Enhanced Detection of Metastatic Liver Disease by Computerized Flow Scintigrams: Concise Communication

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The purpose of this study was to develop a method by which the sensitivity of radionuclide liver imaging for the detection of hepatic metastasis could be enhanced. Routine flow studies were performed before imaging by injecting the usual 2–3 mCi dose of Tc-99m sulfur colloid as a bolus and storing 30 2-sec images in a computer. With regions selected by light pen, curves were generated from the right lobe of the liver, the right kidney, and the descending aorta. The peak of the kidney curve was chosen as a marker to separate the arterial and venous phases on the liver curve. The average slopes of four points on the liver curve before this marker, and four after, were calculated and the ratio of the first slope to that of the second was defined as the arterialization index. In this study with 228 patients, the inclusion of this index raised the sensitivity from 85 to 100%.

J Nucl Med 22: 318–321, 1981

Dynamic hepatic scintigraphy has been described as a method for enhancing diagnostic specificity of hepatic images (*1–6*). These methods are based on the fact that the normal liver receives approximately 25–30% of its blood supply through the hepatic artery and the remainder through the portal vein. When primary or metastatic neoplasms are present in the liver, the normal pattern of blood flow is disrupted and the hepatic artery supplies a larger fraction of the total flow (*2,7–14*). Quantitative assessment of arterial and portal flow fractions has been attempted with digital computers (*13–17*). Assessment of relative arterial and portal blood flow to the liver in patients with neoplastic disease has been reported previously, but the total number of patients evaluated has been limited (*13,14,16*).

This paper describes the increase in sensitivity of liver imaging resulting from inclusion of quantitative assessment of relative arterial to portal blood flow in 228 patients with known neoplastic disease, referred for hepatic scintigraphy as part of their evaluation or follow-up.

Received Sept. 3, 1980; revision accepted Nov. 6, 1980.

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MATERIALS AND METHODS

We have studied 228 patients with known primary neoplasms. They were positioned supine under a large-field scintillation camera equipped with the highest sensitivity parallel-hole collimator* available to us, for anterior views of the liver, kidneys, and aorta. The usual 3-mCi dose of Tc-99m sulfur colloid was injected as a bolus through an antecubital vein. Digital and film acquisition were started simultaneously with injection, and 30 images were acquired at 2 sec per image.

Following the radionuclide angiogram, static images were obtained (800,000 counts each), consisting of anterior, posterior, right lateral, left lateral, right anterior oblique, left anterior oblique, and upright anterior views. These static images were interpreted using strict criteria (focal defects only) (*17*).

The computer data were processed as follows. With regions of interest selected by light pen, time-activity curves were generated for the right lobe of the liver, the descending aorta, and the right kidney (Fig. 1). The largest possible area avoiding the kidney, lung, or portal vein was selected as hepatic region of interest. If the right kidney was not visualized, the left kidney was used. The quality of the bolus was assessed from the aortic time-

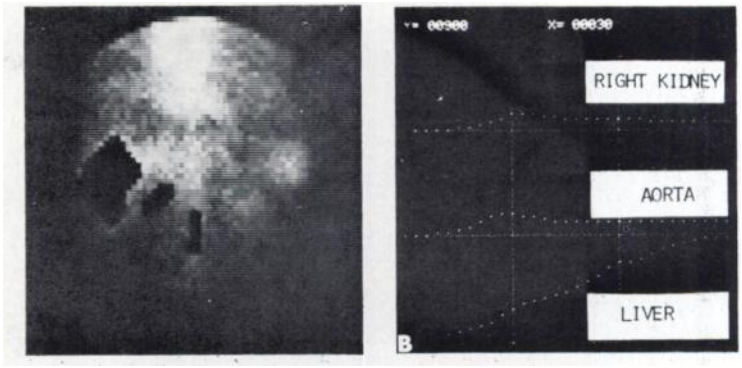

FIG. 1. (A) regions selected over right lobe of liver, right kidney, and descending aorta. (B) time-activity curves for liver, aorta, and right kidney. Time interval between each data point is 2 sec. Note that descending-aorta curve peaks 2 sec before right-kidney curve.

activity curve. If the time to reach peak from the half-maximum point on the ascent of the curve was greater than 8 sec, the study was discarded. This was encountered in less than 4% of the cases investigated. If an early rise in liver activity corresponding to pulmonary activity was seen, the region of interest was redefined to minimize this interference. Once satisfactory curves were obtained, a five-point smooth was performed. The peak time of the renal curve was taken as the demarcation between arterial and portal flow to the liver. The average slopes of four points before and four points after this time were calculated from the hepatic curve. The ratio of the arterial slope to the venous slope was defined as the arterialization index, AI (Fig. 2).

The reproducibility of AI calculation was tested by generating these curves twice on each of 100 patients.

RESULTS

The distribution of AI values is shown in Fig. 3.

