Subtraction Scintigraphy with ^{67}Ga -Citrate and $^{99\text{m}}\text{Tc}$ -Colloid in the Diagnosis of Intrahepatic Masses

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Received March 8, 1980

Subtraction scintigraphy of the liver with ^{67}Ga -citrate and $^{99\text{m}}\text{Tc}$ -colloid ($^{99\text{m}}\text{Tc}$ -phytate) was performed by subtracting the image of the latter from the image of the former in 34 patients who were suspected of having intrahepatic masses, especially hepatoma.

The computer used was Scintipac 1200 (32 KW memories and 2.4MB $\times$ 2 disk memories).

Both images were taken in a digital form (128 $\times$ 128 elements). After normalizing both images, 4 different factors (0.6, 0.8, 1.0, and 1.2) were applied to the $^{99\text{m}}\text{Tc}$ image before the subtraction from the ^{67}Ga image.

We found that this technique was very useful for the detection of abnormal ^{67}Ga accumulation in the liver.

Key Words: subtraction scintigraphy, liver, $^{99\text{m}}\text{Tc}$ -colloid, ^{67}Ga -citrate

1. Introduction

In 1966, Kaplan, et al.¹⁾ reported a technique for subtraction scintigraphy, by which method better images of the pancreas, eliminating liver shadow, appeared on the scintigram. However, the computer processings had to be done by off-line system and were rather troublesome at that time. First of all, there was no suitable radiopharmaceutical for producing pancreas images and this still applies to this day. Consequently, subtraction scintigraphy has not been regularly used for the process of projecting images of the pancreas.

However, as with other technology, image processings in Nuclear Medicine have shared in the benefits of recent advances in computer technology, and subtraction scintigraphy can be easily performed.

In our laboratory, when patients are suspected of having hepatoma, ^{67}Ga scintigraphy is performed as a routine after having completed an ordinary scintigraphy with $^{99\text{m}}\text{Tc}$ -colloid. Until recently, both images were simply com-

pared with each other by visual means to see whether abnormal ^{67}Ga concentration occurred, or not in the defect observed on the $^{99\text{m}}\text{Tc}$ -colloid scintigram.

By installation of a minicomputer, however, we have started applying subtraction technique to ^{67}Ga scintigraphy of the liver. This is to report our results on the subtraction scintigraphy in cases of suspected intrahepatic masses.

2. Materials and Methods

All the patients who were subjected to this study were already known to have definite defects and/or questionable low-uptake areas in their livers on the ordinary liver scintigram taken with $^{99\text{m}}\text{Tc}$ -colloid($^{99\text{m}}\text{Tc}$ -phytate). But no radioactivity of the $^{99\text{m}}\text{Tc}$ was left during this test.

At first, 74 MBq (2mCi) of ^{67}Ga -citrate was given to the patient intravenously 2 or 3 days before the test. The night before the test, the patient was given 30 ml of castor-oil to eliminate intestinal contents. Some of the patients received a glycerine enema just before the test. The pati-

ent kept a supine or prone position under the scintillation camera (Ohio Nuclear $\Sigma 410\text{S}$) with a medium energy collimator (28W08610) which-ever defects were best visualized on the previous scintigram with $^{99\text{m}}\text{Tc}$ -colloid. But in some cases, both projections were used.

A digitized image (128 $\times$ 128 elements) on the ^{67}Ga -citrate was obtained at first by using the computer (Scintipac 1200; 32KW memories, and 2.4 MB 2 disk memories) through the windows (20%) for the peaks of 93, 184, and 296 keV.

The patient was then injected with approximately 74 MBq (2 mCi) of $^{99\text{m}}\text{Tc}$ -phytate (half of the usual dose) intravenously. Ten to 15 minutes later, a digitized image was obtained for the $^{99\text{m}}\text{Tc}$ through the window (20%) for the peak of 140 keV as before. During the time of these data acquisitions, the patient was requested not to move.

Because both images were not balanced in their counts at this moment, normalization was performed by setting "Region of Interest" in the areas where no focal disease was thought to be present, which must be the same geometrically between the two images as indicated in Fig. 1.

Fig. 1 Our procedure for the subtraction scintigraphy.

