¹I-rose bengal by the whole liver.

In some of these patients, gallbladder function was examined, using egg as a gallbladder constrictor. Ninety minutes after the injection of 30 μCi of ¹³¹I-rose bengal, two eggs were given orally to the patients and the chronological changes of radioactivity in the gallbladder were observed for one hour with the 1600 channel analyzer.

Results

Scintiphotos of liver and gallbladder taken with ¹³¹I-rose bengal in various liver and gallbladder diseases.

Fig. 2 (1) through (6) represent the series of scintiphotos in various liver and gallbladder diseases.

Fig. 2 (1) shows the result in a subject with normal liver function. The maximum hepatic uptake of ¹³¹I-rose bengal was observed at 30 minutes. The

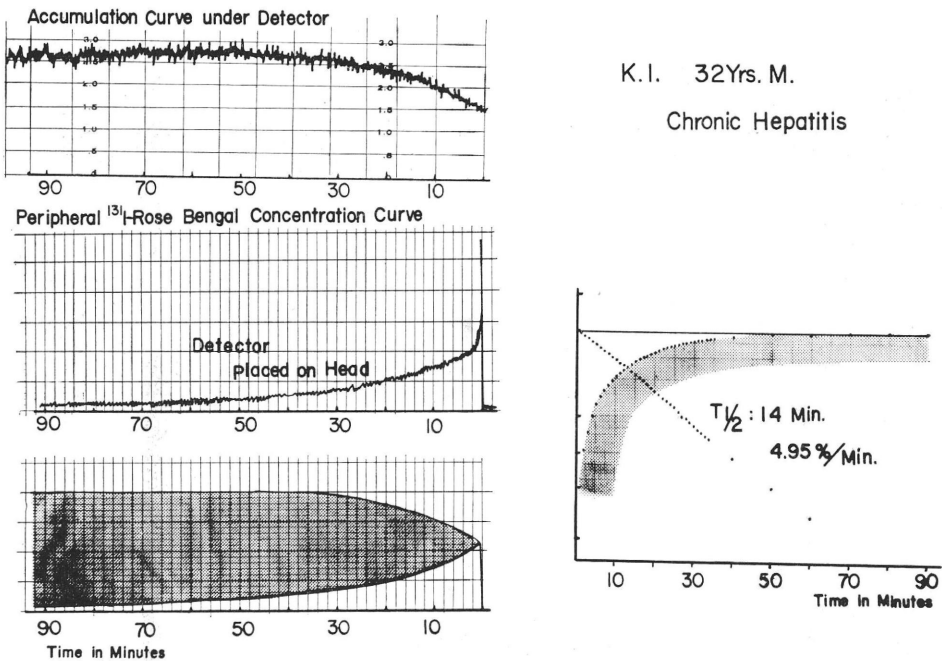
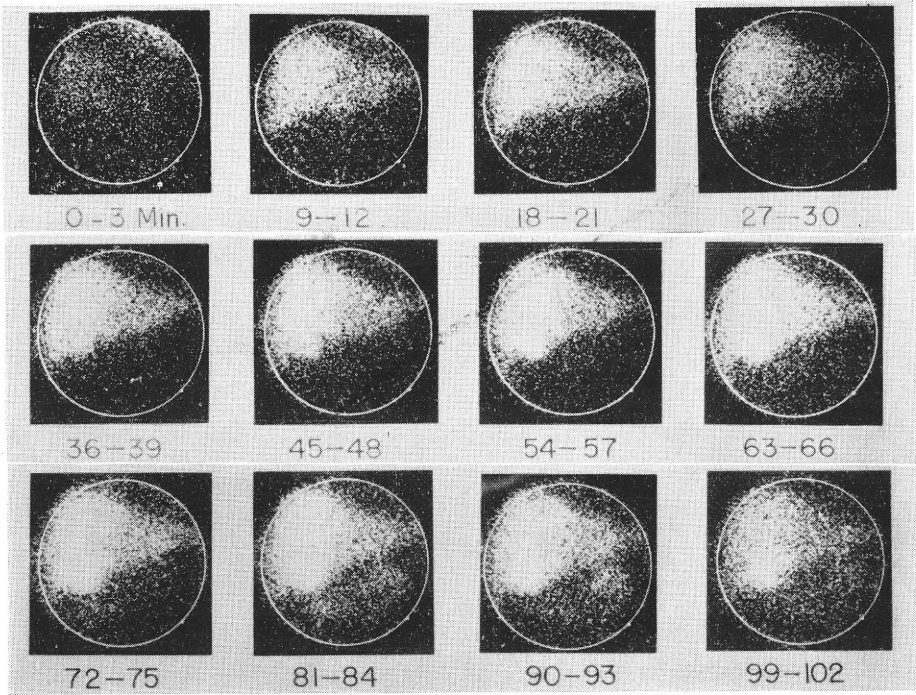
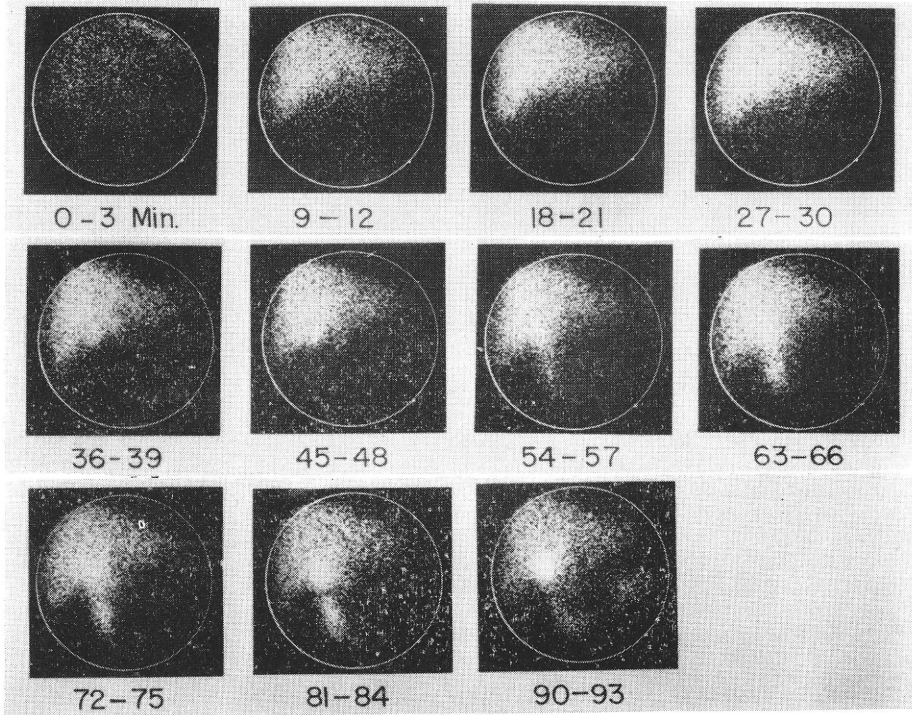


