Improved Detection of Small Cavernous Hemangiomas of the Liver with High-Resolution Three-Headed SPECT

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The purpose of this study was to review our experience with ^{99m}Tc-red blood cell scintigraphy for diagnosis of cavernous hemangiomas of the liver using a new three-headed, high-resolution dedicated SPECT system. Of 19 patients referred with a total of 38 lesions seen on CT, US, or MRI, 14 patients had 24 lesions that were hemangioma-positive with SPECT (all true-positives). Six of these 14 patients also had 9 hemangioma-negative lesions; all were ≤1.3 cm in size and false-negative. The remaining five patients had hemangioma-negative lesions only (1 false-negative, 4 true-negatives). Two hemangiomas were seen by SPECT that were not detected by CT, US, or MR. The sensitivity for hemangiomas ≥1.4 cm. was 100% (20/20). The sensitivity was 33% for lesions 0.9–1.3 cm, and 20% for lesions ≤0.8 cm. The smallest hemangioma detected was 0.5 cm. These results show a definite improvement in sensitivity with high-resolution triple-headed SPECT over previously reported results using single-headed SPECT. High-resolution SPECT has improved our ability to detect small cavernous hemangiomas of the liver.

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Technetium-99m-labeled red blood cell (Tc-RBC) liver scintigraphy has been previously reported to be very useful for diagnosing cavernous hemangiomas of the liver (*1–10*). Although the specificity of this technique approaches 100%, the sensitivity is dependent on lesion size and the technology used. Generally, planar imaging is able to detect hemangiomas 3 cm in size and larger, while single-photon emission computed tomography (SPECT) has been routinely able to diagnose hemangiomas down to a size of about 2 cm (*1–8*). Although some recent studies, using single-headed SPECT systems, have reported detection of liver hemangiomas less than 2 cm in size, the sensitivity for these small lesions has been poor (*9–10*).

New high-resolution three-headed rotating SPECT systems recently have become commercially available. Initial experience with this three-headed gamma camera showed an improved ability to detect smaller liver lesions compared to conventional single-headed SPECT (*11*). The purpose of this study is to review our overall experience using Tc-RBC scintigraphy with this high-resolution SPECT system to diagnose hemangiomas of the liver with emphasis on determining the sensitivity of this new camera for detecting small hemangiomas of the liver.

METHODS

Twenty-seven patients with indeterminate hepatic lesions seen on computed tomography (CT), ultrasonography (US), and/or magnetic resonance imaging (MRI) were referred for Tc-RBC scintigraphy between August 1988 and April 1990. In 19 patients adequate imaging, clinical and pathologic follow-up were available to establish a definitive diagnosis, and these patients form the basis for this report. The patients were referred because of findings on imaging studies that were suggestive but not necessarily specific for hemangioma of the liver. The patient population included 7 men and 12 women ranging in age from 27 to 74 yr (mean 51). Eight patients had a known primary diagnosis of malignancy, including breast cancer (4), colon cancer (2), hepatoma (1), and squamous-cell cancer of the lung (1).

Tc-RBC liver scintigraphy was performed after labeling the patient's RBCs with 925 MBq (25 mCi) [^{99m}Tc]pertechnetate using the modified in-vivo technique (*12*). An initial 60-sec flow study was performed (1-sec frames), followed by immediate planar images in at least four views (usually anterior, posterior, right lateral, and left lateral). This was followed by delayed planar images for one million counts 20–30 min after injection in the same projections. SPECT was performed, starting 30–60 min after injection, using a three-headed rotating gamma camera (Triad, Trionix Research Laboratories, Twinsburg, OH) with ultra high-resolution collimators. Acquisition time was 26 min, 40 sec with 120 images acquired over 360° (40 images/120°/detector). Reconstruction was performed using filtered backprojection and first-order Chang attenuation correction.

