Acute Gastrointestinal Bleeding

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Radionuclide bleeding scintigraphy remains a simple yet powerful method of localizing sites of gastrointestinal hemorrhage and is most commonly performed today using the red blood cell technique. Radionuclide techniques for detecting bleeding remain safe, sensitive, and noninvasive. Based on several simple concepts, including the use of cine-mode imaging over the abdomen, it is possible to achieve excellent accuracy in localizing the site of bleeding. Studies often contain additional ancillary information, which is helpful for diagnosis and patient treatment.
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FOR OVER 20 years, bleeding scintigraphy has been used as an effective method for localizing sites of gastrointestinal bleeding and until today maintains an important clinical niche. This review will consider the technical methodology for performing bleeding scintigraphy, guidelines of interpretation, and clinical results.

CLINICAL ROLE OF BLEEDING SCINTIGRAPHY

Localization of the site of acute gastrointestinal bleeding is important to patient treatment. The origin of the bleed is helpful for determining the initial catheter placement at angiography and is critical for directing a surgical approach if emergency resection is required. When a patient presents with significant gastrointestinal hemorrhage, a gastric etiology should be excluded clinically by evaluation of the nasogastric aspirate. Bleeding scintigraphy then has a useful role to play in localizing the bleed to small or large bowel, originating in either the right or left colon.

Radiopharmaceuticals

Historically, 2 radiotracers have predominated in the radionuclide localization of acute gastrointestinal bleeding, ^{99m}Tc-labeled red blood cells (RBC)[1] and ^{99m}Tc-labeled sulfur colloid (SC).[2] Localization of ectopic gastric mucosa, such as in Meckel's diverticulum, will be discussed later. It is amusing to reflect that intravascular clearances of RBC and SC radiopharmaceuticals are polar opposites. RBC have a stable persistence within the blood pool, while the predominant characteristic of SC as a blood pool label is rapid intravascular clearance, with a half-time of approximately 2 to 3 minutes. By 10 to 15 minutes after administration, SC has completely cleared from the blood pool into the liver, spleen, and, to a lesser degree, the bone marrow, while RBC activity is essentially unchanged. Relevant features of bleeding scintigraphy follow from these fundamental differences. Crenated RBC have also been proposed for use in bleeding scintigraphy, with blood pool clearances intermediate between SC and RBC.[3] Their half-time of clearance of 6 to 11 minutes allows for an intermediate period of imaging. Clearance of these large particles is primarily to the spleen, with relatively less activity accumulating in the right upper quadrant in the liver. Although interesting conceptually, the use of this radiopharmaceutical has not been widespread.

Because gastrointestinal bleeding is typically intermittent and episodic, the ability to image over a prolonged period is attractive, which theoretically favors RBC scintigraphy.[4] In many current protocols, red cell imaging is performed to 90 minutes, based on early clinical studies that suggested that the yield of positive studies will plateau by that time, detecting 83% of all active hemorrhage.[5] Some investigators have advocated retrieving patients for further-delayed imaging, such as at 6 and 24 hours. However, the clinical value of detecting previously extravasated blood in the colon, without observing the actual episode and site of extravasation, is negligible.

The relative disadvantage of using RBC is the persistence of background activity in vessels and blood pool throughout the study, which will theoretically increase the threshold for the amount of bleeding needed for detectability. In contrast, SC, which completely clears the blood pool by 10 to 15 minutes after injection, will be easier to detect in the absence of background activity. In reality, because of the intense uptake in the liver and spleen, bleeding may be difficult to detect in the upper abdominal region when using SC, while marrow background activity is also noted in the remainder of the abdomen. The importance of these theoretical considerations on the imaging of gastrointestinal bleeding has been studied in animal models and human studies.