Fig. 1. The calculation of liver ¹³¹I-rose bengal uptake from liver accumulation curve of ¹³¹I-rose bengal below NaI (Tl) crystal of the scinticamera and ¹³¹I-rose bengal concentration curve in peripheral blood monitored with 2" x 2" NaI (Tl) scintillation detector.

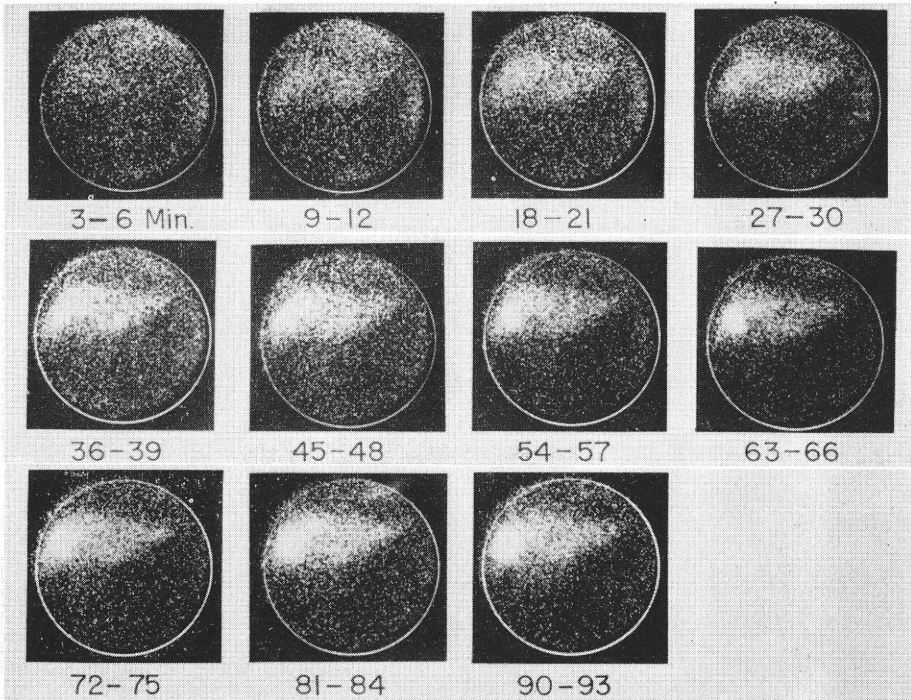


(1) A 35-year-old healthy female.

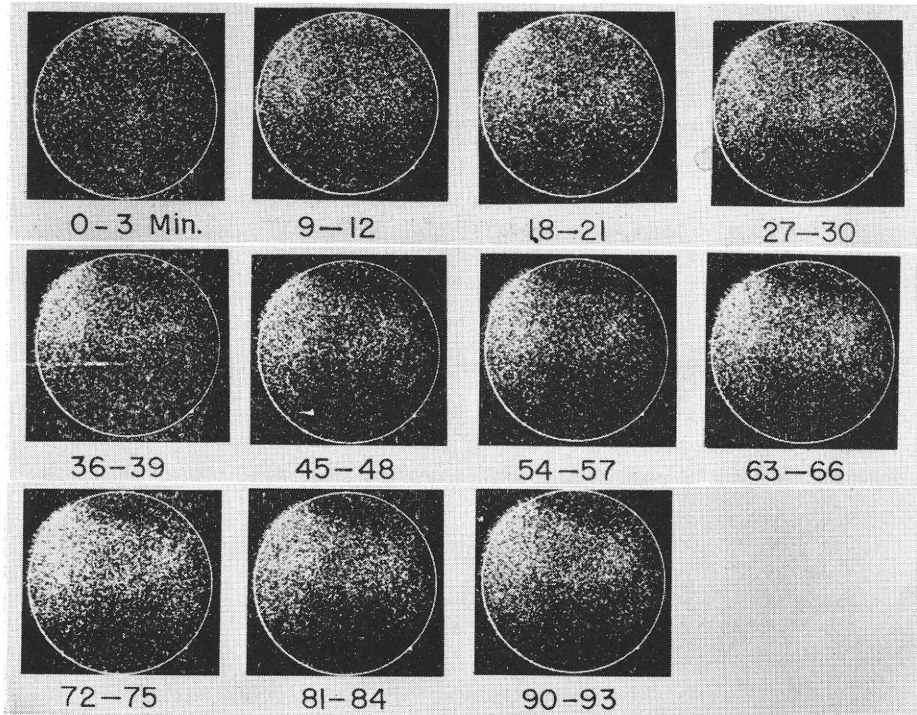


(2) A 44-year-old male with chronic hepatitis.