The SPECT studies were reviewed and interpreted on a Sun Computer (Sun Microsystems, Mountain View, CA) by consensus of at least two experienced nuclear medicine physicians. All cross-sectional transaxial, coronal, and sagittal slices were reviewed. A lesion was interpreted as hemangioma-positive if ra-

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diotracer uptake within the lesion seen on correlative US, CT, or MRI was greater than adjacent liver and clearly differentiated from normal vascularity. Planar analog images were also interpreted as positive if delayed imaging showed uptake greater than adjacent liver. The flow phase and presence or absence of a "filling-in" from immediate to delayed imaging were not used as diagnostic criteria.

US was performed using commercially available real time sector scanners. Imaging was performed at 3.5 or 5.0 MHz. CT was performed using a GE 9800 CT/T (General Electric Medical Systems, Milwaukee, WI) (400 mas, 120 kVP, 10 mm collimation). Non-contrast scans followed by dynamic, enhanced images and delayed scans to a maximimum of 30 min were selectively performed. Contrast (60% urographic) was injected via a power injector at a rate of 1.2–1.5 cc/sec up to a total of 150 cc. MR was performed with a Siemen's Magnetom (Siemen's Medical Systems, Iselin, NJ) operating at 1.5 Tesla. T1-weighted scans (400–600/15, 4 acquisitions, 256 × 256 matrix) and triple echo T-2 weighted scans (2000/45,90 or 2000/30,80,150, 2 acquisitions, 256 × 256) were performed. Gradient movement reduction was used to supress motion on the T-2 weighted images.

The CT, MR, and US studies were reviewed by two experienced abdominal imaging radiologists. All lesions were sized in two dimensions. The mean diameter was used for lesion size comparison.

The final diagnosis was determined by either autopsy, biopsy, aspiration with cytology, serial US, CT, and/or MR imaging, and clinical follow-up. A true-positive study was defined as a Tc-RBC study interpreted as positive for hemangioma and the diagnosis confirmed. A false-positive study was read as positive on Tc-RBC scintigraphy, but another diagnosis was determined. True-negative studies were defined as hemangioma-negative with Tc-RBC, and a diagnosis other than hemangioma was established. A false-negative study was hemangioma-negative with Tc-RBC, no definitive diagnosis other than hemangioma was made, and the patient had 12–24 mo of benign clinical and imaging follow-up. All such lesions were considered to be hemangiomas for the purpose of this study, although a number of other benign etiologies were possible. This could serve to overestimate the false-negative rate. The overall and size-dependent sensitivity [(TP/(TP + FN)] and specificity [TN/(TN + FP)] were then calculated.

TABLE 1
SPECT Lesion Size, Scan Interpretation and Final Diagnosis

Patient no.	Lesion size	Hemangioma Pos.	Hemangioma Neg.	TP	TN	FN
1	4.0	+		X		
2	2.0	+		X		
3	4.0	+		X		
4	3.0	+		X		
5	1.9	+		X		
	0.9		–	X		X
6	3.5	+		X		
7	1.5	+		X		
	1.3		–			X
	1.0		–			X
	0.5	+		X		
8	1.5	+		X		
	1.3		–			X
	0.8		–			X
9	1.7	+		X		
	1.3	+		X		
	1.1		–			X
10	6.5	+		X		
	0.9	+		X		
11	3.6	+		X		
	1.3		–			X
12	2.5	+		X		
	1.8	+		X		
	1.5	+		X		
	0.7		–			X
	0.5		–			X
13	2.9	+		X		
	1.8	+		X		
	1.0	+		X		
14	3.5	+		X		
	2.9	+		X		
	2.4	+		X		
	1.4	+		X		
15	3.6		–		X	
16	5.5		–		X	
17	6.8		–		X	
18	1.8		–		X	
19	1.2		–			X
Total		24	14			

RESULTS

A total of 19 Tc-RBC SPECT studies were reviewed. The patients had been referred for lesions seen on CT (9), US (4), both US and CT (4), or MR (2). There were a total of 38 lesions ranging in size from 0.5 cm to 6.8 cm (mean 2.2 cm).