Studies in anesthetized dog models have estimated that the amount of blood necessary for detection during SC scintigraphy is 0.05 to 0.1 mL/minute.[6] In an analogous study, the minimum bleeding rate required for detection of RBC was quite comparable, although at the lowest detectible bleeding rate of 0.04 mL/minute, 55 to 63 minutes elapsed before detection after an estimated total extravasation of 2.0 to 2.4 ml.[7] Smith and colleagues have also observed in patients that the intensity of visualization of bleeding on RBC scintigraphy and time of appearance correlate with transfusion requirements and bleeding rates.[8] Clinical studies that have

Table 1. Sensitivity for Detecting Gastrointestinal Bleeding

	Experimental and Clinical Models	
	Time	Investigator
Angiography	0.5-1 ml/min	
^{99m}Tc-SC	0.05-0.1 ml/min*	Alavi et al[6]
^{99m}Tc-RBC	0.04 ml/min* (seen at ~1 hr)	Thorne et al[7]
	2–3 ml Blood necessary	
	Rate-dependent time until positive	
^{99m}Tc-RBC	Minimal rate 0.1 ml/min†	Smith et al[8]

*Anesthetized animal models.
†Clinical study.

directly compared SC and RBC when sequentially performed in the same patients have favored RBC over SC.[5,9] In one study of 100 patients referred for suspicion of gastrointestinal bleeding, from whom good surgical, radiologic, and clinical follow-up was obtained, RBC detected 38 true positive sites of bleeding, while SC only detected 5.[5]

Currently, most clinical imaging laboratories have adopted RBC scintigraphy as the preferred method of localizing gastrointestinal bleeding, and this is the primary method cited in the Society of Nuclear Medicine's Procedure Guideline.[10] Nonetheless, proponents of SC bleeding scintigraphy still maintain its advantage, citing easier and quicker preparation, and comparable accuracy. In a recent article reviewing the experience at the University of Pennsylvania, no statistically significant difference was noted between sensitivity of the 2 examinations (24.4% for SC and 27.5% for RBC; $P = 0.71$).[11] Of interest is that sensitivity for both examinations was higher during the day than during the evening call, a phenomenon the investigators attributed to an increased delay before test performance when performed in the evening.

In comparison with radionuclide studies, angiography is approximately 10-fold less sensitive for detecting bleeding (Table 1).[6] Various reasons have been postulated for the limited sensitivity of angiography for detecting gastrointestinal hemorrhage (Table 2). Both SC and RBC scintigraphy can detect venous as well as arterial bleeding, which is not the case for contrast angiography.

Occasionally, bleeding scintigraphy has been combined with anticoagulation to increase diagnostic yield.[12] This method was only moderately successful and has not been widely embraced, although it may have merit in a particular clinical situation.

Technique

The Society of Nuclear Medicine's guidelines represent an important consensus on optimal technique and form the basis of recommendations regarding RBC scintigraphy.[10] Optimal red cell tagging is of critical importance and is best achieved using the in vitro method, while the modified in vivo method is a less favored alternative. Because of poor tagging resulting in artifacts from free pertechnetate, the standard in vivo method is not recommended.

Technique should be optimized to extract the maximal information available from the study. It is worthwhile to obtain dynamic scintiphotographs of the anterior abdomen at a few seconds per frame for 1 minute after bolus injection of 20 to 30 mCi (750 to 1100 MBq) of radiotracer, to show flow to the abdominal viscera.[13] Only rarely will bleeding be identified on the dynamic blood flow images (Fig 1). Historically, multiple static images have then been acquired at several minute intervals throughout the period of observation, such as images of 1 minute duration taken at 5 minute intervals. Today, with the widespread use of computer-based gamma-cameras, it is preferable to leave the patient under the gamma-camera and acquire dynamic images at a frequency of 1 image per minute or higher. When replayed in cine-mode, these images provide a "movie"-type display of extravasation and peristalsis of labeled blood, and are more accurate than static images in the localizing of gastrointestinal bleeding.[15] Subtraction of baseline activity has been suggested as a helpful modification in patients who lie still.[16]