Fig. 2.

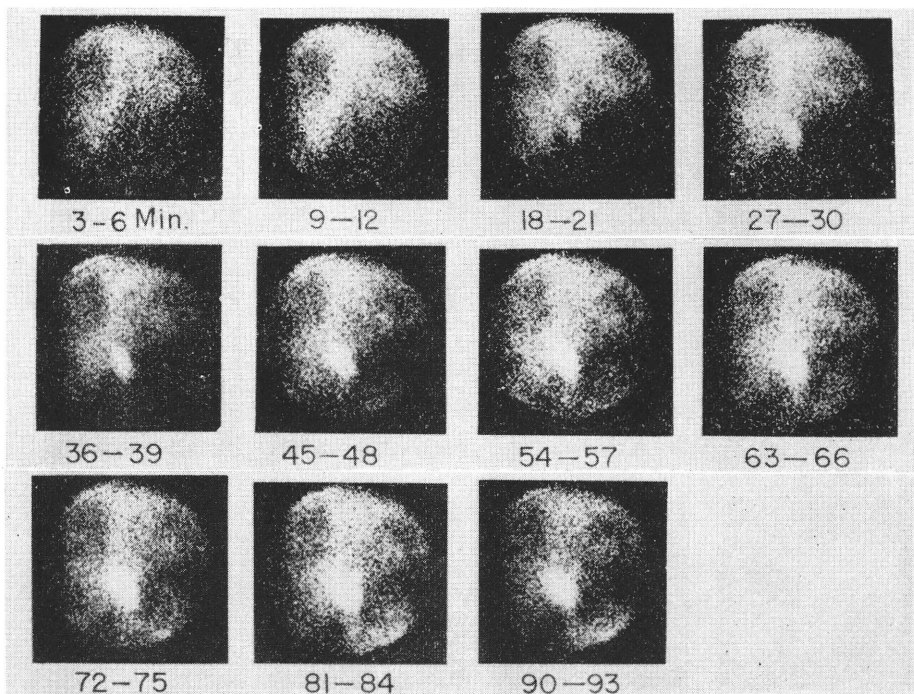


(3) A 34-year-old female with liver cirrhosis.

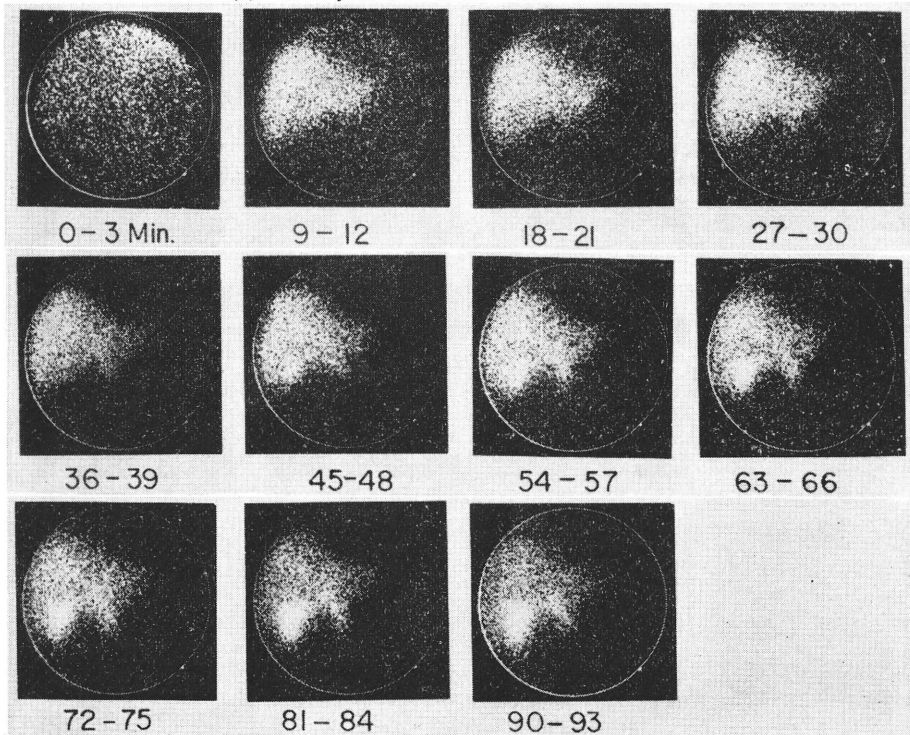


(4) A 60-year-old male with extrahepatic obstructive jaundice.

Fig. 2.



(5) A 61-year-old female with metastatic liver.



(6) A 60-year-old female with cholelithiasis.

Fig. 2. The serial liver scintiphotos after the injection of $100\mu\text{Ci}$ of ^{131}I -rose bengal in various liver and gallbladder diseases.

