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# Clinical assessment of hepatic functional reserve using $^{99m}$Tc DTPA galactosyl human serum albumin SPECT to prognosticate chronic hepatic diseases —Validation of the use of SPECT and a new indicator—

Yuya ONODERA,* Kazuei TAKAHASHI,** Tadashi TOGASHI,*** Yukio SUGAI,**
Nagara TAMAKI* and Kazuo MIYASAKA*

*Department of Radiology and Nuclear Medicine, Hokkaido University School of Medicine
**Department of Radiology, Yamagata University Hospital
***Department of Second Internal Medicine, Yamagata University School of Medicine

***Rationale:*** It is generally known that scintigraphy of $^{99m}$Tc diethylenetriamine pentaacetic acid-galactosyl human serum albumin ($^{99m}$Tc-GSA) is useful for assessing hepatic functional reserve. For hepatic functional indicators, the index of the calculated planar image has been used in previous studies. However, there have been few reports that suggest that the indicators calculated from static SPECT data would be useful for the assessment of hepatic function. The aims of this study were to establish a simple method for assessing hepatic functional reserve using the liver SPECT of $^{99m}$Tc-GSA and to apply this method for rich stratification in patients with chronic hepatic diseases. ***Methods:*** A liver phantom (a 50% concentration of $^{99m}$Tc solution) was used to compare the planar and SPECT methods. According to the definition of the new indicator, the liver SPECT of $^{99m}$Tc-GSA was divided by a syringe SPECT of $^{99m}$Tc-GSA and was called the liver uptake ratio (LUR). We correlated the LUR and the liver uptake ratio calculated according to the blood-sampling method. $^{99m}$Tc-GSA SPECT was performed in 137 patients with hepatic diseases, including chronic hepatic diseases, and 20 healthy volunteers. The LUR was correlated between the formed subtypes for all subjects. ***Results:*** The acquired phantom-count ratio calculated by the SPECT method was more accurate than that acquired by the planar method. A good correlation was obtained between the LUR and the blood-sampling method ($r = 0.971$). The LUR was significantly lower in subjects with severe cirrhosis than in healthy subjects or those with chronic hepatitis and mild cirrhosis, and it was significantly lower in subjects with chronic hepatitis and mild cirrhosis than in healthy subjects. The LUR was significantly correlated with other hepatic function tests. Based on LUR, the chronic hepatic diseases were divided into two groups: Group A, with LURs 30% and higher, and Group B, with LURs below 30%. An LUR of 30% marked the 25th percentile of the mild-cirrhosis group. The cumulative survival rates were lower in Group B than in Group A. ***Conclusion:*** The SPECT method was superior to the planar method for assessing LURs. LUR was a suitable indicator of $^{99m}$Tc-GSA clearance from the blood pool and of binding to the asialo-glycoprotein receptor. LUR is a simple and clinically useful indicator for the assessment of hepatic functional reserve in chronic hepatic diseases.

**Key words:** $^{99m}$Tc DTPA galactosyl human serum albumin, SPECT, hepatic functional reserve

## INTRODUCTION

ASSESSMENT of hepatic functional reserve is most frequently done to assist with the management of patients of chronic hepatic diseases. $^{99m}$Tc DTPA galactosyl human serum albumin ($^{99m}$Tc-GSA) scintigraphy is clinically available for the assessment of hepatic function because

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For reprint contact: Yuya Onodera, M.D., Department of Radiology, Hokkaido University School of Medicine, N 15 W 7, Kika-ku, Sapporo 060–8638, JAPAN.
E-mail: y-ono@radi.med.hokudai.ac.jp

$^{99m}$Tc-GSA specifically binds to the hepatic asialo-glycoprotein receptor, which decreases with chronic hepatic disease. Many analyses using planar $^{99m}$Tc-GSA scintigraphy or dynamic $^{99m}$Tc-GSA SPECT are clinically available.[1–8] The planar method is simple, and so it is used more widely.

However, with the planar method, data acquisition is affected by a patient's size and liver volume because of photon attenuation.[9] Therefore, the planar method might produce an inaccurate clinical index. In addition, the planar method cannot be used to assess regional hepatic function. We have reported that static SPECT provided a simple and reliable functional parameter.[9–11] Our method is especially superior for assessing regional hepatic function, including preoperational liver function and postoperative outcome.[11]

Another disadvantage of the planar method is that it cannot distinguish the tracer distribution in the hepatic blood pool from the tracer uptake of the hepatic parenchyma. This is a potential cause of assessment error; however, there have been very few reports regarding this problem. The present study was carried out to solve this problem by using the static liver SPECT method. One of the goals of the study was to clarify the validity of the static liver SPECT method and compare it to that of a phantom study and the blood-sampling method.