If no site of bleeding is apparent but the patient continues to pass blood per rectum during the study, it can be helpful to image the bed pan or a rectal glove to see if it contains radiolabeled material. If so, a rectal source should be further pursued. As a general rule, lateral or steep oblique views may be helpful for differentiating rectal from bladder activity. If by 90 minutes of imaging no bleeding site is observed, imaging may be terminated. Recalling the patient for further delayed images at 6 or 24 hours is not generally useful because bleeding that has occurred during the intervening period cannot be localized accurately. If there is evidence that the patient is subsequently rebleeding, it is worthwhile to restart a series of dynamic images to detect acute extravasation, possibly after reinjection of additional activity.

In the case of SC imaging, 10 mCi (370 MBq) of freshly prepared radiotracer are administered. Dynamic blood flow images should be acquired, followed by static imaging during a 20-minute period.

Table 2. Potential Causes of Angiographic Failure to Detect Gastrointestinal Bleeding (after Sos et al[4])

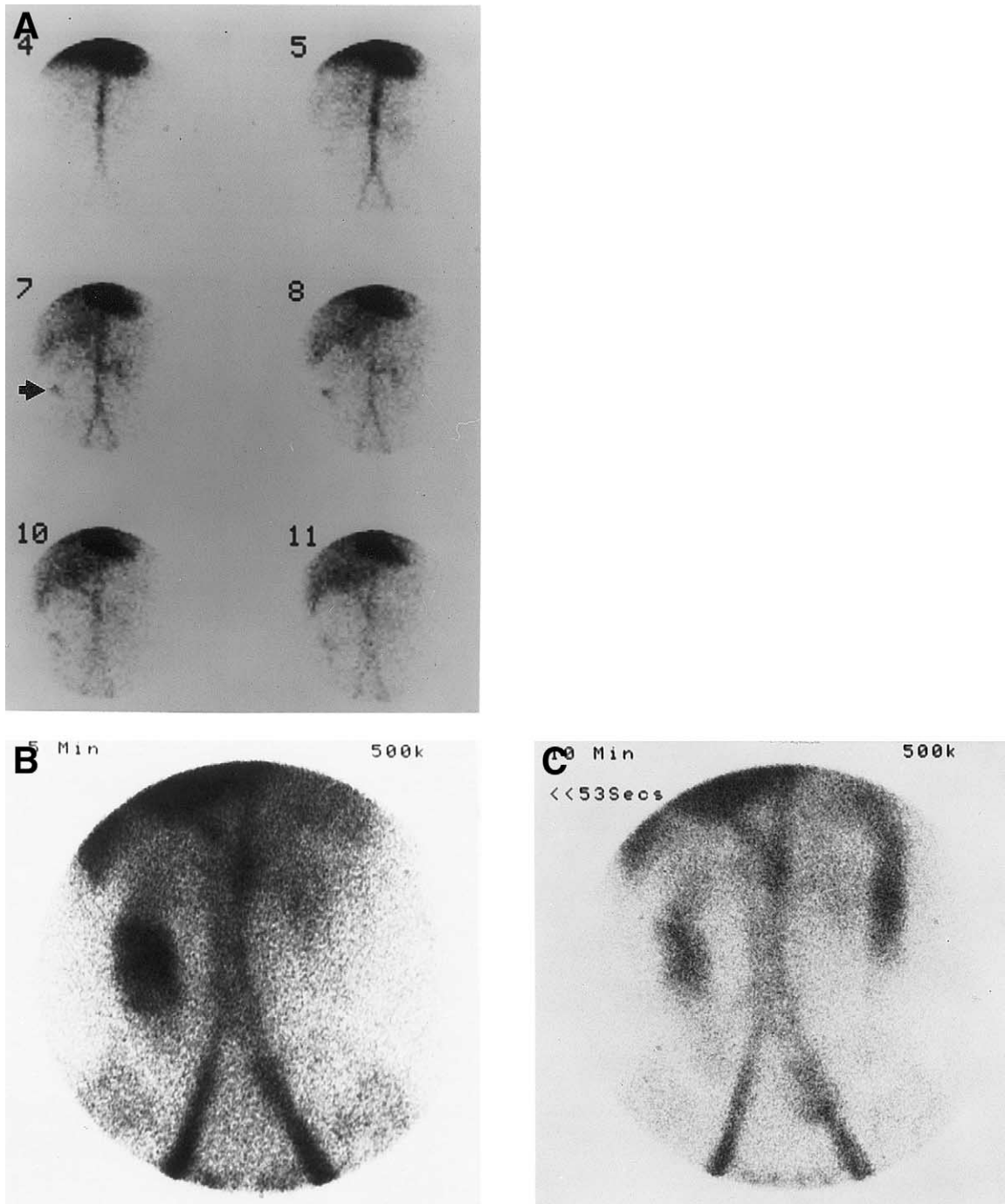| |
| --- |
| Hemorrhage < 0.5 ml/min |
| Venous (variceal) bleeding |
| Technical failure |
| Resolution of bleeding |
| Temporary cessation of bleeding |
| Hypotension |
| Intermittent source |