The range of AI for 150 patients with definitely abnormal static liver images was from 0.50 to 3.70. The range for 50 patients with normal static liver images, and no other evidence for metastatic liver disease over a period of 6 mo, was 0.14 to 0.60. Twenty-eight patients had normal static images but elevated AI values ranging from 0.61 to 2.30. These groups are summarized in Table 1. Seven of the 28 patients with discordant AI and static images (Table 2) were further studied by biopsy; two of these had TCT scans, one of which was normal. In another patient (with breast cancer) the AI suggested metastatic disease but liver chemistry and liver images were normal. Nevertheless, within 3 mo her alkaline phosphatase increased, and it appears clinically that she has hepatic involvement, although the liver scan remains normal. Eighteen remaining patients were suspected of having hepatic metastases on a clinical basis. Two of these have been lost to follow-up. Of the remaining sixteen, seven have since developed definite evidence of metastatic disease within 6 mo: four by emission liver scan, two by TCT, and one by liver biopsy. One patient died after 13 mo, and autopsy revealed liver metastases.

The reproducibility of AIs was remarkable in 100 cases that were randomly chosen (correlation coefficient, r = 0.98).

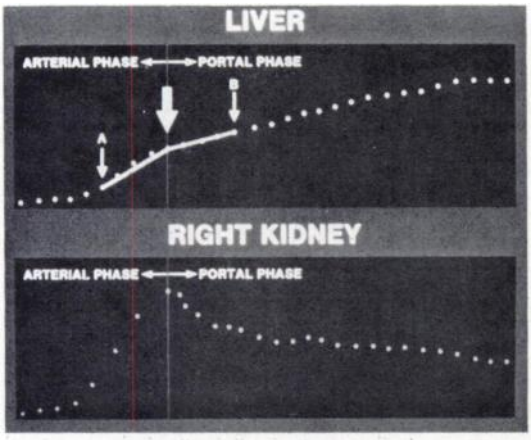

FIG. 2. Drawing of slopes for arterial and portal-venous phases. Peak time of right-kidney curve was defined as demarcation between these two phases. Note relatively sharp arterial rise in this patient with liver metastasis.

DISCUSSION

Technetium-99m sulfur colloid imaging is a well-

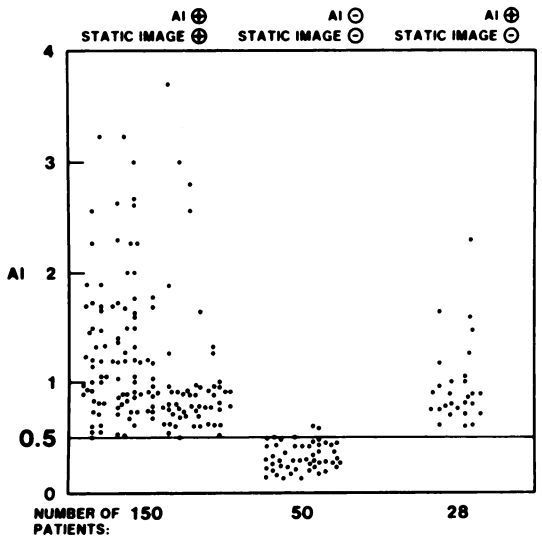

FIG. 3. Distribution of AI values in 228 patients with known neoplastic disease.

TABLE 1. RANGES FOR AI IN 228 PATIENTS

No. of patients	Scan	AI	Range of AI
150	+	+	0.50–3.70
50	−	−	0.14–0.60
28	−	+	0.61–2.30

established screening procedure, but the false-negative rate is still too high. The sensitivity of this procedure has been stated to be between 0.7 and 0.9 (*18*). Phantom studies performed on our equipment show that a lesion under 1 cm would rarely be detected.

The hepatic emission angiogram, with calculation of an arterialization index, was found to be a significant indicator of disease and a reliable index in patient management. An index of greater than 0.50 had a predictive value of 98% for hepatic metastases. The correlation of a high AI and possible metastatic liver involvement can be understood from animal and human studies (*7,10,11*), which show that neoplasms growing in the liver increase the hepatic arterial component of blood flow. This observation has been quantitated by Boyd et al. in six patients (*13*).

Our analysis technique differs from that of Boyd et al. in two ways. First, we chose to use the peak of the renal curve rather than the aortic peak to mark the end of arterial influx into the abdominal organs. This point correlated with prominent inflection points in the liver curves of 32 patients, whereas the aortic peak occurred 2 sec earlier. Second, calculation of the arterial slope from points just before the hepatic inflection point avoided poor statistics at the beginning of the curve and minimized the effects of Compton scatter from the lung.

As depicted in Fig. 3 and Table 1, all definitely abnormal static images had an arterialization index of ≥0.50. All 150 patients with one or more focal defects on static images had abnormal AI values. Of the 50 patients with negative static images and no evidence of metastases after 6 mo, four had AIs in the abnormal range (0.52–0.58); thus there is a specificity of 0.92. The 28 patients with positive AI values and negative static images are summarized in Table 2. Abnormal AI values (≥0.50) predicted liver disease in 27 of the 28 patients clinically suspected of having liver metastasis, and in 16 of these cases this prediction was confirmed by other means. In this clinical study of 228 patients, the sensitivity of static imaging was 84%. The inclusion of the AI raised the sensitivity to 100%.