There have been very few reports indicating that $^{99m}$Tc-GSA results are clinically useful for assessing the prognosis of patients with chronic hepatic diseases. Another goal of the study was to clarify that the new indicator calculated from the static $^{99m}$Tc-GSA liver SPECT is clinically useful as a prognosticator. We investigated the relationship between our new indicator and other hepatic functional test results. The clinical value of our indicator as a prognosticator was evaluated by comparison with the Child-Pugh classification and the prognosis of chronic hepatic diseases using cumulative survival rates.

## MATERIALS AND METHODS

*Subjects*

Twenty healthy volunteers and 137 patients with hepatic diseases participated in this study. All individuals gave informed consent according to institutional guidelines and the principles of the Helsinki Declaration. A total of 137 patients had chronic hepatic disease; 28 had chronic hepatitis; and 109 had cirrhosis. Most of the cases of chronic hepatic disease had underlying infections with hepatitis B or C virus. Sixteen subjects had acute hepatitis. One had primary sclerosing cholangitis. Two had autoimmune hepatitis. One had hepatic failure due to congestive heart failure. The cirrhotic patients were divided into three groups according to the Child-Pugh classification: Child-Pugh A, 41; Child-Pugh B, 48; Child-Pugh C, 12; and unknown, 8. Hepatocellular carcinoma was diagnosed in 102 patients (one had a combined type of cholangiocellular carcinoma). According to the Clinical Rules for the Clinical and Pathological Study of Primary Liver Cancer, which was prepared by the Liver Cancer Study Group of Japan, all hepatocellular carcinoma cases ware classified. Only lower staging (i.e. Stage I and II) cases were applied in this study. Hepatitis and cholangitis were diagnosed by liver biopsy. Postoperative pathology, CT, or MRI were used to diagnose liver tumors. Regarding the cause of death, the cancer death cases associated with increased tumor burden were excepted from this study, and only fatal cases associated with liver failure were applied.

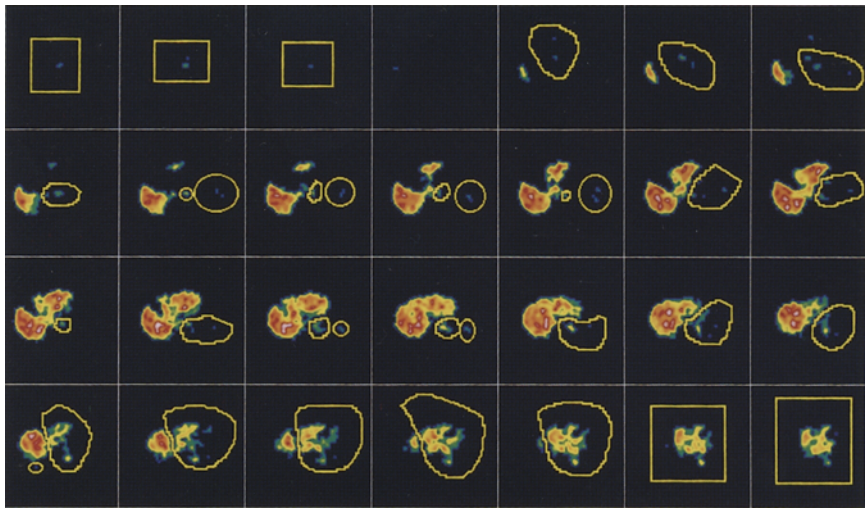
*Data Acquisition and Image Analysis*

Phantom, syringe, and individual SPECT data were acquired on a three-head gamma camera system (MULTISPECT 3/Siemens), equipped with low-energy high-resolution collimators. For the phantom study, a planar image was obtained from one detector in the three-head gamma camera. The projection images were acquired for 12 seconds each at 5° and stored in a 64 × 64 matrix. The acquired data were processed on a dedicated computer system (ICON; Siemens). The projection data sets were prefiltered with a two-dimensional Butterworth filter (order, eight; cut off frequency, 0.61 cycle/pixel) and reconstructed with filtered-back projection (Ramp filter). Chang's attenuation collection was added to the reconstructed data in order to obtain more accurate SPECT counts. Scatter correction was not performed. The liver margin was extracted, with 34% of the maximum as the cut off value.[9] Concerning the cut off value, we determined that the accurate volume could be calculated from the result of the phantom study. This process always excludes hepatic tumors. For the clinical study, a region of interest (ROI) was manually selected on the residual extrahepatic region, and the counts in the ROI were excluded. The counts of the liver, syringe, or phantom studies were calculated from the entire acquired image, which enabled us to obtain the count without setting up an ROI. This made it possible for us to develop a program that might produce the desired images individually (Fig. 1).