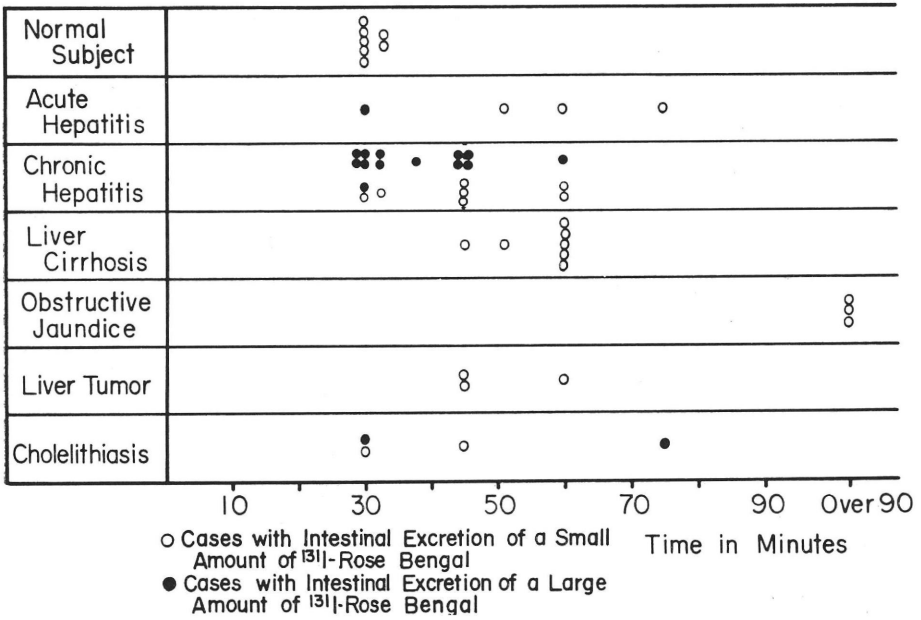


Fig. 3. Time lapse before maximum hepatic uptake of ¹³¹I-rose bengal in various liver and gallbladder diseases.

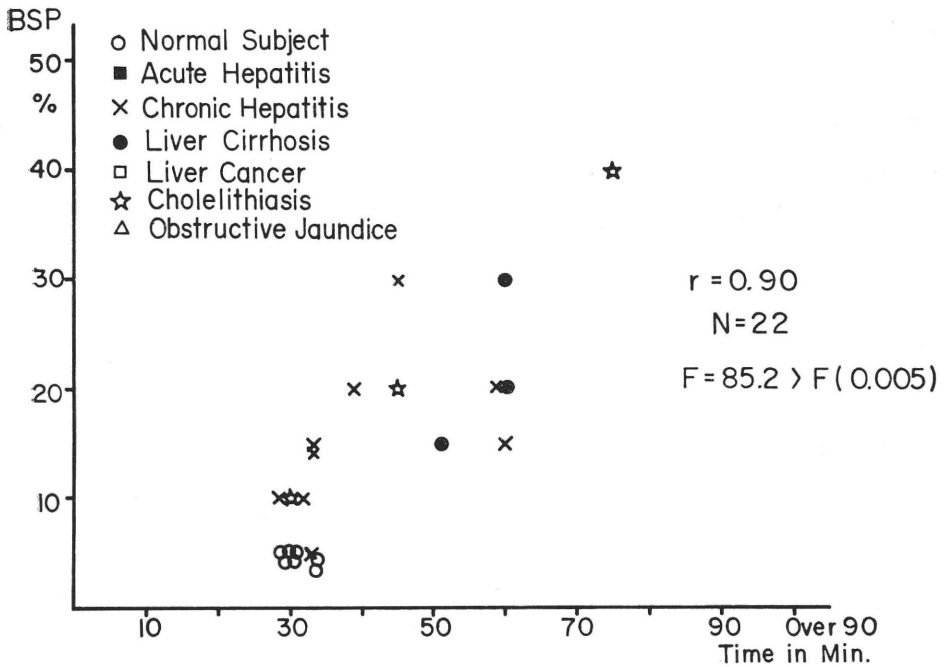


Fig. 4. Correlation between the time lapse before maximum hepatic uptake of ¹³¹I-rose bengal and the Bromsulphalein values at 45 minutes.

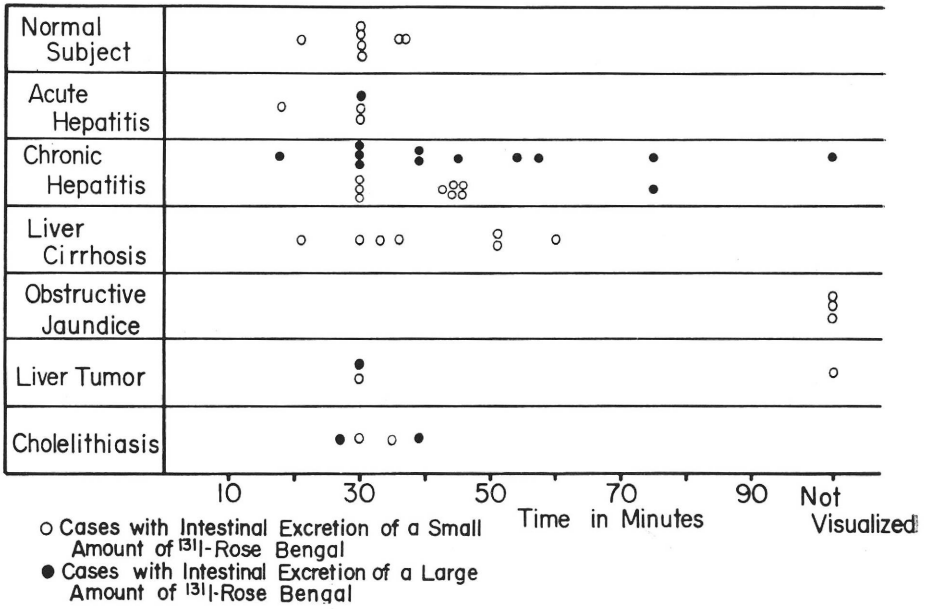


Fig. 5. The appearance time of radioactivity in the gallbladder in various liver and gallbladder diseases.