After normalization, the image with $^{99\text{m}}\text{Tc}$ -phytate was multiplied by 4 different factors (0.6, 0.8, 1.0, and 1.2). Each image from a different factor was subtracted from the image with ^{67}Ga -citrate. Finally, 4 different subtraction images were reproduced on one film by the micro dot imager through the computer.

Following the above-mentioned procedure, the subtraction scintigraphy was performed on

34 patients.

There were 17 patients on whom histological diagnoses were obtained (Table 1). Fourteen of them were proved to have hepatocellular carcinoma. One patient was found to have combined hepatocellular and cholangiogenic carcinoma at autopsy. One patient was later proved to have had a liver abscess by an emergency surgery after its spontaneous rupture. In one patient, diagnosis of chronic hepatitis was made on the biopsy specimen.

There were 6 patients on whom clinical diagnosis of hepatocellular carcinoma was made on the basis of clinical data which included findings on angiography, X-ray CT, echography, scintigraphy, etc. (Table 2). There was one patient with clinical diagnosis of liver cirrhosis. Two patients were thought to be free of liver disease. On the remaining 8 patients, diagnosis has not been established yet at the time of this report.

3. Results

As seen in Table 1, all four factors were effective in visualizing abnormal accumulations of ^{67}Ga in the liver of some cases, whereas only one or two factors were useful in some of the others. The smallest hepatocellular carcinoma visualized on the subtraction scintigraphy was 3.5 cm in diameter, which was not recognized by conventional image study. There were 5 hepatomas (in 3 patients) which were not recognized on both conventional and subtraction images. The smallest one was 1.0 cm in diameter, located in the hepatic dome and the largest was about the size of a grapefruit which was pedunculated under the visceral surface and was fully necrotic. The remaining 3 were located close to the visceral surface and the colonic radioactivity probably confused the images.

A case of hepatoma is shown in Fig. 2., for which 3 factors (0.6, 0.8, and 1.0) were thought to be useful. But factor 1.2 was interpreted as being too much because the tumor size seemed to be smaller on the image than it should be as compared with the surgical specimen. Figure 3 indicates a case of hepatoma for which the conventional method failed to depict the tumor. The subtraction scintigraphy however

Table 1 Cases proved with the pathological examination

Name & No.	Age & sex	Pathological diagnosis (specimen)	Conventional judgment on Ga-67 accum.	Better factor on subtraction image	Size of tumor (cm) & other remarks
H. S. 95426	47 M	HCC* (surgery)	+1	1.0, 1.2	8×8.5×7
N. M. 209910	63 M	HCC (surgery)	uninterpretable	0.8(larger mass)	3.5 & 1 each in diameter
K. U. 228555	75 M	HCC (surgery)	+2	0.8, 1.0	8×6.5
K. M. 229627	28 M	HCC (surgery)	+2	0.6, 0.8, 1.0, 1.2	17×10 on formalin-fixed sp.
Y. S. 229788	65 M	HCC (surgery)	uninterpretable	not depicted	4 in diam. visc. surf., grapefruit size. pedunculated below visc. surf., necrotic
S. M. 230053	47 M	HCC (surgery)	uninterpretable	not depicted	4×3 & 2×1.9 Both were close to visc. surf.
N. I. 230342	50 M	HCC (surgery)	+1	0.8	2.3×5
W. N. 231800	50 M	HCC (surgery)	+1	1.0***	7×5.5×4.5, in post. segment
H. A. 233310	56 M	HCC (surgery)	+2	0.8, 1.0	5×3
E. A. 54867	58 M	HCC (autopsy)	+2	well with 0.8, 1.0, 1.2	combined type
Y. I. 229865	67 M	HCC & CHC** (autopsy)	+1	well with 1.0, 1.2	
S. S. 95419	59 M	HCC (biopsy)	+2	well with 1.0, 1.2	
S. H. 227405	78 M	HCC (biopsy)	+2	well with 0.8, 1.0, 1.2	
M. H. 229519	65 M	HCC (biopsy)	+2	well with 0.6, 0.8, 1.0, 1.2	
H. A. 232243	57 M	HCC (biopsy)	+2	well with 0.6, 0.8, 1.0, 1.2	
S. H. 227708	53 M	liver abscess (surgery)	+2	well with 1.0, 1.2	
T. K. 228191	46 M	chronic hepatitis (biopsy)	no focal lesion		

+1: =normal liver

* hepatocellular carcinoma; ** cholangiogenic carcinoma;

+2: >normal liver

*** anterior projection for the tumor in post. segment

is thought to have successfully visualized one of the tumors compared with findings of the surgical specimen.

