Diagnosis and Evaluation of Portal Hypertension by Administration of Tc-99m-MIBI Per Rectum

Shao-Liang Chen, Lan-Wen Xu, Xue-fen Chen
Gang Jin, Ji-yao Wang*[1], Hou-Yu Liu*[1],
Wei-gang Xu*[2], Norihisa Tonami*[3]

Abstract

A new method for evaluating portal systemic circulation by administration of Tc-99 m-MIBI per rectum was applied to 10 normal control subjects and to 81 patients with various liver diseases. Tc-99m-MIBI 370 MBq (10 mCi) was administered to the rectum through a catheter. Images of the abdomen and low chest were obtained for up to 90 minutes with a scintillation camera interfaced with a computer. In order to obtain the quantity of portal-systemic shunt, the heart-to-liver uptake ratio (H/L ratio), the per-rectal portal shunt index of heart (S. I. h), and the shunt index of whole set of organs except the liver (S. I. w) were calculated in radionuclear rectum-portal imaging. In the case of normal controls, the image of the liver appeared within 5 minutes, becoming clearer and clearer as time went on, whereas the images of other organs such as the heart, spleen and lungs were only very faint. In the case of patients with liver cirrhosis associated with portal-systemic shunt, the image of the liver was not so clearly defined, whereas radioactivity in other organs became evident, especially in heart and spleen. The values of H/L, S. I. h and S. I. w were significantly higher in liver cirrhosis than those in normal controls ($p<0.01$) and in acute and chronic hepartitis ($p<0.01$). There was a good correlation between these values and the results of indocyanine green (ICG) tests ($r=0.94$). Also, there was a very good correlation between these values and the results of direct evaluting of portal pressure during operation ($r=0.93$). Radionuclear, rectum-portal imaging with Tc-99 m-MIBI appears to be a useful method for non-invasive and quantitative evaluation of portosystemic shunting in portal hypertension.

Introduction

In recent years there have been several major innovations in the diagnosis and evaluation of portal hypertension, including the application of nuclear medicine methods[1)–8)]. There have been many clinical reports by per-rectum administration of radioactive tracers. However, conventional radioisotope tracers such as $^{99m}TcO_4^-$ or ^{201}Tl are not quite suitable for quantitative evalu-

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Shao-Liang Chen, Lan-Wen Xu, Xue-fen Chen, Gang Jin, Ji-yao Wang, Hou-yu Liu, Wei-gang Xu*[2], Norihisa Tonami*[3]

Department of Nuclear Medicine, *Department of Internal Medicine, and *Department of Surgical, Zhon-Shan Hospital, Shanghai medical university, Shanghai, China, ***Department of Nuclear Medicine, Kanazawa University School of Medicine, Kanazawa,
Address for correspondence: Shao-Liang Chen, Associate Professor, Department of Nuclear Medicine, Zhong-Shan Hospital, Shanghai Medical University, Shanghai 200032, China.
*[3] 金沢大学医学部核医学学科 〒920 金沢市宝町 13-1

ation of portosystemic shunting[9)10)]. Recently, the use of ^{123}I-IMP seems to be superior to previous tracers[11)12)], but IMP does not stay in the heart, spleen and other related organs, which precisely are the most imaportant organs of portosystemic shunting when people suffer from portal hypertension. A new and efficient tracer that could permit the precise quantitative evaluation of portosystemic shunting of all organs is therefore most desirable.

Recently we tried the Tc-99 m-MIBI, which is widely used for myocardial imaging[13)14)], in transrectal portal scintigraphy on a number of patients without and with liver diseases, and estimated the indices for the degree of portosystemic shunting.

Patients and Methods

Ninety-one patients were studied, including ten patients without liver diseases and eighty-one patients with various liver diseases. The diagnosis of liver diseases were made on the basis of clinical findings, liver function tests, liver scintigraphy, liver biopsy and operation. Patients with liver diseases were classified into five subgroups, including acute hepatitis, chronic hepatitis, cirrhosis, hepatic coma, and primary liver carcinoma. The age, sex and number distribution of each group is shown in Table 1.

After the patient had fasted for at least 3 hours, an enema was performed to empty the rectum. With the patient in the left lateral decubitus position, a special catheter was inserted 20 cm into the upper part of the rectum and 185-370 MBq (5-10 mCi) of Tc-99 m-MIBI (1-2 m*l*), followed by 15 m*l* of air, was administered through the catheter.