*Phantom Study*

We simulated a liver phantom study (volume, 1,000 m*l*) and a syringe-phantom study. A liver phantom has the shape of the column type. The syringe phantom was the $^{99m}$Tc-GSA syringe itself that is usually used. The liver phantom was filled with a 150 MBq $^{99m}$Tc solution, and the syringe phantom was filled with a 300 MBq $^{99m}$Tc solution. The activity of the $^{99m}$Tc solutions was calculated using a scintillation counter. The planar scanning and SPECT of the liver and syringe phantoms were performed for 5 minutes. The phantom-count ratio was calculated by dividing liver-phantom counts by syringe-phantom counts.

a



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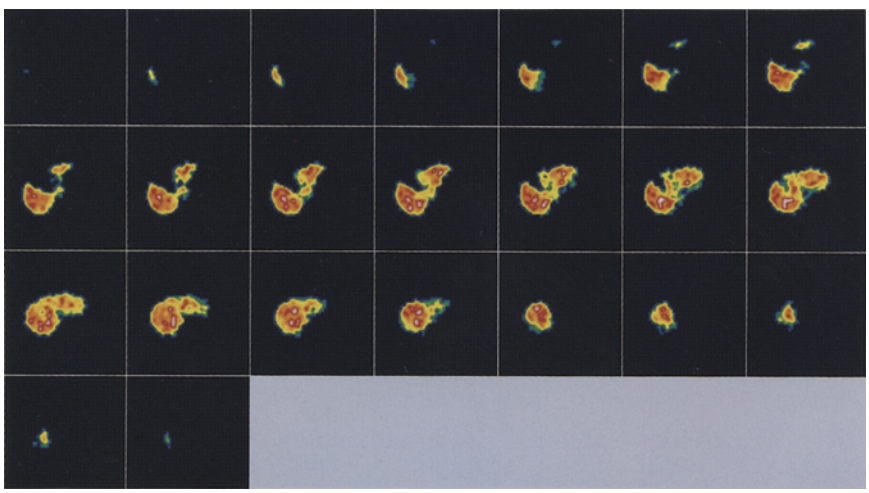

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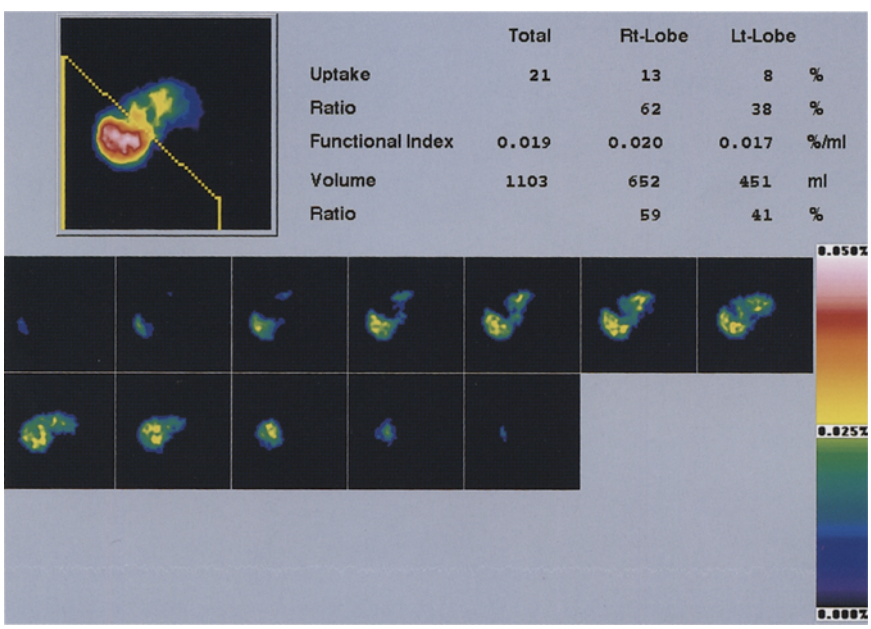


**Fig. 1** a: The region of interest is established over the extrahepatic counts. b: The extrahepatic counts in each image are removed. c: LUR is calculated based on the whole liver SPECT images.