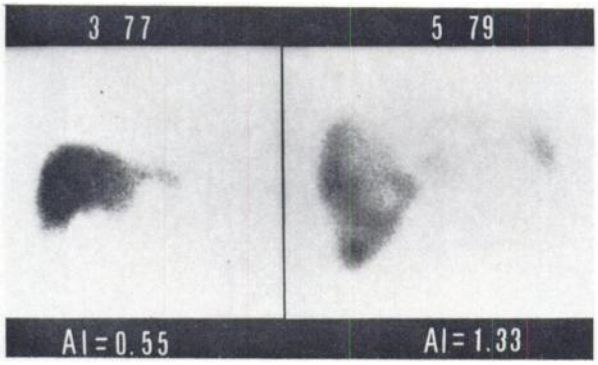

FIG. 4. Left: liver image in patient with known breast carcinoma, who showed no evidence of liver metastases and gave normal AI. Right: 2 yr later patient's liver image shows obvious disease and AI is definitely elevated.

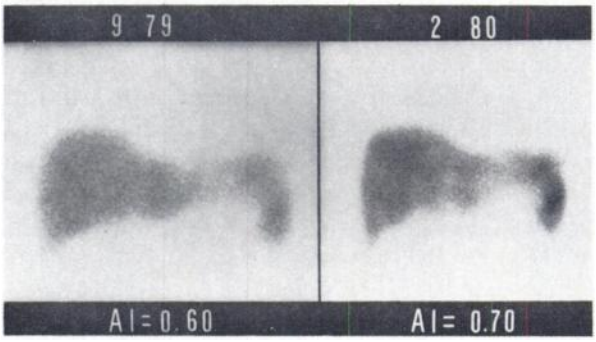

FIG. 5. Left: liver image in patient with known breast carcinoma is inhomogeneous, with slightly elevated AI. Right: 5 mo later there is inhomogeneity again and AI has risen. Biopsy showed metastatic disease.

Elevation of AI from a previously normal level, and coinciding with the development of metastic liver disease in a patient with breast cancer, is shown in Fig. 4. Figure 5 shows an abnormal liver scan, with elevated AI, in a

TABLE 2. FOLLOW-UP OF 28 PATIENTS WITH DISAGREEMENT BETWEEN AI AND STATIC IMAGES

No. of patients	Scan	AI	TCT	Path	Clinical
18	−	+(0.60–2.30)	none	none	+
4	−	+(0.75–1.64)	none	+	+
1	−	+(0.78)	+	+	+
1	−	+(1.0)	−	+	+
1	−	+(0.75)	none	+	+
2	−	+(0.61–0.70)	+	none	+
1	−	+(0.89)	none	none	?

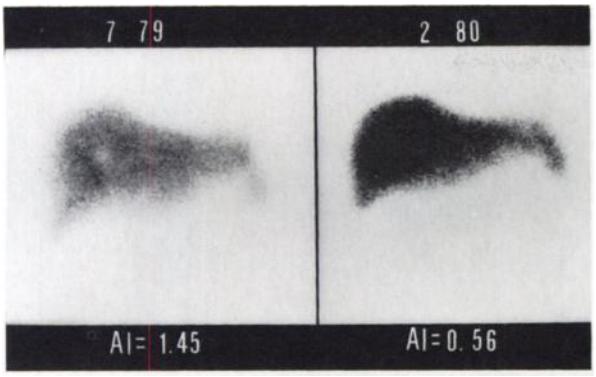

FIG. 6. Left: liver image in patients with malignant melanoma shows definite lesion in right lobe; AI is obviously elevated. Right: after treatment, image reverts to normal and AI has decreased considerably.

breast cancer patient with biopsy-proved metastic disease. Figure 6 shows the decrease in AI as liver metastases from melanoma improve with chemotherapy.

The inclusion of these routine quantitative liver-flow studies is a simple way of enhancing sensitivity of liver imaging in the detection of metastatic disease in patients with known malignancy. Each individual laboratory must establish its own criterion for abnormality if this test is to be used effectively. Further work is obviously necessary to ascertain whether patients with primary liver disease, extrahepatic disease other than neoplasia, or no disease, can be separated from those with metastatic disease.

FOOTNOTE

* Dynamic Low Energy-No. 615-252, Picker Corporation.

ACKNOWLEDGMENT

The assistance of Dr. Peter J. Sones, Jr. in obtaining the TCT images is gratefully acknowledged.

This work was supported in part by NIH Grant No. RR39.

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ERRATUM

In "Early Recollections of the Manhattan Project—Day of Criticality. Excerpts from an Address to the Society of Nuclear Medicine, 20 June 1977, Chicago, Illinois," by Harold M. Agnew (*J Nucl Med* 22:82-87, 1981) Dr. Agnew's name appeared incorrectly. His name should be Harold M. Agnew.