Of the 19 SPECT studies, 14 were hemangioma-positive with a total of 24 hemangioma-positive lesions that corresponded to the lesions seen on CT, US, and/or MR. The number of hemangioma-positive and negative lesions for each patient is shown in Table 1. Eight patients had one positive lesion, three patients had two, two patients had three, and one patient had four hemangioma-positive lesions. The 24 hemangioma-positive lesions ranged in size from 0.5 cm to 6.8 cm in size (Table 1). Half (12) of the hemangioma-positive lesions detected measured less than 2 cm in size and five were less than 1.5 cm (1.4, 1.3, 1.0, 0.9, 0.5 cm, see Figs. 1–2).

All 24 SPECT hemangioma-positive lesions seen in 14 patients were determined to be true-positives. One patient had autopsy and another patient had biopsy confirmation. The remainder had lesions on correlative imaging consistent with hemangioma and unchanged imaging and clinical follow-up of 12–24 mo (mean 18 mo). Two of the 14 SPECT-positive patients had one additional positive lesion assumed to be hemangiomas that were not detected by either CT, US, or MRI, one located at the tip of the right lobe and the other at the distal tip of the left lobe. These could not be accurately sized, but appeared to be less than 2 cm in size. These were not included in the statistical analysis. Six of the 14 hemangioma-positive patients also had 9 hemangioma-negative lesions. All were ≤1.3 cm in