*Clinical Study*

$^{99m}$Tc-GSA (3 mg, 185 MBq) syringe SPECT scanning was performed for 30 seconds before the subjects received a bolus injection of $^{99m}$Tc-GSA into an antecubital vein. Next, the subjects' SPECTs were performed for 5 minutes beginning at 12.5 to 17.5 minutes after the injection. Because, in previous reports, the time activity curve of $^{99m}$Tc-GSA was gradually flatter at 10 minutes after injection, we fixed the central acquisition time at 15 minutes after injection.[1-9] Based on acquired data, we calculated a new hepatic function indicator called the liver uptake ratio (LUR), which we obtained by dividing the syringe SPECT counts into the liver SPECT counts.

LUR = Liver SPECT counts/Syringe SPECT counts

*Blood-Sampling Method*

For the validation of an LUR, it is necessary to control the method. We defined the liver uptake ratio calculated from the blood-sampling method as the control index. The blood-sampling method was used for 51 subjects (20 normal volunteers and 31 subjects with chronic hepatic diseases). A blood-sampling point was placed on an antecubital vein against the $^{99m}$Tc-GSA injection site. Seven samples were taken at 3, 5, 7, 10, 15, 20, and 30 minutes. The acquired samples were divided to the plasma and the blood cell. A count for each sample was taken by measuring the plasma with a scintillation counter. The $^{99m}$Tc-GSA plasma-disappearance rate was calculated from a formula approximated from the no-linearity method of least squares using plasma sample counts. In other words, a disappearance rate curve was looked for from the sample counts, and the disappearance rate at the moment was calculated.

When the expected liver uptake rate of the $^{99m}$Tc-GSA was supposed as (1 – $^{99m}$Tc-GSA plasma-disappearance rate), the expected liver uptake of $^{99m}$Tc-GSA was defined as the dose of the $^{99m}$Tc-GSA that disappeared from blood. The expected liver uptake dose of the $^{99m}$Tc-GSA was calculated from the following formula:

The expected liver uptake of the $^{99m}$Tc-GSA (mg)
= $^{99m}$Tc-GSA dosage of the syringe (3 mg)
× (1 – $^{99m}$Tc-GSA plasma-disappearance rate)

The liver uptake ratio of the blood-sampling method was calculated from the following formula. We used a 15-minute value of the blood-sampling method for the correlation.

$$\text{Liver uptake ratio of a blood-sampling method (\%)} = \frac{\text{the expected liver uptake of the } ^{99m}\text{Tc-GSA}}{^{99m}\text{Tc-GSA dosage of the syringe}} \times 100$$

In addition, we investigated the comparison of the $^{99m}$Tc-GSA plasma-disappearance curve calculated by using the mean counts of normal volunteers and the mean counts of subjects.

*Statistical Analysis*

The correlation between the blood-sampling method and LUR was analyzed using Pearson correlation analysis, and the significance of the difference was determined using the Student's unpaired t-test. $p < 0.05$ was considered significant.

Spearman rank correlation analysis was applied to analyze the correlation between LUR and each laboratory test result (plasma-retention rates of indocyanine green at