Figure 4 indicates the case of liver abscess for which factors 1.0 and 1.2 were thought to be useful.

In our series, there was a case of histologically proven chronic hepatitis. In this case the subtraction scintigraphy showed a gradual decrease in density of the liver shadow as the factor increased, and no significant focal accumulation appeared (Fig. 5).

There were 6 cases with clinically diagnosed hepatocellular carcinoma. They are shown in Table 2. All were visualized by both conventional and subtraction scintigraphies.

In one case with clinically diagnosed liver cirrhosis, the subtraction scintigraphy showed no focal accumulation except in the vertebral region on the posterior projection. This pattern was noted also in the case of Fig. 1. In two cases of clinically normal liver, the subtraction scintigraphy showed no significant accumulation of ^{67}Ga on any of the images.

Fig. 2

Fig. 3

Fig. 4

Fig. 2 K.U., No. 228555. HCC. 8×6.5 cm. Posterior view with $^{99\text{m}}\text{Tc}$ -colloid reveals a clear-cut defect in lateral portion of right lobe, where accumulation of ^{67}Ga is noted.

Fig. 3 N.M., No. 209910. HCC. Two tumors close to hepatic dome having 3.5 and 1 cm each in diameter. Original scintigrams with $^{99\text{m}}\text{Tc}$ -colloid and ^{67}Ga can not show either defect or accumulation. Subtr. scintigraphy depicts the larger tumor.

Fig. 4 S.H., No. 227708. Liver abscess. Original scintigram with ^{67}Ga reveals a doughnut-shaped deposit in the area, where $^{99\text{m}}\text{Tc}$ -colloid scintigram shows a large defect. Subtr. scintigrams reveal better delineation of ^{67}Ga deposit compared to that of ^{67}Ga original.

Table 2 Cases with clinical dagnosis of hepatocellular carcinoma

Name & No.	Age & sex	Diagnosis	Conventional judgment on Ga-67 accum.	Better factor on subtraction images
Y. K. 28763	70 M	HCC	+2	0.8, 1.0, 1.2
K. H. 217242	46 M	HCC	+1	1.0, 1.2
M. N. 225521	50 M	HCC	+2	0.6, 0.8
M. O. 230443	63 M	HCC	+2	0.8, 1.0, 1.2
M. K. 233207	53 M	HCC	+1~+2	0.8, 1.0
K. T. 233959	56 M	HCC	+2	0.6, 0.8, 1.0, 1.2

4. Discussion

Recently, the minicomputer designed for Nuclear Medicine practice has become gradually

Fig. 5 T.K., No. 228191. Chronic hepatitis. Shrinkage of anterior margin of right lobe is seen on original scintigrams with ^{99m}Tc -colloid and ^{67}Ga . Subtr. scintigrams reveal no abnormal accumulation of ^{67}Ga .

more popular, resulting in the fact that even complicated data processings are now conducted as a kind of routine work. These include dynamic studies of the brain, heart, lung, liver, kidney, etc. as well as static image studies of certain organs such as the liver and pancreas.

a) Digitized data for ^{67}Ga was obtained by using 3 peaks before ^{99m}Tc -phytate was injected.

b) Digitized data for ^{67}Ga was obtained by using 2 peaks after ^{99m}Tc -phytate was injected.

Fig. 6 Y.I., 69 years old female. No. 233613. Subtraction images from the two different methods on the clinically normal liver.

When the defect found on the ordinary liver scintigram with $^{99\text{m}}\text{Tc}$ -colloid is suspected of hepatoma, the second scintigram with ^{67}Ga -citrate is often taken to check whether the defect presents ^{67}Ga concentration or not. These two images are visually compared with each other in general. However, this method is largely dependent on the subjectivity of each person, resulting in the lack of universal validity.

Such a problem can now be virtually eliminated by the computer processings which reproduce a new image by subtracting the image obtained with $^{99\text{m}}\text{Tc}$ -colloid from the image with ^{67}Ga -citrate.