Fig 1. A 35-year-old man with 2 recent negative bleeding studies was recalled to the nuclear medicine department after recurrence of profuse rectal bleeding. (A) Selected 2-second anterior abdominal flow images after injection of radio-labeled red blood cells (RBCs) show sequential visualization of the abdominal aorta, kidneys, and liver. An abnormal accumulation of activity is seen in the right flank by frame 5 that subsequently increases in intensity by frames 7 (arrow) and 8, and represented the source of bleeding. (B) Five-minute static image shows marked extravasation into the cecum. (C) By 10 minutes, extravasation has spread throughout the colon, thereby obscuring the original source of bleeding. Reprinted with permission.[14]
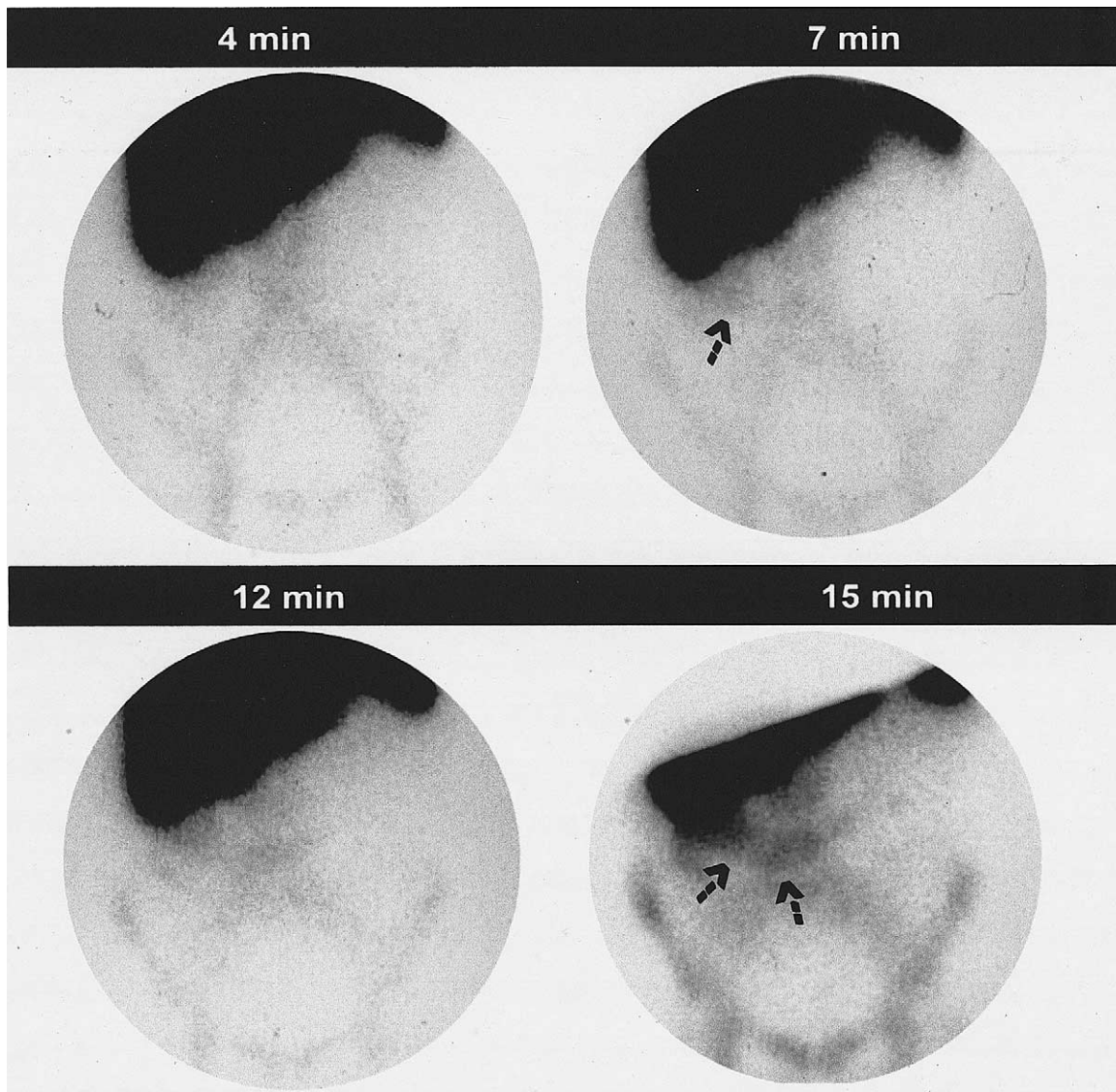
Fig 2.   Sulfur colloid (SC) bleeding scan was performed in an 80-year-old women on anticoagulants who presented with rectal bleeding. Extravasated blood is partially seen in the hepatic flexure on the 7-minute image (arrow) but is best seen in the transverse colon at 15 minutes after peristalsis and with increased image intensity (double arrows).