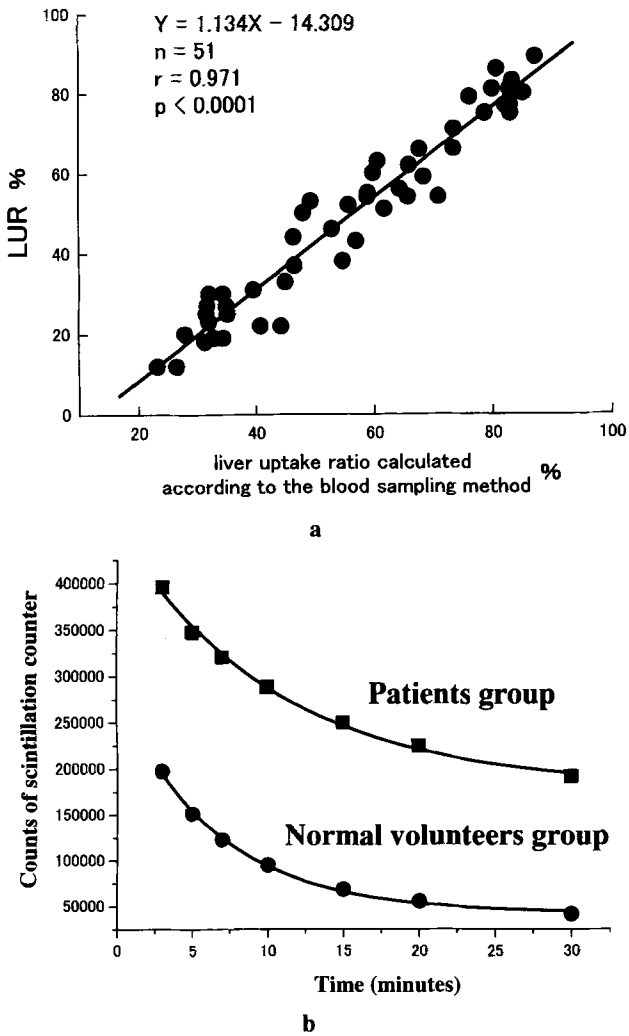


**Fig. 2** a: Correlation between LUR and the blood-sampling method. The results showed a significant correlation; r = 0.971, p < 0.0001. The gradient of the regression line was very close to one, but the LUR indicated that it was lower than that shown by the blood-sampling method. b: The $^{99m}$Tc-GSA plasma-disappearance curves using the mean counts of the normal volunteers group and the patients group were approximated in the mono exponential function. Both curves flattened within 15 minutes of the $^{99m}$Tc-GSA injection. The normal volunteers mean curve: $y = 42460.1 + 244152.4 \exp(-x/6.4)$ ($R^2 = 0.998$), the patients mean curve: $y = 179392.1 + 280838.8 \exp(-x/10.5)$ ($R^2 = 0.996$)

**Table 1** Shows the results of the correlation between LUR and conventional hepatic function tests

| | ICG $R_{15}$ | $K_{ICG}$ | Alb | ChE | PT | Tbil |
|---|---|---|---|---|---|---|
| LUR | R = –0.711 | R = 0.751 | R = 0.524 | R = 0.710 | R = 0.544 | R = –0.120 |
| | n = 119 | n = 107 | n = 160 | n = 160 | n = 161 | n = 161 |
| | p < 0.0001 | p < 0.0001 | p < 0.0001 | p < 0.0001 | p < 0.0001 | p = 0.12914 |

15 min [ICG $R_{15}$], plasma-disappearance rates of ICG [$K_{ICG}$], cholinesterase, serum albumin, prothrombin time, and total bilirubin) for all patients. We divided an applicable group (in which the prognoses for 147 subjects were known) into a normal group (20 normal volunteers), a chronic hepatitis group (26 patients), and a cirrhosis group (101 patients). The cirrhosis group was based on the Child-Pugh classification and was further divided into three groups (Child-Pugh A, 41; Child-Pugh B, 48; and Child-Pugh C, 12). In total, five groups were evaluated. We correlated the LUR mean for each group, and the significance of the difference was determined using Kruskal-Wallis and multiple comparison tests (Scheffe's F method). The results were expressed as the medians with 25th and 75th percentiles. For each test result, $p < 0.05$ was considered to show a significant difference.

We investigated the cumulative survival rate of the 127 patients with chronic hepatic diseases. Patients were divided into two groups based on LUR and ICG $R_{15}$. The LUR border was the 25th percentile of the Child-Pugh A group, and the ICG $R_{15}$ border was the mean + one standard deviation of the Child-Pugh A group. The survival rates were calculated using the Kaplan-Meier method. The significance of the difference was determined using a Logrank test; $p < 0.05$ was considered significant.

## RESULTS

*Phantom Study*

The phantom-count ratio was calculated by dividing the liver-phantom counts by the syringe-phantom counts. The actual ratio should be 50.0% because the ratio was calculated by dividing a 150 MBq $^{99m}$Tc solution by a 300 MBq $^{99m}$Tc solution. The SPECT method ratio was 49.3%, which was almost the actual ratio, whereas the planar method ratio was only 29.1%. Thus, the SPECT method was superior to the planar method for calculating liver uptake ratios.

*Correlation between LUR and the Blood-Sampling Method*

A significant and strong correlation was observed between the LUR and the blood-sampling method: r = 0.971, p < 0.0001, n = 51 (Fig. 2a). The gradient of the regression line was very close to one, but the LUR determined by SPECT was slightly lower than that determined by the blood-sampling method.

The $^{99m}$Tc-GSA plasma-disappearance curves of two groups were approximated in the mono exponential function (Fig. 2b). Both curves flattened within 15 minutes of the $^{99m}$Tc-GSA injection.