The patient was then placed supine under a large field-of-view gamma camera (technicare Omega-500 or Aplx SP-6), fitted with a low-energy, multipurpose parallel-hole collimator. The collimator was positioned over the patient's abdomen so that the field of view would include the heart, liver, spleen and the lower parts of the lung.

Images were obtained every 5 minutes up to 120 minutes at least. In addition, data were collected and stored in a computer. Regions of interest (ROI) were placed on the heart, liver, spleen and right lung. Areas of these ROI were normalized. Time-activity curves in each normalized ROI were then obtained.

To evaluate the degree of portal-systemic shunt, we use the equations as follows:

$$H/L=\frac{\text{ROI counts of heart}}{\text{ROI counts of liver}} \quad (1)$$

$$\text{S. I. h}=\frac{\text{ROI counts of heart}}{\text{ROI counts of heart}+\text{ROI counts of liver}} \quad (2)$$

$$\text{S. I. w}=\frac{\text{ROI counts of heart}+\text{spleen}+\text{lung}}{\text{ROI counts of heart}+\text{spleen}+\text{lung}+\text{liver}} \quad (3)$$

were H/L is the heart-to-liver ratio, S. I. h is the portal shunt index of heart, and S. I. w is the portal shunt index of whole set of organs excpet the liver. All results were expresses as means±s. d., and student's t-test was used for the statistical analysis.

Table 1 Clinical Status and Results of Shunt Indices in Liver Diseases and in Normal Controls

Diagnosis	n	Age(Yr)	Sex(M/F)	H/L	S.Ih	S.I.w
Normal Controls	10	42±12.4	6/4	0.20±0.08	0.17±0.06	0.22±0.07
Acute Hepatitis	8	45±10.7	5/3	0.47±0.10**	0.32±0.05**	0.41±0.06**
Chronic Hepatitis	6	48±9.4	4/2	0.58±0.13**	0.37±0.05**	0.48±0.07**
Cirrhosis	43	52±9.0	35/8	1.00±0.26**	0.50±0.07**	0.71±0.14**
Hepatic Coma	6	50±11.2	4/2	1.40±0.17**	0.55±0.08**	0.85±0.11**
Primary Liver Carcinoma	18	47±9.9	16/2	0.53±0.20*	0.34±0.09*	0.46±0.12*

(*P<0.05 ; **P<0.01)

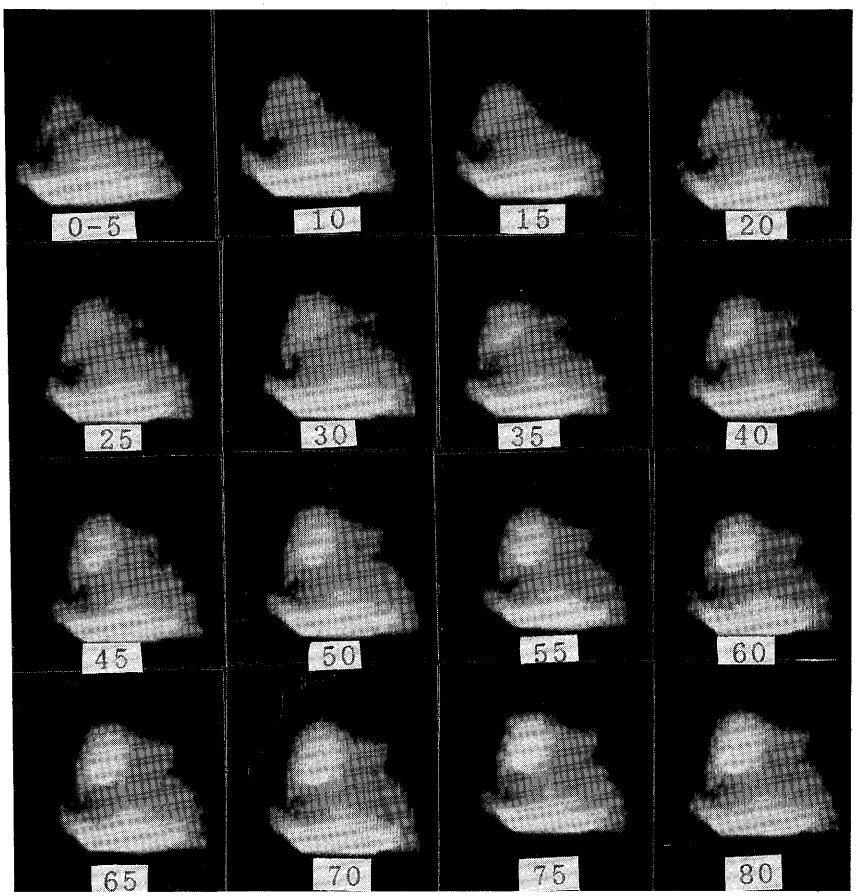

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Fig. 1 Sequential scintigrams after transrectal administration of MIBI in a normal subject without liver disease. Liver is observed in 0～5 min image and becomes clear thereafter. Other organs are not visualized even on the 75～80 min image except gallbladder.