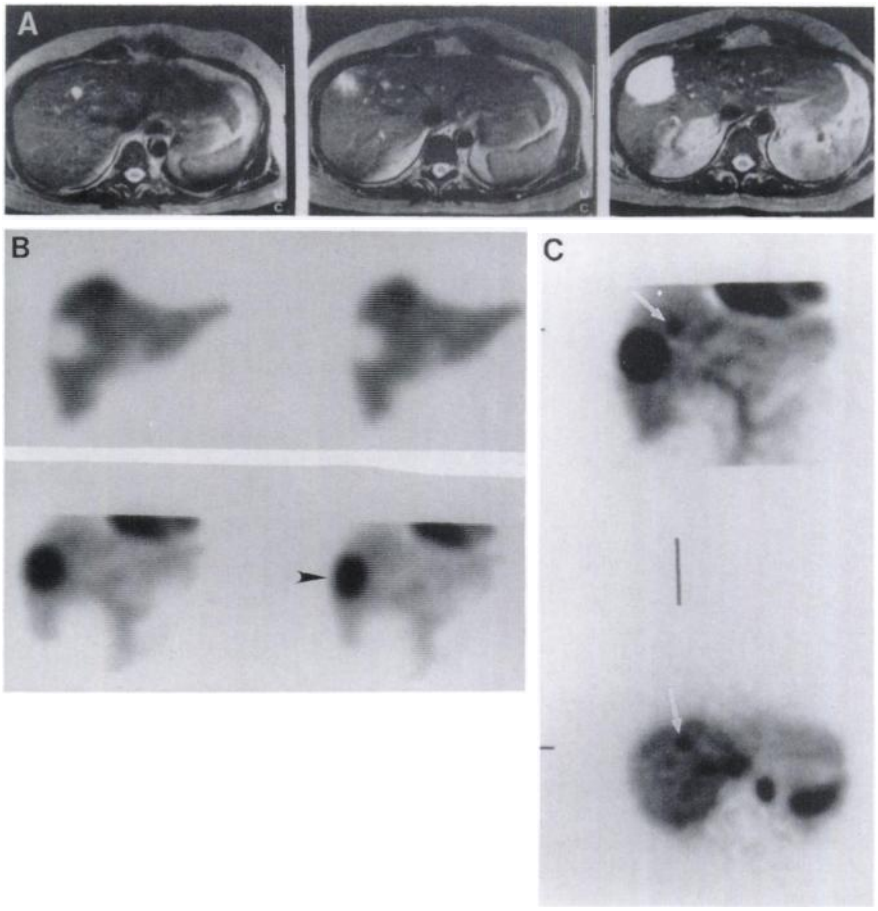

FIGURE 1. (A) T2-weighed MR image. Three selected sequential transaxial slices showing two lesions adjacent to each other, one large (6.5 cm) in the right slice and one small (0.9 cm) in the left slice.. The middle slice has partial volume images of both lesions, but shows their close proximity. (B) Single-headed conventional SPECT showing two coronal slices: (above) the patient's ^{99m}Tc-SC liver spleen scan and (below) comparable ^{99m}Tc-RBC slices. The large lesion is clearly seen as hemangioma-positive on the Tc-RBC study (arrowhead), however, the smaller lesion was not seen. (C) Triple-headed SPECT. The coronal (above) and transaxial (below) slices clearly resolve the small 0.9 cm hemangioma (arrows) not seen in B with the single-headed SPECT camera. The other "hot" regions in the transverse slice are, from left to right, the portal vein, inferior vena cava, aorta, and spleen.

size and were determined to be false-negatives, as described above.

The five patients with hemangioma-negative SPECT studies had one hemangioma-negative lesion each (no positive lesions). One was false-negative, determined by serial imaging and clinical follow-up of 24 mo. Four were true-negatives. The true-negative diagnoses included hepatic cyst (2), colon cancer (1), and hepatoma (1). The malignant tumors were diagnosed by biopsy, the cysts by ultrasound with aspiration and cytology and 12 mo follow-up.

Eight patients with 15 lesions had a history of an underlying primary malignancy. Of these, only two patients had true-negative lesions (2) due to cancer. The other six patients had ten true-positive lesions and four false-negative lesions. No patient had both a hemangioma- and a true-negative lesion.

With SPECT there were a total of 24 true-positives, 4 true-negatives, 10 false-negatives, and no false-positives. The specificity for hemangiomas was 100% (4/4). The sensitivity of SPECT for detecting one hemangioma per true-positive patient was 100% (14/14). The sensitivity for detecting individual hemangiomas was 71% (24/34). The sensitivity for detecting hemangiomas was very dependent on lesion size (Table 2). The sensitivity for lesions ≥1.4 cm was 100% (20/20), for hemangiomas 1.0–2.0 cm, 65% (11/17), and for lesions 0.9–1.3 cm, 33% (3/9). We detected one of five lesions ≤0.8 cm (20%).

Planar imaging diagnosed nine hemangioma-positive lesions in nine patients. Two patients with five lesions on correlative imaging did not have planar images adequate for interpretation. The planar hemangioma-positive lesions ranged in size from 1.9 to 6.8 cm. The sensitivity of planar imaging for diagnosing at least one hemangioma per true-positive SPECT patient was 75% (9/12). For individual hemangiomas, the overall sensitivity of planar imaging was 30% (9/30). The sensitivity for hemangiomas ≥1.9 cm was 69% (9/13) and for hemangiomas ≥ 1.4–2 cm, 20% (2/10). All but one patient had normal flow; a large cyst (6.8 cm) had relatively decreased flow.

DISCUSSION

Cavernous hemangiomas are the most common benign tumor of the liver and usually require no specific therapeutic interventions. However, differentiating hemangiomas from more serious metastatic involvement of the liver is a frequent clinical dilemna. Hemangiomas are often detected incidentially on US or CT examinations during routine investigation for a variety of unrelated clinical problems or in the staging of a known primary malignancy. Although US is quite sensitive for detecting liver hemangiomas, it is not at all specific (*13–15*). CT, on the other