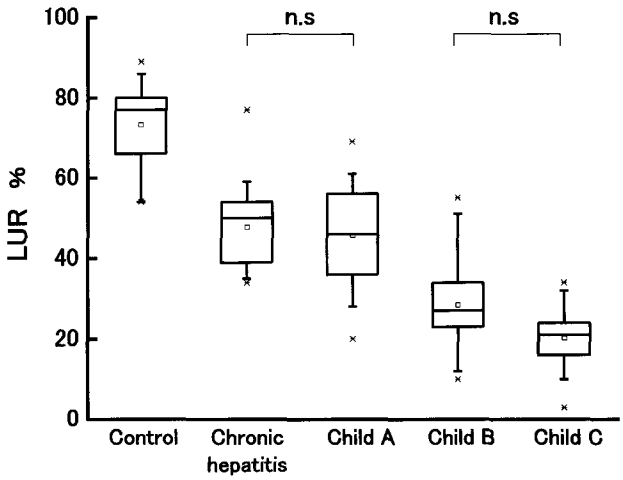


**Fig. 3** The median with the 25th and 75th percentiles of LURs was divided into five groups, i.e., normal, chronic hepatitis, and Child-Pugh groups A, B, and C. Except for two combinations (chronic hepatitis and Child-Pugh A group, and Child-Pugh B and C groups), the combination of any two groups had statistically significant differences in the Kruskal-Wallis and multiple comparison tests (Scheffe's F method); p < 0.0001.

*Correlation between LUR and Conventional Hepatic Function Tests*

Table 1 shows the results of the correlation between LUR and a conventional hepatic function test. The LUR showed a significant correlation with the conventional hepatic function test. Good correlations were shown, especially with the ICG tests and cholinesterase (ICG $R_{15}$: r = 0.711, p < 0.0001, n = 119; $K_{ICG}$: r = 0.751, p < 0.0001, n = 107; ChE: r = 0.710, p < 0.0001, n = 160).

The median with the 25th and 75th percentiles of the LURs was calculated for each of the five patient groups, i.e., normal, chronic hepatitis, and Child-Pugh A, B, and C, as shown in Figure 3. The median (25th and 75th percentiles) of the LUR was 78% (65% and 80%) in the healthy volunteer group, 50% (38% and 55%) in the chronic hepatitis group, 46% (38% and 55%) in the Child-Pugh A group, 28% (25% and 35%) in the Child-Pugh B group, and 20% (15% and 22%) in the Child-Pugh C group. Except for two combinations (chronic hepatitis and Child-Pugh A group, and Child-Pugh B and C groups), the combination of any two groups showed statistically

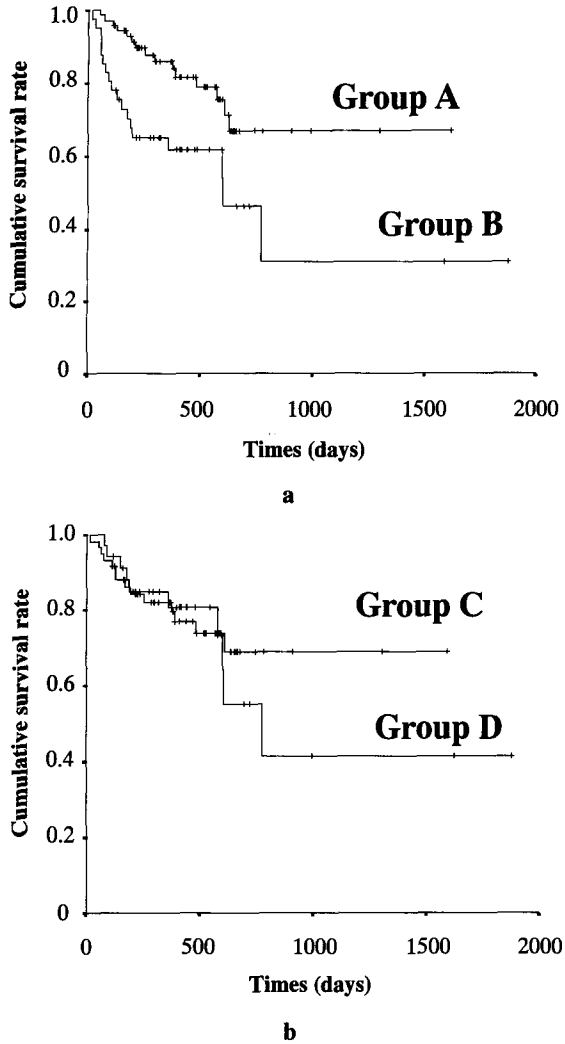


**Fig. 4** a: The cumulative survival rates in two groups: Group A had LURs above 30%, and Group B had LURs below 30%. The survival rates were lower in Group B than in Group A; the Logrank test showed a significant difference between the two groups ($p < 0.05$). b: The cumulative survival rates in two groups: Group C had ICG $R_{15}$ above 32%, and Group D had ICG $R_{15}$ below 32%. The Logrank test showed no significant difference between the two groups

significant differences in the Kruskal-Wallis and multiple comparison tests (Scheffe's F method); $p < 0.0001$.