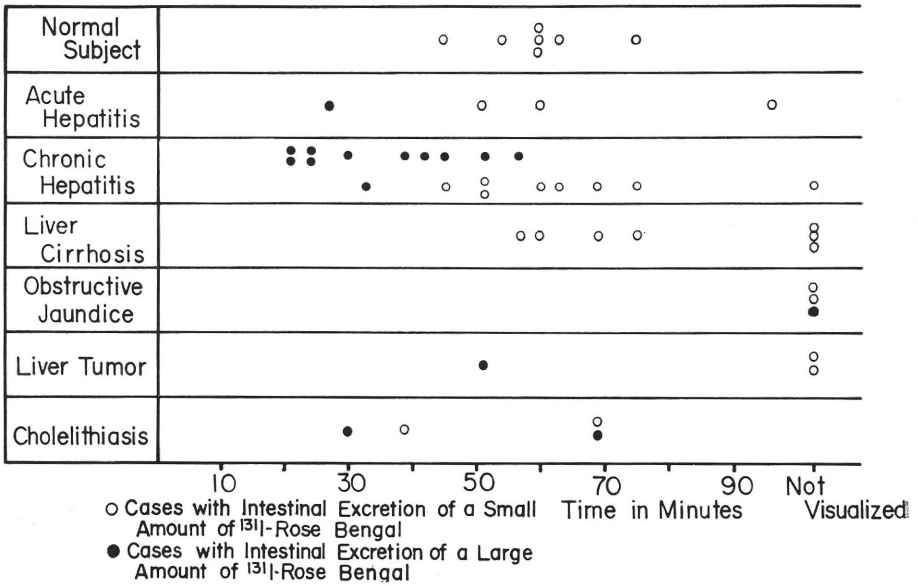


Fig. 6. The appearance time of radioactivity in the intestine in various liver and gallbladder diseases.

radioactivity in the gallbladder appeared at 36 minutes, and the first discernible intestinal excretion of ¹³¹I-rose bengal occurred at 60 minutes.

Fig. 2 (2) and (3) show the results in a patient with chronic hepatitis and liver cirrhosis, respectively. In both cases, the maximum hepatic uptake of ¹³¹I-rose bengal was delayed and prolonged, occurring at 45 and 63 minutes, respectively. In liver cirrhosis, marked deformity of the liver contour was observed. In chronic hepatitis, the excretion of a large amount of ¹³¹I-rose bengal into the bowel was noted. But, in liver cirrhosis, no excretion of radioactivity into the bowel occurred within the test period of 90 minutes. In a patient with complete occlusion of the common bile duct, the hepatic uptake of ¹³¹I-rose bengal increased slowly up to 90 minutes, and no appreciable excretion into the gallbladder or bowel was apparant in 90 minutes, as shown in Fig. 2 (4). Fig. 2 (5) shows the scintiphotos of a patient with metastatic liver cancer. A filling defect in the liver was distinctly shown, and the excretion of a large amount of ¹³¹I-rose bengal into the bowel was noted 45 minutes after injection. In a patient with chol-

elithiasis, dilatation of the bile duct filled with ¹³¹I-rose bengal was observed, as shown in Fig. 2 (6).

Fig. 3 shows the time lapse before maximum hepatic uptake of ¹³¹I-rose bengal in various liver diseases. The maximum hepatic uptake occurred at 30 minutes in normal subjects, at 30-70 minutes in patients with acute hepatitis, at 30-60 minutes, with a mean of 45 minutes, in patients with chronic hepatitis, at 45-60 minutes in patients with liver cirrhosis, at more than 90 minutes in patients with extrahepatic obstructive jaundice, at 45-60 minutes in patients with liver tumor, and at 30-75 minutes in patients with cholelithiasis. As shown in Fig. 4, a good correlation was noted between these times and Bromsulphalein values at 45 minutes (P<0.005).

Fig. 5 and 6 show the appearance time of radioactivity in the gallbladder and intestine in various liver diseases. Radioactivity appeared in the gallbladder in 30 minutes in normal subjects, in 15-30 minutes in patients with acute hepatitis, in 15 over 150 minutes in patients with chronic hepatitis, in 15-60 minutes in patients with liver cirrhosis, in more than 90 minutes in patients with extrahepatic

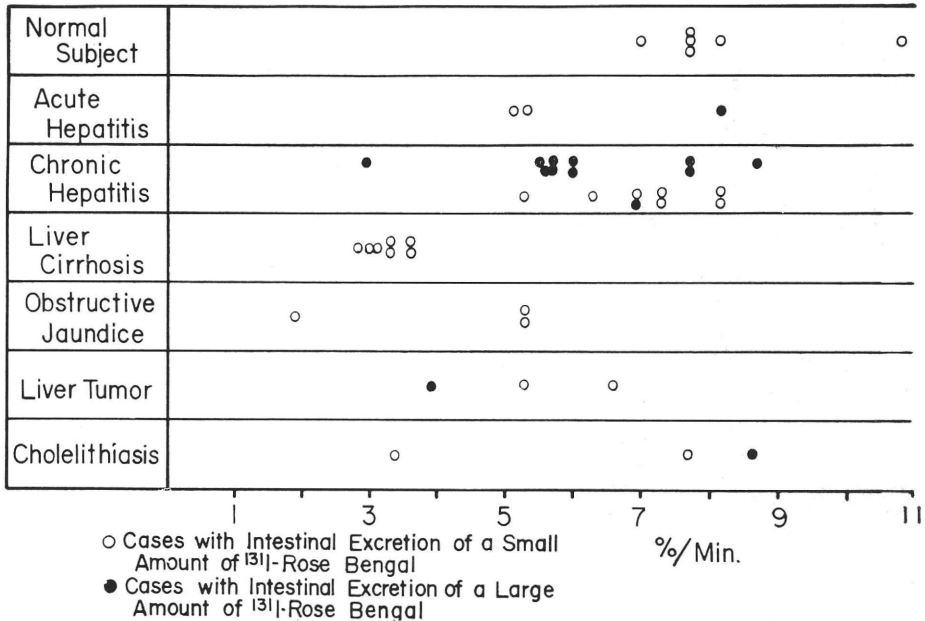


Fig. 7. The liver uptake rate of ¹³¹I-rose bengal in various liver and gallbladder diseases.