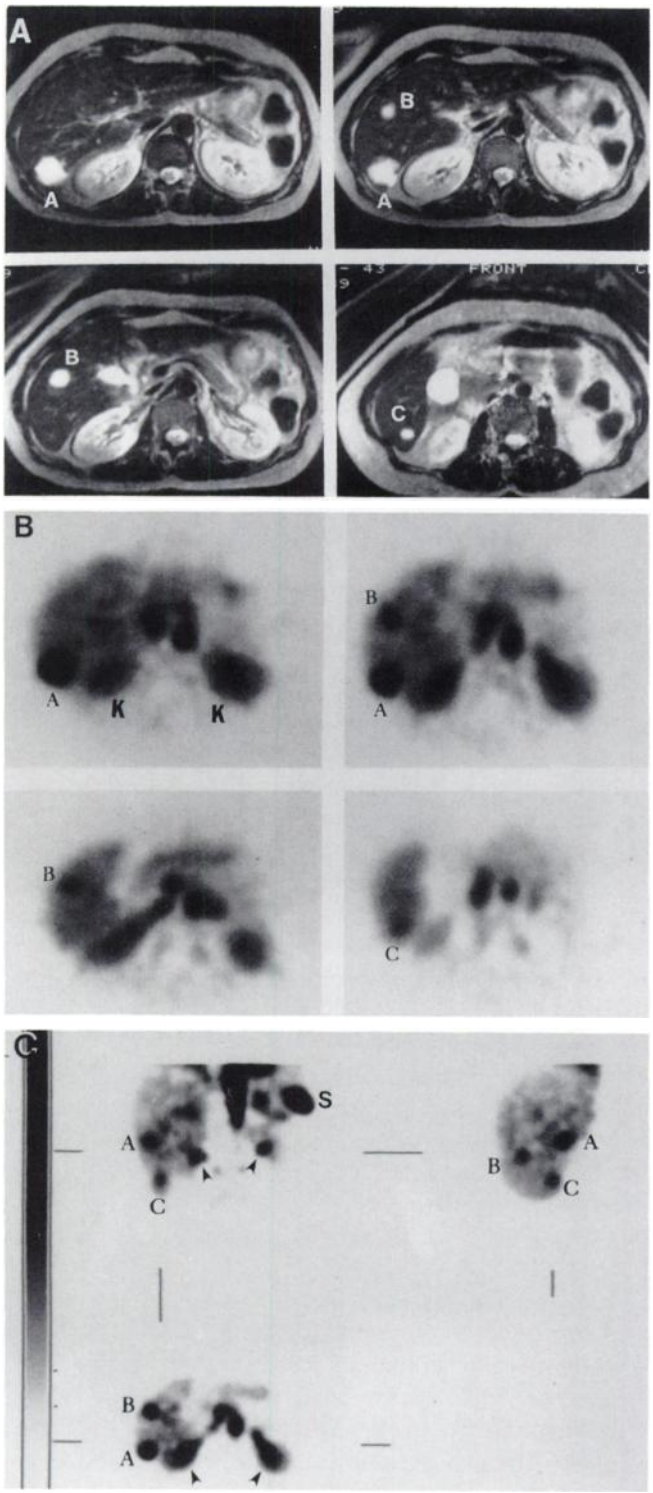

FIGURE 2. (A) T2-weighted MR study with four selected slices (from top left to bottom right) showing three hemangiomas measuring 2.5 (A), 1.8 (B), and 1.0 cm (C) in size. The MR and Tc-RBC studies were ordered as a result of abnormal ultrasonography demonstrating the two larger lesions. (B) Three-headed SPECT with transaxial slices comparable to the selected MR cuts in A. All three images (A, B, C) are hemangioma-positive. The kidneys (K) are noted. (C) Three-view computer display with triple-headed SPECT (same patient in B). Two lesions are clearly seen in the coronal and transaxial views, and all three hemangiomas are seen in the sagittal slice. The hemangiomas are again marked as A, B, C. The spleen (S) and adjacent kidneys (arrowheads) are noted. Reviewing all cross-sectional slices ensures differentiation of small hemangioma from normal vascularity.