After Kaplan, et al.¹⁾ reported the method for subtraction scintigraphy, several papers^{2)~7)} concerning this subject have appeared, using either the scintillation scanner or the scintillation camera. In 1972, Hamamoto, et al.⁴⁾ presented good results in detecting liver tumor by subtracting ^{198}Au -colloid image from ^{67}Ga -citrate image. They divided the field into 40×40 elements for digitized data acquisition and printed the final image after converting this field into 120×80 elements. In 1978, Dhawan, et al.⁵⁾ also reported the results of subtraction scintigraphy by using ^{67}Ga -citrate and $^{99\text{m}}\text{Tc}$ -compounds on the bone, liver, spleen, and kidney. They divided the field into 128×128 elements. Both Hamamoto, et al. and Dhawan, et al. normalized two images at the elements of the highest counts before the subtraction. Furthermore, the latter group applied variable weighting factors from 10 to 60% to the $^{99\text{m}}\text{Tc}$ images, and they mentioned that the useful range of subtraction was 10 to 30%. In 1979, Kawai, et al.⁶⁾ also reported the superiority of subtraction scintigraphy over the conventional method in detecting abnormal ^{67}Ga accumulation in the liver. They used ^{198}Au -colloid for ordinary liver scanning.

In our method, to normalize both images we set "Region of Interest" as mentioned before, and applied 4 different factors (0.6, 0.8, 1.0, and 1.2) to the normalized $^{99\text{m}}\text{Tc}$ -colloid images.

Although we found that the subtraction images obtained with the factors of 0.8 and 1.0 were most often acceptable for making diagnosis, other factors (0.6 and 1.2) were also useful for detecting abnormal accumulation of ^{67}Ga in some

cases. These factors are apparently different from those by Dhawan, et al.⁵⁾ The reason for this difference seems to be due different normalization. At present, we prefer to use four kinds of factors for precise judgment.

In our procedure, when the data for ^{67}Ga was collected the patient was free from $^{99\text{m}}\text{Tc}$ -colloid. Therefore, 3 peaks (93, 184, and 296 keV) were utilized with 20% windows for each. Then, the data for $^{99\text{m}}\text{Tc}$ -colloid was collected 10 to 15 minutes after the injection. But we have also tried another procedure in several cases, in which the data collections for ^{67}Ga -citrate were performed after the injection of $^{99\text{m}}\text{Tc}$ -colloid. In such cases, two peaks (184 and 296 keV) were used for the ^{67}Ga . We compared the subtraction images obtained by these two different methods with each other, and found that there was not much difference between them (Fig. 6).

Vertebral accumulations of ^{67}Ga were sometimes noted on the subtraction images, especially on the posterior projection. In such cases, we were not able to make an assessment on this area, though, fortunately no tumors were present in our series.

Although we failed to point out small hepatomas in three cases even by our subtraction scintigraphy, two of them had tumors close to the visceral surface of the liver and colonic radioactivity obstructed the images. In the remaining one, the tumor was apparently too small to be detected (1.0 cm).

The subtraction scintigraphy with ^{67}Ga -citrate and $^{99\text{m}}\text{Tc}$ -colloid is very useful for detecting abnormal accumulations of ^{67}Ga in the liver.

This work was supported in part by a Grant-in-Aid for Cancer Research (Showa 54, designated) from the Ministry of Health and Welfare.

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要 旨

肝内腫瘍の診断における ^{67}Ga -citrate と $^{99\text{m}}\text{Tc}$ -colloid を用いての 引き算シンチグラフィについて

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日常の肝スキャンでは $^{99\text{m}}\text{Tc}$ -colloid シンチグラム上の欠損像の部位に ^{67}Ga が集積するかどうかで, 肝内の mass lesion についてのある程度の定性的診断が行われている。通常は視覚的に判断しているが, その方式だと読影者の主観に左右されることが多い。そこでわれわれはコンピュータによって ^{67}Ga シンチグラムから $^{99\text{m}}\text{Tc}$ シンチグラムを引き算することを行っている。われわれの方法は両者の画像を normalize したあと, 引き算をする前に $^{99\text{m}}\text{Tc}$ シンチグラムのほうに factor として 0.6, 0.8, 1.0, 1.2 をかけ, 4 種類の引き算シンチグラムを作成している。この方法によれば客観的な判断が可能で日常の診断にたいへん有効である。