The intensity of the gamma-camera should be adjusted so that the marrow is visualized. After 10 minutes, it is worthwhile to obtain oblique images of the upper abdomen to help separate activity within the bowel from intense liver and spleen uptake. Slightly delayed images also allow for migration of upper bowel activity into a more readily observable location (Fig 2). If possible, the liver and spleen should be imaged at appropriately windowed levels to look for relevant pathology, such as evidence of cirrhosis or metastatic disease (Figs 3 and 4).

Interpretation of Bleeding Scintigraphy

The end point of interpretation of RBC and SC scintigraphy is the identification and localization of extravasation of activity from the blood pool into the bowel lumen, which is a topographically segregated space within the body. Heuristically, it is worthwhile to break down interpretation of bleeding scintigraphy into finite, discrete steps. Radionuclide methods for detecting gastrointestinal bleeding sequentially depend on visualization of the extravasation of radiotracer from the
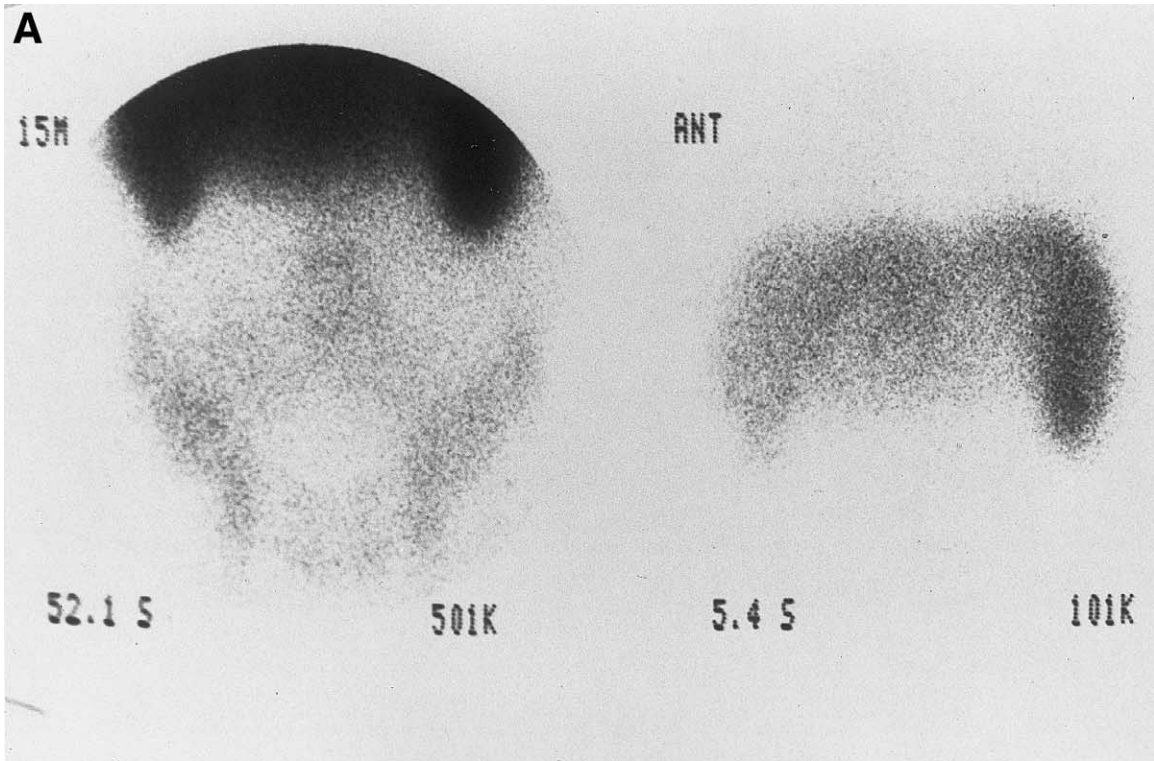
Fig 3. (A) Sulfur colloid (SC) study at bleeding intensity (left panel) and liver intensity (right panel). On properly windowed images, the liver is noted to be small, with a colloid shift to the spleen, indicative of hepatic cirrhosis. (B) CT shows a small liver with prominent ascites. Reprinted with permission.[16]
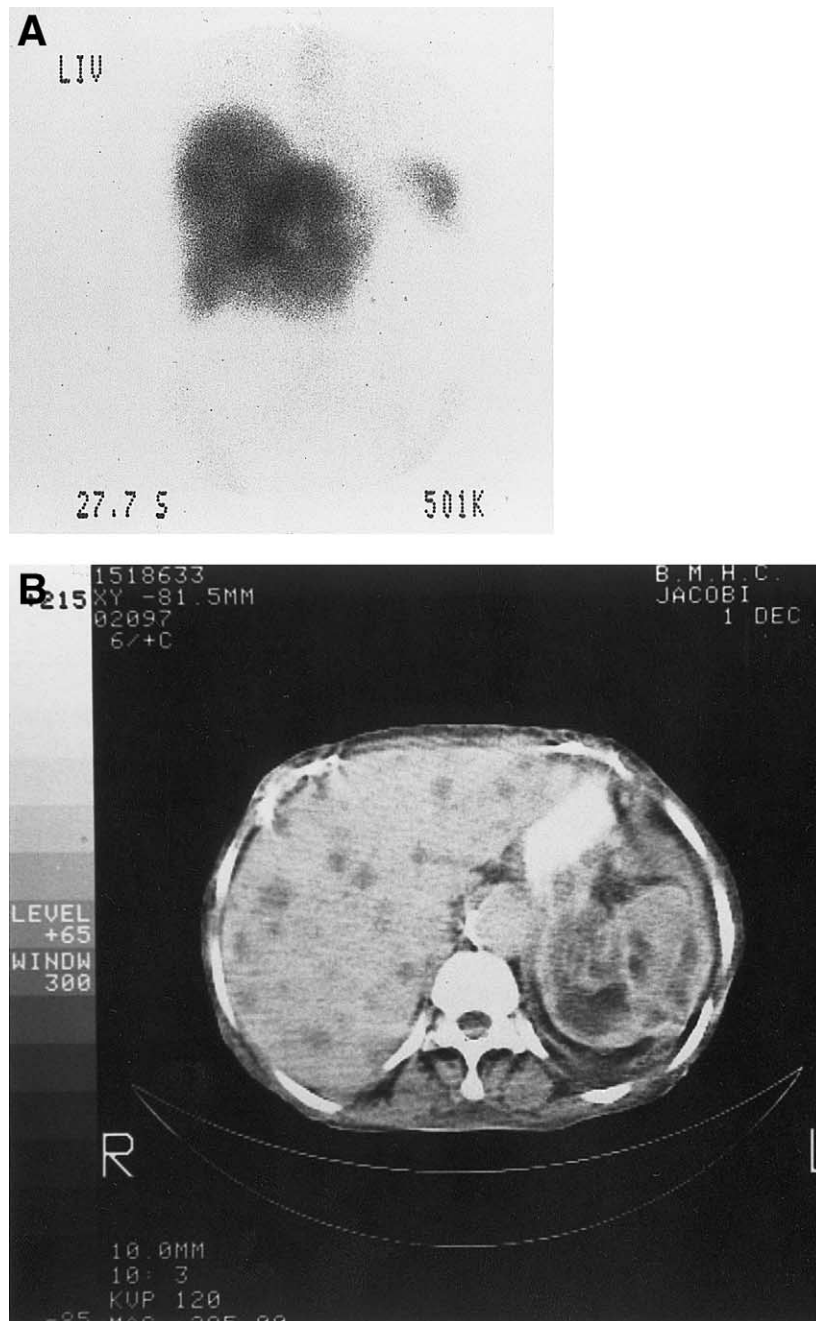
Fig 4. (A) Anterior view of abdomen, obtained at optimal intensity setting for liver and spleen, after the administration of SC in a 71-year-old woman demonstrates multiple focal defects in the liver. (B) CT scan of the liver, obtained with oral and intravenous contrast, demonstrates multiple focal hepatic defects, proven at percutaneous liver biopsy to be metastatic adenocarcinoma. Reproduced with permission.[17]