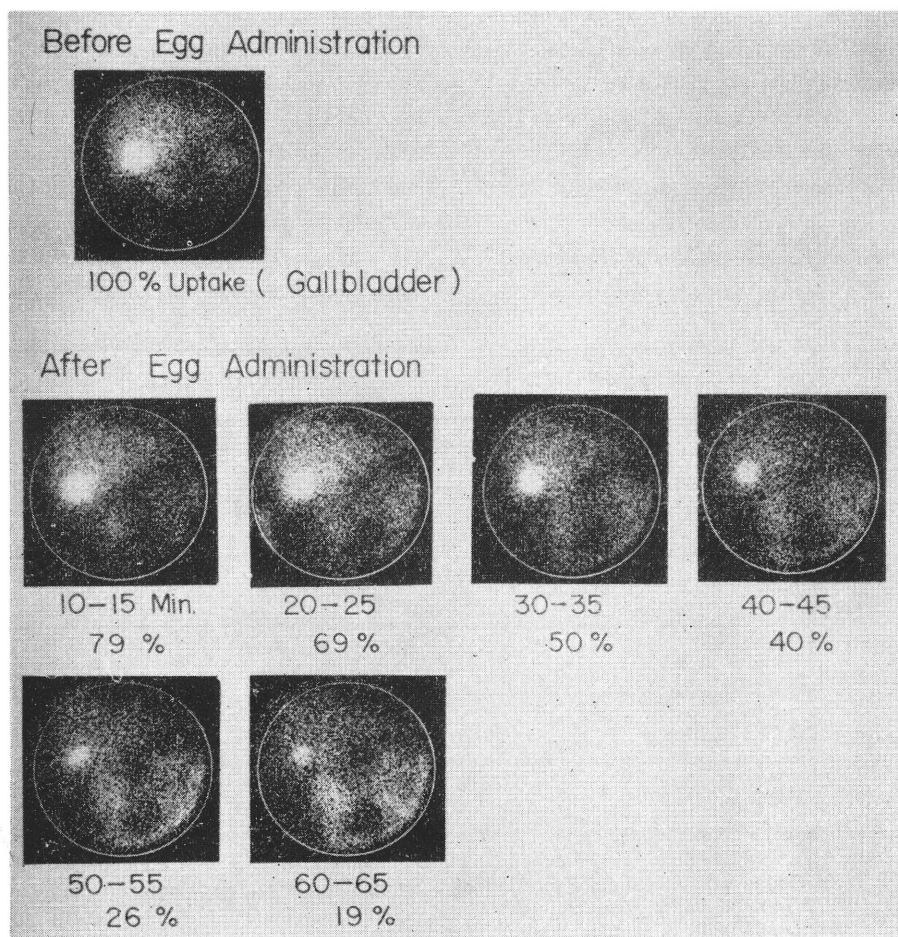
obstructive jaundice, in 30 over 90 minutes in patients with liver tumor, and in 30-45 minutes in patients with cholelithiasis.

Radioactivity appeared in the bowel in 50-75 minutes in normal subjects, in 30-100 minutes in patients with acute hepatitis, in 20 over 90 minutes in patients with chronic hepatitis, in 55 over 90 minutes in patients with liver cirrhosis, in more than 90 minutes in patients with extrahepatic obstructive jaundice, in 50 over 90 minutes in patients with liver tumor, and in 30-70 minutes in patients with cholelithiasis. In half of the patients with chronic hepatitis, a large amount of ^{131}I -rose bengal in the bowel was observed, and radioactivity

in the bowel appeared earlier than in the normal subjects.

Liver uptake rates from the analysis of the chronological changes in all radioactivities below the detector of the scintillation camera and the blood radioactivity curve monitored on the head of patients with various liver and gallbladder diseases.

Fig. 7 shows the liver uptake rate in various liver and gallbladder diseases. The liver uptake rate was 7.0-10.5% per minute in normal subjects, 5.0-8.0% per minute in patients with acute hepatitis, 3.0-8.5% per minute in patient with chronic hepatitis, 2.8-3.5% per minute in patients with liver cirrhosis, 2.0-5.0% per minute in patients with



(1) A 36-year-old healthy female.

Fig. 8. The serial liver scintiphotos after the ingestion of egg following the injection of $30\mu\text{Ci}$ of ^{131}I -rose bengal.

extrahepatic obstructive jaundice, 3.9-6.7% per minute in patients with liver tumor, and 3.3-8.7% per minute in patients with cholelithiasis.

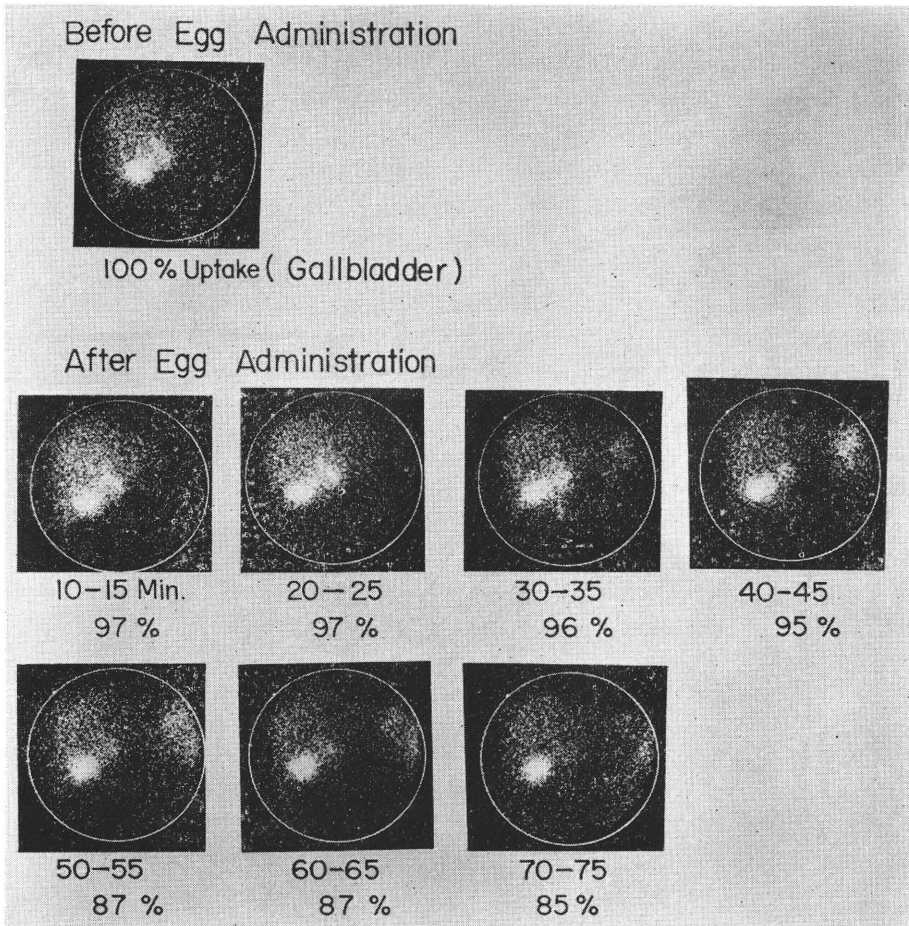
Effect of egg ingestion on decrease in radioactivity in gallbladder.