Results

After the administration of Tc-99 m-MIBI, images of the 10 normal control subjects without any liver disease were observed every 5 minutes over a period of 180 minutes. It was found that the image of the liver appeared within 5 minutes, becoming clearer and clearer as time went on, whereas the images of other organs such as the heart, spleen and lungs were only very faint (Fig. 1). Time-activity curve for the normalized ROI in liver showed that the liver activity increased more rapidly than that in heart and persistently with time for at least 90 minutes, but the activities of other organs increased much more slowly (Fig. 2).

In contrast to the normal controls, in patients with liver diseases associated with portal systemic shunt, in addition to activity in the liver, activity was also seen in the heart, spleen, lungs, and sometimes in stomach (Fig. 3). Time-activity curves of the heart, spleen, and lung increase rapidly with time (Fig. 4).

The calculated indices (H/L, S. I. w) became essentially constant after 20-30 minutes and remained so until 180 minutes both for patients without and with liver diseases (Fig. 5). Therefore, these indices for each patient were deter-

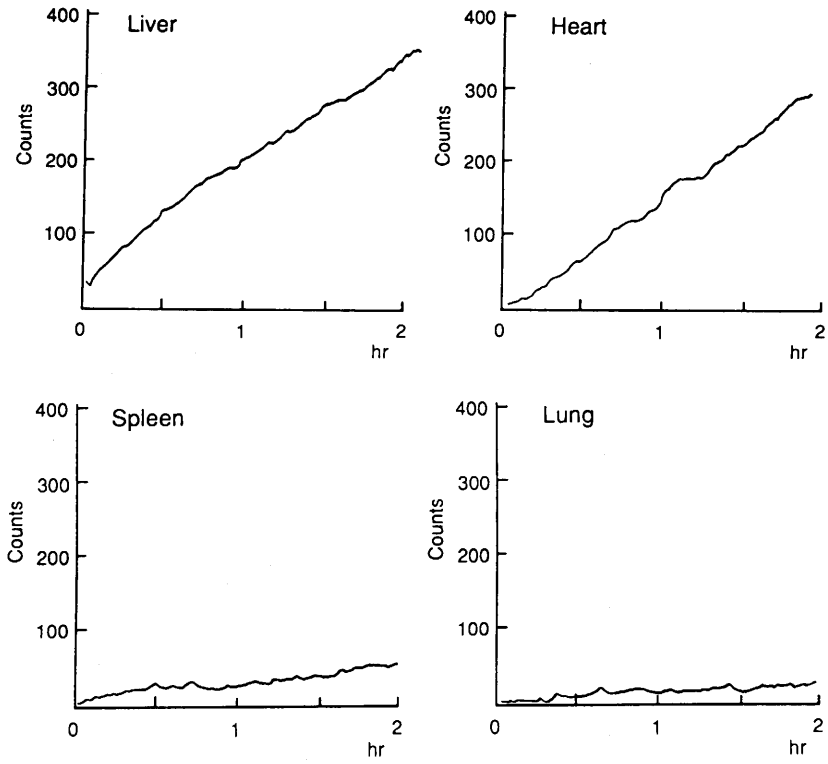

Fig. 2 Time-activity curves in ROIs of liver, heart, spleen and lung in normal control subject. Liver activity increases more rapidly with time than heart activity whereas activities of other organs increase much more slowly.

mined by mean values obtained every 5 minutes over the period between 60 and 90 minutes after MIBI administration. The standared deviation of these indices in each patient was less than 5%. Table 1 lists out the mean values of H/L, S. I. h and S. I. w found in the groups with various diseases and in the normal controis. For patients with liver liver cirrhosis, the values significantly increased, espicially in pre-hepatic come. These mean values were significantly higher than those in normal control subjects ($p<0.01$), and also higher those in chronic hepatitis ($p<0.01$), acute hepatitis ($p<0.01$), but significantly lower than those in hepatic come ($p<0.01$). For patients with primary hepatoma, the values vary according to the liver conditions, e. g., with or without cirrhosis.