TABLE 2
Sensitivity by Lesion Size with Three-Headed SPECT

Lesion size (cm)	Sensitivity
≥1.4	100% (20/20)
≥1.3	91% (21/23)
1.0–2.0	65% (11/17)
0.9–1.3	33% (3/9)
0.5–0.9	20% (1/5)

hand, is very specific for the diagnosis of hemangioma when strict criteria are used, however, the diagnosis of hemangioma can only be made with certainty 55%–76% of the time (*16,17*).

Tc-RBC scintigraphy is the most specific test available for the noninvasive diagnosis of cavernous hemangioma of the liver. In over 10 years of routine clinical use, few false-positive studies have been reported (*2,6,18,19*). Early studies suggested a 100% sensitivity. However, as larger and more general referral populations were studied it became obvious that the ability to detect hemangiomas with Tc-RBC scintigraphy was dependent on two factors: (1) whether planar or SPECT imaging was performed and (2) the size of the lesion.

Many studies have now shown the clearcut superiority of SPECT over planar imaging for detection of cavernous hemangiomas of the liver (*4–9*) (Table 3). SPECT is better able to detect hemangiomas that are small, multiple, centrally located, and those adjacent to the heart, spleen, kidney, and large vessels (*4–9,20*). Since most hemangiomas are less than 3 cm in size, the sensitivity and predictive value of a negative study for smaller lesions is an important concern and the main thrust of this paper. Studies using single-head SPECT technology have reported a high sensitivity for diagnosis of cavernous hemangiomas of the liver measuring 2 cm in size and larger, but have found a poorer sensitivity for smaller lesions (*9,10*). Kudo et al. reported SPECT sensitivity of 83% for detecting hemangiomas between 2.1–3.0 cm, but only 38% for lesions 1.1–2.0 cm in size (*9*). Another recent study by Birnbaum et al. reported a 92% sensitivity for hemangiomas 2.0–2.9 cm in size, but only 58% for lesions 1.0–1.9 cm (*10*). The results of our study compare quite favorably. The triple-headed SPECT camera was able to detect smaller hemangiomas than previously reported with single-headed SPECT. Half of the hemangiomas detected were smaller than 2 cm in size and five were less than 1.5 cm (1.4, 1.3, 1.0, 0.9, 0.5 cm). Most importantly, in our study, the sensitivity for cavernous hemangiomas 1.4 cm and larger was 100%. In contrast, the single-headed SPECT studies discussed above detected only 50%–67% of the

TABLE 3
SPECT Versus Planar Sensitivity for Liver Hemangiomas and Size of Smallest Hemangioma Detected by SPECT

First author	Year	Reference	Sensitivity		Smallest hemangioma
			Planar	SPECT	
Tumeh	1987	4	43% (20/23)	100% (23/23)	1.3
Malik	1987	5	77% (10/13)	100% (13/13)	
Brodski	1987	7	44% (8/18)	78% (14/18)	1.0
Brown	1987	21			1.0
Itenzo	1988	6	88% (14/16)	100% (16/16)	
Brunetti	1988	8	69% (27/39)	100% (39/39)	0.7
Kudo	1989	9	42% (36/85)	74% (63/85)	1.4
Birnbaum	1990	10			1.0
Ziessman	1991		30% (9/30)	71% (24/34)	0.5

hemangiomas in the size range of 1.4–2.0 cm (*9–10*). The 0.5 cm hemangioma detected in our study is the smallest hemangioma reported to date with SPECT RBC scintigraphy (*4,7–10,21*) (Table 3). The resolution of our camera system using ultra-high collimators is about 11 mm. A new super-fine high-resolution collimator with even better resolution is being developed which could further improve these results.

Lesions adjacent to major vessels may be difficult to resolve. A recent study found limited sensitivity with single-headed SPECT for lesions 2.5 cm and smaller adjacent to the heart, spleen, kidney, and major vessels (*10*). Although we did not have difficulty with lesions adjacent to these organs unless they were smaller than 1.4 cm, small centrally located lesions adjacent to major vessels within the liver were sometimes difficult to diagnose with certainty. Correlation with CT or MRI at the time of interpretation is critical in differentiating hemangiomas from normal vascular anatomy.