*Cumulative Survival Rate*

The patients were divided into two groups based on LURs and ICG $R_{15}$. The border value of the LURs was 30%, so an LUR of 30% was the 25th percentile of the Child-Pugh A group, for which the prognosis was comparatively good. The mean – standard deviation of ICG $R_{15}$ was 32% in the same way.

Group A had LURs above 30%, and Group B had LURs below 30%. The results are shown in Figure 4A. The cumulative 1-y survival rate was 90% in Group A and 62% in Group B. The cumulative 3-y survival rate was 65% in Group A and 45% in Group B. The cumulative 5-y survival rate was 65% in Group A and 32% in Group B. The survival rates were lower in Group B than in Group A; a significant difference was shown between the two groups in the Logrank test ($p < 0.05$).

Group C had ICG $R_{15}$ above 32%, and Group D had ICG $R_{15}$ below 32%. The results are shown in Figure 4B. No significant difference was shown between the two groups in the Logrank test.

## DISCUSSION

Our results clarified four important points: the superiority of SPECT in quantification, the hemodynamics of $^{99m}$Tc-GSA was approximated in the mono exponential function, the validation of using static SPECT, and the clinical usefulness of LUR for prognosticator of chronic hepatic diseases.

*Superiority of SPECT in quantification*

Our phantom study indicated that the SPECT method is better than the planar method for the assessment of the $^{99m}$Tc-GSA liver uptake ratio.

In chronic liver disease, liver uptake is gradually lower because of the asialo-glycoprotein receptor (AGR). In contrast, the extrahepatic tracer concentration in the spleen, inferior vena cava, or aorta increases gradually. The planar method may be used for data acquisition from a gamma camera set up in the liver anterior face so that the tracer in the blood pool cannot be separated and mix in the liver. Generally, an index of $^{99m}$Tc-GSA is found directly from the counts in the planar image. An ROI is identified on the liver and the heart. An ROI of the heart indicates the $^{99m}$Tc-GSA distribution in the blood pool.

However, the phantom study showed that the data were lower than actual data on the planar method. The results show that body-size variance and the depth of the liver might also cause technical errors because the planar method cannot routinely add the attenuation correction. An ROI of the heart might be used as the blood pool because the dimension of the ROI varies from individual to individual.[12]

Using the static SPECT method could reduce these problems. The static liver SPECT led to accurate liver counts, except for extrahepatic counts and enhanced attenuation correction. Moreover, the SPECT is useful for regional assessment. We used syringe counts to take the place of the blood-pool counts *in vivo* so that the examiners would not be affected by the dimensions of regions of interest, such as the heart. All counts were calculated after the attenuation correction, and a liver margin was extracted to remove less than 34% of maximum counts in all counts on the basis of a phantom study for calculating the accurate volume.[9] Residual extrahepatic counts were manually removed using an ROI with horizontal and coronal view; therefore, an ROI for the whole liver could be obtained almost actually. This method is simple for

clinical assessment of hepatic function and non-invasive, without blood sampling.

*Hemodynamics of $^{99m}$Tc-GSA*

The liver uptake ratio, according to the blood-sampling method, was approximated in the mono exponential function; as a result, the $^{99m}$Tc-GSA dynamics within 30 minutes of administration can be explained in a 1-compartment model that reflects the transmission from the blood pool to the liver parenchyma. $^{99m}$Tc-GSA uptake into the hepatocyte is only caused by binding to the asialoglycoprotein[1-8]; then, $^{99m}$Tc-GSA clearance on the 1-compartment-model pharmacokinetically reflects $^{99m}$Tc-GSA uptake into the hepatocyte with the binding to the asialo-glycoprotein receptor. Therefore, the liver uptake ratio of the blood-sampling method reflects $^{99m}$Tc-GSA binding to AGR.

*Validation of using static SPECT*

Clarifying the validity of using the static SPECT technique is necessary in order to compare the LUR with a reference, such as the blood-sampling method.[16] There have been very few comparisons of simple methods to the blood-sampling method. The correlation between LUR and the blood-sampling method indicated that $^{99m}$Tc-GSA in the hepatic blood pool does not affect LUR. Moreover, the gradient of the regression line between the LUR and the blood-sampling method is very close to one. Therefore, the LUR is also considered to be an indicator reflected by $^{99m}$Tc-GSA binding to AGR.

The $^{99m}$Tc-GSA time activity curve does not meet equilibration during the data acquisition time of the $^{99m}$Tc-GSA liver SPECT. The data-acquisition time of the LUR was 5 min, beginning anywhere from 12.5 min to 17.5 min after tracer injection. These factors might cause error, but the $^{99m}$Tc-GSA plasma-disappearance curve showed that the amount of change in the blood pool is small at approximately 15 minutes after administration. It is indicated that liver uptake of $^{99m}$Tc-GSA is also small. Although the acquisition time of SPECT is not an equilibrium phase, any possible clinical problem will be prevented by a good correlation of LUR with the blood-sampling method, which is not likely affected by the acquisition time.