No significant correlation was identified between H/L ratio, S. I. h, S. I. w and bilirubin, SGPT, SGOT, ZnT, etc. There was relatively good correlation between these values and the results with indocyanine green (ICG) test ($r=0.94$).

Ten patients received surgical operations one week after radionuclear rectum-portal imaging. The portal pressure was measured directly during the surgical operation. The relation between H/L ratio and the portal pressure is shown in Fig. 6. There was a relatively good correlation ($r=0.93$, $p<0.01$).

Discussion

A number of substances, such as Na-24, Xe-133, I-131, etc., have been given per rectum to evaluate the portal systemic circulation. Kuroki et al reported using Technetium-99 m pertechnetate as a radiotracer and obtained the portosystemic shunt index[2]. They calculated the liver-to-

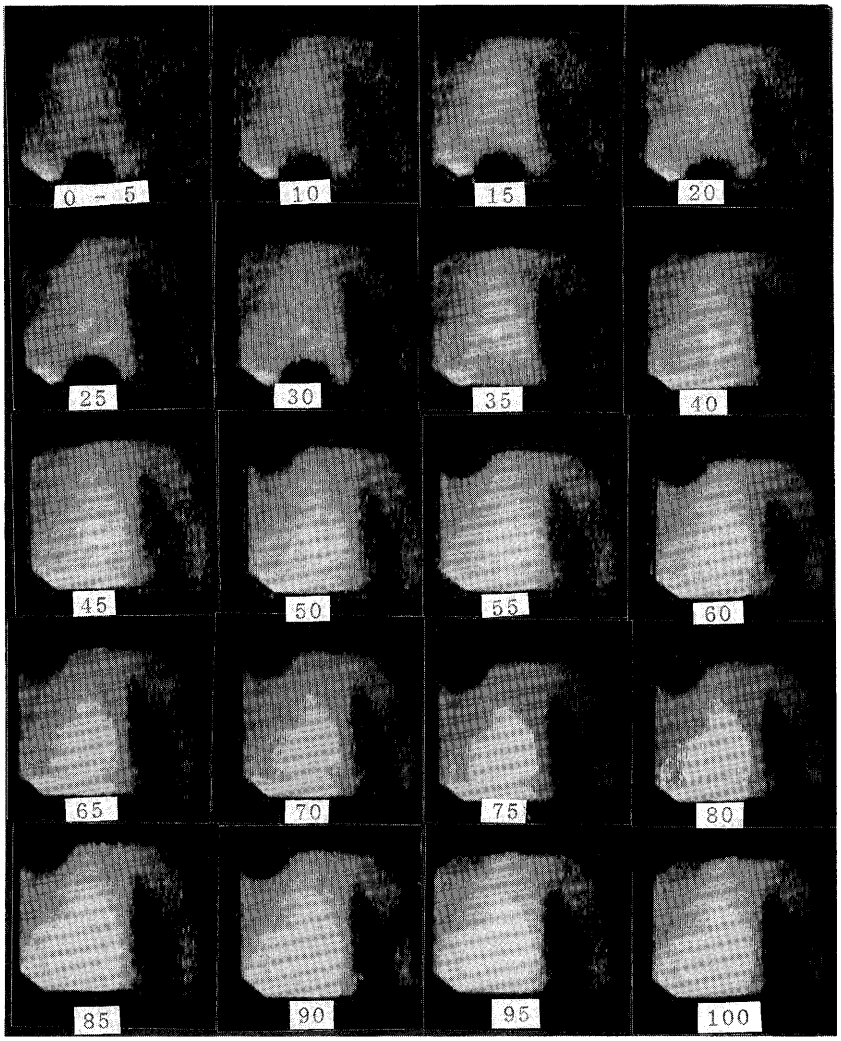

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Fig. 3 Sequential scintigrams after transrectal administration of MIBI in a patient with liver cirrhosis with portal-systemic shunt. Heart, lungs, spleen, and stomach were observed.

heart count ratio from initial rising count curves over liver and heart after rectal administration of $^{99m}TcO_4^-$. $^{99m}TcO_4^-$ has very good physical characteristics for imaging, and this method provides visualization of the portal venous system in some cases. However, some main factors influence the rise of radioactivity over the liver, such as adsorption of Technetium-99 m from the rectum, portal circulation time, and so on. So, this index is not stritly reliable. Furthermore, Technetium-99 m passes through the liver rapidly and does not remain there, but a significant amount of it remains in the abdomen area following administration. It seems, therefore, that Technetium-99 m pertechnetate is not an ideal tracer for studying portal circulation[9].