In normal subjects, ^{131}I -rose bengal in the gallbladder was rapidly excreted into the bowel after the ingestion of egg, and radioactivity in the gallbladder fell to 19% in one hour, as shown in Fig. 8 (1). Fig. 8 (2) shows the serial scintiphotos in a patient with cholelithiasis. A large amount of ^{131}I -rose bengal in the gallbladder was observed after the ingestion of egg. Fig. 9 shows the chro-

nological changes of the amount of ^{131}I -rose bengal retained in the gallbladder after the ingestion of egg in various diseases of the liver and gallbladder. When the gallbladder showed normal constriction, the radioactivity in the gallbladder fell to less than 20% by one hour after ingestion of the egg, but in some patients with cholelithiasis, the level of radioactivity in the gallbladder remained high 50-80%.

Discussion

Tapiln and co-workers (1) described the ^{131}I -rose bengal uptake-excretion test of liver function in 1956. Employing external γ -ray scintillation counting techniques, they obtained different uptake-excretion



(2) A 42-year-old female with cholelithiasis.

Fig. 8.

patterns in patients with various types of liver disease. Englert and associates (2) extended these studies and concluded that the technique of external measurement of ^{131}I -rose bengal in the liver afforded a reproducible method for quantitating the rate of hepatic excretion under carefully controlled conditions. These authors pointed out, however, that careful attention to collimation and positioning of the patient was crucial in determining the accuracy and reproducibility of the study, and this has remained the major limitation to the clinical applicability of this test. More recently, Eyler and co-workers (4) have reported their experience with ^{131}I -rose bengal liver scan as an aid in the differential diagnosis of jaundice. It was found that liver size, intrinsic isotope distribution, and demonstration of the labeled dye in bile ducts, gallbladder, and small bowel were most helpful in differential diagnosis. In regard to liver scanning with ^{131}I -rose bengal, Tauxe and Hamamoto (6) reported that two scans

in succession gave more accurate information of liver function. Immediately after the injection of ^{131}I -rose bengal the first scan started from bottom to top, and then the second scan was performed from top to bottom. They pointed out that in diffuse parenchymal disease the second scan was hotter than the first, and activity in the bowel was not visualized on the second scan; the findings were vice versa in localized liver diseases.

The scintillation camera, invented by Anger (5), reduced the radioisotope scanning time required with the conventional scanner, and permitted a more precise localization of the lesion. Moreover, it should be particularly valuable for stop-motion studies of dynamic processes. Burke and co-workers (7) reported dynamic liver function studies with ^{131}I -rose bengal and the scintillation camera. This approach permitted constant visual monitoring of hepatic uptake of ^{131}I -rose bengal from the circulation and its excretion into the biliary tree and intestine.

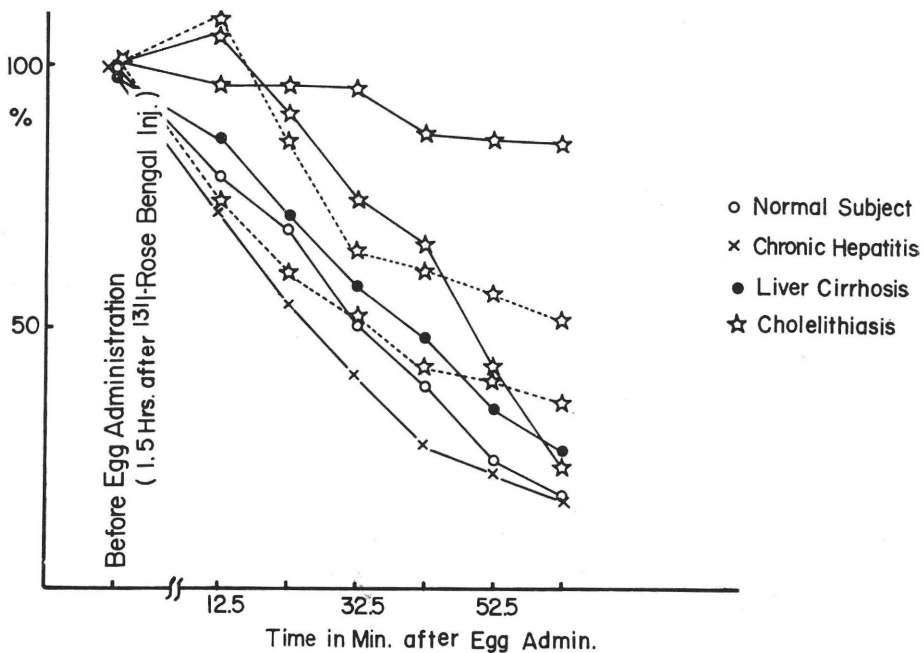


Fig. 9. The chronological changes of the amount of ^{131}I -rose bengal retained in the gallbladder after the ingestion of egg following the injection of ^{131}I -rose bengal in various liver and gallbladder diseases.