*Clinical usefulness of LUR*

A comparison of LUR and clinical studies indicated that the LUR is clinically useful for assessing hepatic functional reserve. In addition, there was a statistically significant difference in the cumulative survival rates of the two groups on LUR. Furthermore, the LUR may be a good prognosticator for assessing chronic hepatic disease.

In the clinical study, the good correlation between the LUR and the indocyanine green (ICG) test results indicated that the value of our new indicator as a prognosticator is high. The ICG tests are standard methods for the assessment of chronic hepatic diseases, and these test results showed that the hepatic functional reserve reflected hepatocyte volume.[13-15] LUR tends to have a stronger correlation to the ICG test results and cholinesterase than indicated in previous reports.[1-8] We believe that the SPECT method is better than the planar method and that a better method leads to a more accurate outcome.

Our results were especially reasonable considering that the numbers of hepatocytes decrease with cirrhosis.[1-4] Patients with serious cirrhosis had significantly lower LURs than patients with mild cirrhosis and chronic hepatitis. The mean LUR of each group tended to gradually decline according to liver dysfunction, although no significant correlation was shown by the chronic hepatitis and the Child-Pugh A group or by the Child-Pugh B and C groups. The survival rate was significantly lower in the low-LUR group than it was in the high-LUR group, indicating that LUR can be used as a practical prognosticator for patients with chronic hepatic diseases. In contrast, the survival rate of the two groups on ICG $R_{15}$ was not significantly different. These results suggest that LUR might reflect the hepatic functional reserve better than the ICG test.

It is important to assess hepatic functional reserve to determine the prognosis for patients with chronic hepatic diseases. $^{99m}$Tc-GSA scintigraphy is useful for clinical assessment because the total number of functioning hepatocytes, which reflects the amount of AGRs, might define the hepatic binding capacity of $^{99m}$Tc-GSA. Many studies have analyzed $^{99m}$Tc-GSA uptake to hepatocytes and its clinical value.[1-8] However, there have been few reports comparing $^{99m}$Tc-GSA indicators of the Child-Pugh classification and practical patient prognosis, especially using a simple method such as the LUR.[7,9] Comparison with these factors is necessary to clarify a useful indicator reflecting the hepatic functional reserve because the Child-Pugh classification is widely used as a clinical assessment index for hepatic functional reserve of chronic hepatic diseases, and the practical patient's prognosis is closely related to the hepatic functional reserve. LUR showed a good correlation for these factors, which suggested that our new indicator could be used to assess hepatic functional reserve.

The SPECT method is routinely available for the assessment of regional hepatic function that cannot be directly assessed by the planar method. The clinical usefulness of the $^{99m}$Tc-GSA indicator has been reported; for example, the indicator is useful in determining a change in regional liver function that is related to fulminant hepatitis and the status after portal-vein embolization, thus providing a therapeutic window.[10,11] LUR may be used as a therapeutic monitor when a situation such as severe cirrhosis requires treatment that results in minimal damage to the liver.

*Limitation*

The LUR was slightly lower than the blood-sampling method. We think that the omitted counts may have caused this difference in the determination of the threshold required to obtain the liver margin.

The present study showed no significant correlation between chronic hepatitis and the Child-Pugh A, B, and C groups. This fact is not important for clinical assessment. The mean LUR of each group tended to decrease according to liver dysfunction and a classification based on LUR reflected the patient's practical prognosis. These results suggest that LUR is a useful indicator for hepatic functional reserve. The purpose of the LUR is to assess hepatic functional reserve and not to determine pathological diagnosis. The scores for the Child-Pugh B and C groups were very close, even overlapping, so it was difficult to discriminate among them.

Patient prognosis is most greatly affected by complicating hepatocellular carcinoma. In this study, an LUR of 30% was established as the borderline, but a decision concerning an optimal borderline would require a more in-depth analysis of patients without hepatic tumors or with clinical tumor staging.

## CONCLUSION

Assessment of liver function using $^{99m}$Tc-GSA should be performed with the SPECT method because it is more accurate than the planar method. LUR is a suitable indicator of $^{99m}$Tc-GSA clearance from the blood pool and of the binding to the asialo-glycoprotein receptor. LUR is a simple and clinically useful indicator for the assessment of hepatic functional reserve and determining prognosis in cases of chronic hepatic diseases.

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