Tonami N. et al reported a method for evaluating portal circulation by administration Thallium -201 per rectum[1]. Tl -201 is absorbed and retained by the liver and heart, being trapped

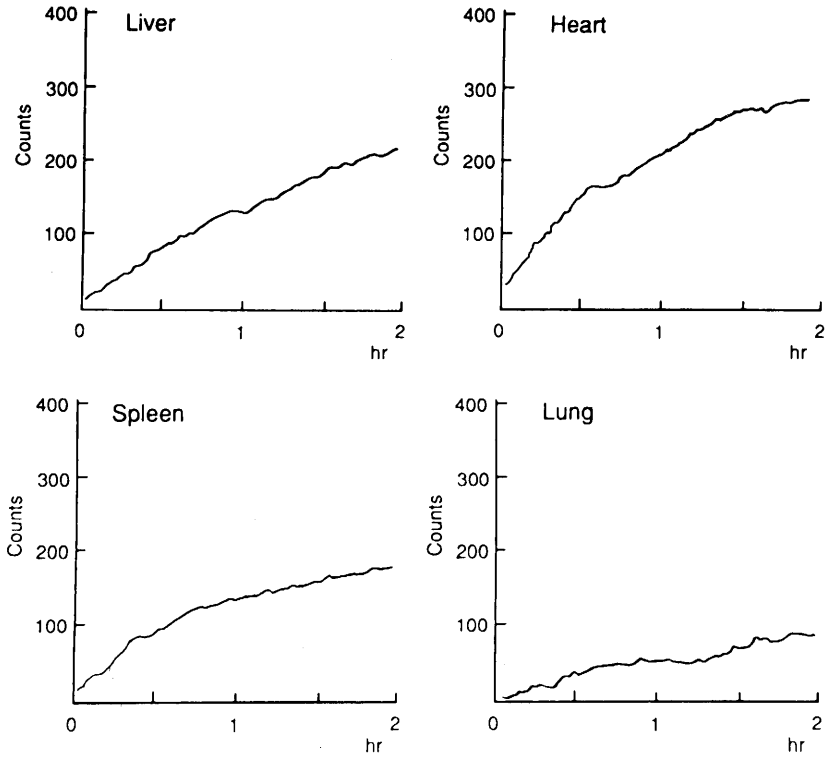

Fig. 4 Time-activity curves in ROIs of liver, heart, spleen and lung in patient with liver cirrhosis with portal-systemic shunt. Activies in heart, spleen and lung increase rapidly with time.

there at least for a couple of hours and cannot readily be washed out[1]. T1-201 provides heart-to-liver ratio and seems to be a valuable and reliable index for evaluationg the amount of shunting form the rectal veins to the systemic circulation. This method was supported by Urbain D[15] and our ealy investigation. However, Tl -201 is too expensive to be used as a routine tracer, especially in the developing countries such as China.

Recently several new myocardial perfusion radiophamaceticals labled Tc-99 m were reported, among which the MIBI is one of the best agent[13][14]. It can accumulate and retain myocardium in proportion to the blood flow. Besides myocardium, other organs such as liver, lungs spleen and kidney also absorb this agent partially, and can secrete it to the gallbladder and intestines.

Since Tc-99 m-MIBI can be mainly distributed in its initial passage to the organ by virtue of the local blood flow and the cell viability, we believe it is an appropriate tracer for evaluating the rectum-to-hepatic vascular pathways when given rectally.

When Tc-99 m-MIBI is delivered at the upper part of the rectum of a normal control subject, it can be absorbed by the rectal lumen and most of it is carried to the liver via the inferior mesenteric and portal veins. The radioactivity does not appear in the systemic circulation, because most of the Tc-99 m-MIBI remains in the liver. As to the patients with portosystemic shunts, the tracers can appear in the circulation and be distributed to the whole body through collateral routes (via the portosystemic shunts). In our studies, all control subjects only showed liver imagings and did not reveal the heart, lung, spleen