They postulated that the rates of decline in blood radioactivity and of hepatic isotope uptake have been characterized in normal subjects and distinguished from those obtained in patients with parenchymal dysfunction, and the technique was of significant value in the differentiation of jaundice which could be corrected surgically from that which could not.

This report deals with the usefulness of ^{131}I -rose bengal and the scintiscamera in evaluating the liver and gallbladder function. Time lapse moving pictures exposed at three-minute intervals showed the chronological changes in the distribution of ^{131}I -rose bengal in the liver, gallbladder and bowel; the liver contour and the presence of space-occupying lesions could also be visualized. The time lapse before maximum hepatic uptake of ^{131}I -rose bengal was precisely determined from the chronological changes in radioactivity in the liver by the 1600 channel analyzer. The maximum hepatic uptake occurred at 30 minutes in normal subjects, at 30-60 minutes (with a mean of 45 minutes) in patients with chronic hepatitis, at 40-60 minutes in liver cirrhosis, and over 90 minutes in patients with extrahepatic jaundice. In patients with acute hepatitis, liver tumor or cholelithiasis, these times widely distributed depending on the degree of parenchymal damage in the liver. A good correlation was observed between these times and the Bromsulphalein values in various liver and gallbladder diseases. On the basis of these results, it can be pointed out that the time when maximum hepatic uptake of ^{131}I -rose bengal occurs reflects liver function exceedingly well. The time of appearance of radioactivity in the gallbladder or the bowel was determined from the serial scintiphotos. These times in normal subjects were 30 and 60 minutes, respectively. In half of the patients with chronic hepatitis, a large amount of ^{131}I -rose bengal in the bowel was observed, and radioactivity in the bowel appeared earlier than in the normal subjects. In these cases, the time of appearance of radioactivity in the gallbladder showed a wide distribution. These facts suggest that there is dysfunction of the gallbladder and bile duct in

patients with chronic hepatitis. Additional investigations are necessary to interpret these relationships. In patients with liver cirrhosis, both times were longer than normal because of the slow prolonged liver uptake of ^{131}I -rose bengal.

In this study, the liver uptake rate was calculated from the chronological changes of all radioactivity below the detector and the blood radioactivity curve monitored on the head. This rate was considered to reflect the function of the whole liver. Of course, the uptake and excretion rates in each compartment in the liver can be calculated from the chronological changes of radioactivities in 1600 matrices from the 1600 channel analyzer. Further studies with the 1600 channel analyzer, magnetic tape system and digital computer should give us a greater knowledge of regional hepatic activity.

In a few cases, gallbladder function was examined with eggs to constrict the gallbladder. With the scintillation camera the excretion of ^{131}I -rose bengal from the gallbladder into the bowel after the ingestion of egg could be visualized, and the excretion rate could be calculated from the chronological changes of radioactivity in the gallbladder region with the use of the 1600 channel analyzer. This rate shows quantitatively the power of constriction of the gallbladder.

References

- 1) Taplin, G.V., Meredith, O. M. Jr., and Kade, H.: The radioactive (^{131}I -tagged) Rose Bengal uptake excretion test for liver function using external gamma-ray scintillation counting techniques. *J. Lab. Clin. Med.* 45; 665, 1956.
- 2) Englert, E. Jr., Burrow, B.A., and Ingelfinger, F. J.: Differential analysis of the stages of hepatic excretory function with gamma-emitting isotope. 1. Method and validations. *J. Lab. Clin. Med.* 56; 181, 1960.
- 3) Eyler, W. R., et al.: The radioiodinated liver scan as an aid in the differential diagnosis of jaundice. *Amer. J. Roentgen.* 94; 469, 1965.
- 4) Eyler, W. R., et al.: Rose Bengal. ^{131}I liver

- scan. An aid in the differential diagnosis of jaundice. *J. A. M. A.* 194; 141, 1965.
- 5) Anger, H. O.: Gamma-ray and positron scintillation camera. *Nucleonics* 21; 56, 1963.
- 6) Tauxe, W. N. and Hamamoto, K.: Personal

Communication

- 7) Burke, G. and Halko, A.: Dynamic clinical studies with radioisotopes and the scintillation camera. II. Rose Bengal ^{131}I liver function studies. *J. A. M. A.* 198; 608, 1966.

Summary

The scintillation camera and the 1600 channel analyzer were employed with ^{131}I -rose bengal in dynamic studies of liver and gallbladder function in various liver and gallbladder diseases.

The series of scintiphotos showed chronological changes of distribution of ^{131}I -rose bengal in the liver, gallbladder, and intestine, liver contours and the presence of space occupying lesion in the liver. The time of maximum hepatic uptake of ^{131}I -rose bengal was determined from the chronological changes of radioactivity with the 1600 channel analyzer. This and the liver uptake rate calculated from the chronological changes in all radioactivity below the detector and the blood radioactivity curve

monitored on the head reflected liver function exceedingly well.

In a few cases, gallbladder function was examined with eggs used to constrict the gallbladder. The power of constriction of the gallbladder could be determined quantitatively with the 1600 channel analyzer from the chronological changes of radioactivity in the gallbladder region.

Determination of liver and gallbladder function with the scintillation camera connected with the 1600 channel analyzer and ^{131}I -rose bengal is a useful method of evaluating liver and gallbladder function quantitatively.

* * * * *

* * * *