Seven patients in our study with lesions positive for hemangioma also had hemangioma-negative lesions. All were less than 1.4 cm in size and were false-negatives. Although the diagnosis of a hemangioma on Tc-RBC scintigraphy does not rule out other concommitant disease, it does seem to increase the likelihood that the other liver lesions are also hemangiomas.

As previously reported, we confirmed a poorer sensitivity for planar imaging than with SPECT. In this series it was somewhat less than previously published reports (Table 3), which is probably due to several factors. First, we had a larger number of small lesions referred for evaluation compared to many previous studies. We also usually limited our planar imaging to four standard views and performed delayed planar imaging relatively early (20–30 min after injection). Although previous reports have found that most hemangiomas will have diagnostically increased uptake within 15 min after injection (*2*), we have seen exceptions, i.e., planar studies that were negative at 20 min, but positive when repeat planar imaging was performed after SPECT at about 90 min (*20*). SPECT imaging as early as 30 min after injection did not seem to be a problem, although we would still advise starting SPECT imaging at 45–60 min after injection. We did not find the flow or immediate images to be helpful. We feel that SPECT alone is diagnostic and planar imaging is unnecessary.

SPECT's ability to detect small lesions is dependent primarily upon the lesion's contrast relative to background noise. A lesion much smaller than the resolution of the instrument will be detectable if it has high contrast. SPECT is more sensitive than planar imaging for detecting hemangiomas because the reconstruction process greatly enhances lesion contrast. However, if lesion size is less than twice the resolution of the system, its image contrast will be reduced. Therefore it is important to maintain high resolution. There is an optimal compromise between sensitivity and resolution with regard to the detection of small, high-contrast lesions such as hemangiomas. The three-fold increased sensitivity of the three-headed camera relative to a single-headed unit allows the flexibility to obtain adequate counts while imaging with an ultra high-resolution collimator. As a result, our spatial resolution was improved and we were able to detect both smaller and more hemangiomas than single-head SPECT, as well as occasional hemangiomas not seen on contrast CT or MRI.

MRI has been reported to be an accurate test for the diagnosis of cavernous hemangiomas. Although there have been very few comparative studies, one recent report comparing MR with single-headed SPECT found a similar sensitivity and accuracy for hemangiomas 2 cm and larger, however, MRI had better sensitivity for detecting lesions less than 2 cm in size (MR 83% versus SPECT 58%) (*10*). The "light bulb sign" on the T-2 weighted MR image is characteristic of hemangioma, however, its specificity is still less than Tc-RBC scintigraphy. A number of malignant metastatic liver tumors, including islet cell tumors of the pancreas, metastatic carcinoid, pheochromocytoma, metastatic lung cancer, various sarcomas, and adenocarcinomas of the pancreas and uterus have a similar appearance (*10,22,23*).

There were no false-positives encountered in our study. The specificity of Tc-RBC scintigraphy for diagnosing cavernous hemangiomas of the liver is extremely high. Few false-positive studies have been reported, including four hepatomas and one angiosarcoma of the liver (*2,6, 13–14*). Although hepatomas have been the most commonly reported cause of false-positives, in fact, most hepatomas are negative on Tc-RBC scintigraphy. In a recent study of 46 hepatomas less than 5 cm in size, none had increased uptake on delayed Tc-RBC liver imaging (*9*). Angiosarcomas are extremely rare. Therefore, the predictive value of a positive Tc-RBC study approaches 100%.

In conclusion, high-resolution SPECT is the technique of choice for confirming the diagnosis of liver hemangiomas 1.4 cm and larger because of its high specificity and sensitivity for detecting these small lesions. Heman-

giomas down to a size of 0.5 cm may be detected, although SPECT has less sensitivity for detecting these smaller lesions.

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