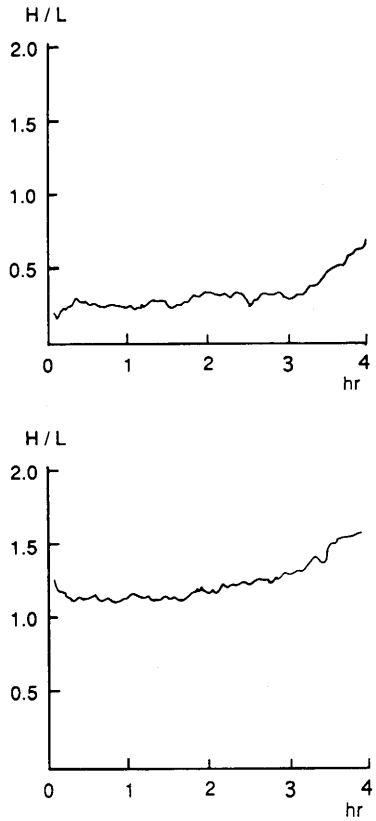

Fig. 5 Curve of heart to liver in normal control subject, and in patient with liver cithosis. Curve becomes constant from 20 min to 180 min.

throughout the process, and values of the shunt indices were low. On the contrary, in the case of cirrhosis, the image of the liver is rather faint, whereas the radioactivities of other organs, especially the heart, significantly increase, and the shunt ratio values also significantly rise. At this time, because of the increase of portal pressure, the collaterals between portal vein systemic circulation open up, indicating a kind of expansion. It is possible for the radioactive tracer to bypass the liver and enter directly into systemic circulation and arrive at the heart, spleen and lungs. The possible route of the collaterals is: from the middle and inferior rectal veins (or the inferior mesenteric vein) to the inferior vena cava, or from the portal vein to the superior vena cava.

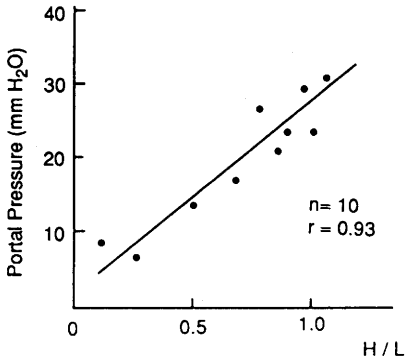

Fig. 6 Relation between H/L ratios and the results of direct evaluating of portal pressure during surgical operation.

Because the abovementioned MIBI can according to the local blood flow quantity retain in the correlated organs, the radioactivities of the heart, lungs and spleen will increase at this time.

In consideration of the fact that the main organs where MIBI can retain, besides the heart, are the spleen, lungs and stomach (these are also the main organs which can reflect the shunt conditions), we hold that, besides calulating the heart/liver ratio, and the shunt index of the heart, the ratio (Sum of radioactivities of all organs except the liver)/Sum of radioactivities of all organs including the liver) should be taken as the shunt index of all organs, and try to use this paramenter to reflect the full picture of the portal systemic shunts. Because of the introduction of the shunt index S. I. w, the difference of the conditions between the groups of liver diseases and the normal control subjects becomes more apparent, compared with the results obtained by using simply the shunt index S. I. h.

Some patients who had received several repeated inspections have indicated that this method seems to have produced reproducible index giving relative steady results. Therefore, this index is quantitative and is a good standard for reflecting the degree of shunting of portalsystemic shunts.

Because this method is simple and non-invasive, it can be employed as a routine method for clini-

cal diagnosis and follow-up of the portosystemic shunting in patients with liver diseases.

The research works of the I-123-IMP in portal scintigraphy have been carried out[12]. Iodine-123-iodoamphetamine (IMP), widely used for brain imaging, mainly distribute in the organs like brain etc. and can also appear in the organisations of the lungs. Kashiwagi T et al used the lung/liver shunt index as the main paramenter for estimation of the portal hypertension. They think IMP is too expensive and is difficult to be popularised in developing countries. Furthermore, IMP does not enter into the heart. And MIBI seems to be somewhat better than IMP because it can be directly taken up by the heart.

The major drawback of this method in some patients is lower absorption from the rectum. Rectum absorbs $^{99m}TcO_4^-$ at a higher speed and a larger quantity than MIBI. And this is the shortage of MIBI as an image agent for portal scintigraphy, especially in the case of patients with not so good absorption power.

In our dynamic research work, the shunt index revealed between 20 minutes and 12 minutes remained essentially steady with only slight fluctuations, therefore it is possible to collect static data during this period. This not only further simplifies the operating process, but also can prolong the time for collecting data, which is particularly useful in obtaining satisfactory images for patients with not so good absorption power. The results of our study demonstrate that portosystemic shunt quantitation can be carried out using the transrectal administratioin of Tc-99 m-MIBI.

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