vascular space into the bowel lumen, classification of the involved segment of bowel, and, subsequently, identification of the regional subsegment of bowel involved. Bleeding into the bowel must first be differentiated from other collections of activity that appear on RBC or SC scintigraphy. The chief feature specific for characterizing a focus of activity as being located in the bowel is the prompt movement of the extravasated blood within the
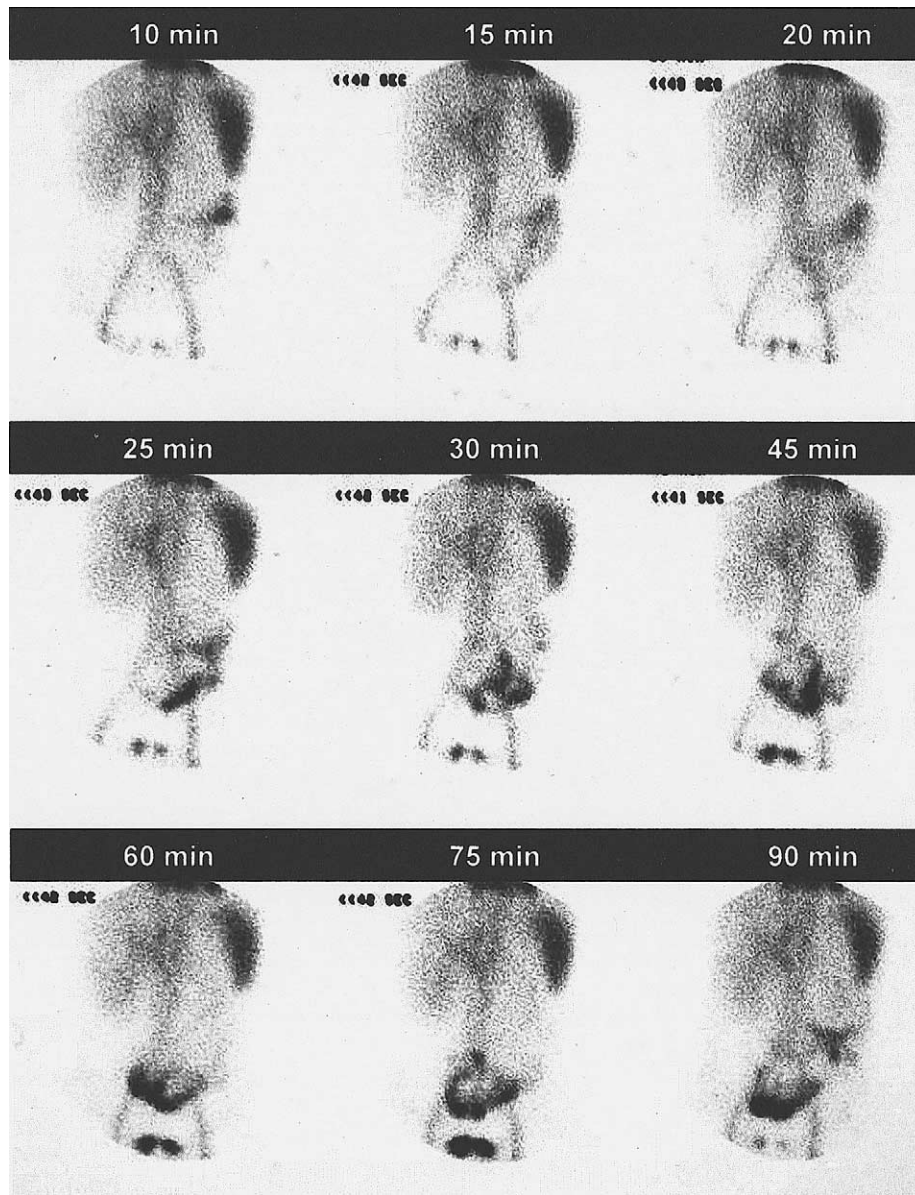
Fig 5.   Red blood cell (RBC) study was performed in a 45-year-old male with known cirrhosis. Findings typical of small bowel bleeding are noted, including central location, and rapidly changing appearance of small bowel segments from frame to frame.

lumen, stimulated by its cathartic properties (Figs 5 and 6). In contrast, static areas of abnormality generally represent other physiologic and pathophysiologic processes, such as varices, excreted renal activity, or areas of inflammation or tumor blush. Occasionally, the static area of abnormality may reveal the underlying pathology responsible for the bleed, although movement of extravasated blood is not seen during the study (Fig 7).

Other incidental abnormalities contributory to patient care are frequently observable on bleeding scintigraphy.[17] In a 5-year retrospective review of 132 RBC and SC studies performed for acute gastrointestinal hemorrhage at the Bronx Municipal Hospital Center, approximately half the patients had incidental abnormalities relevant to diagnosis or further investigation. These findings were related to the vascular system (Figs 8 and 9), soft tissues (Fig 10), and, in the case of SC studies,
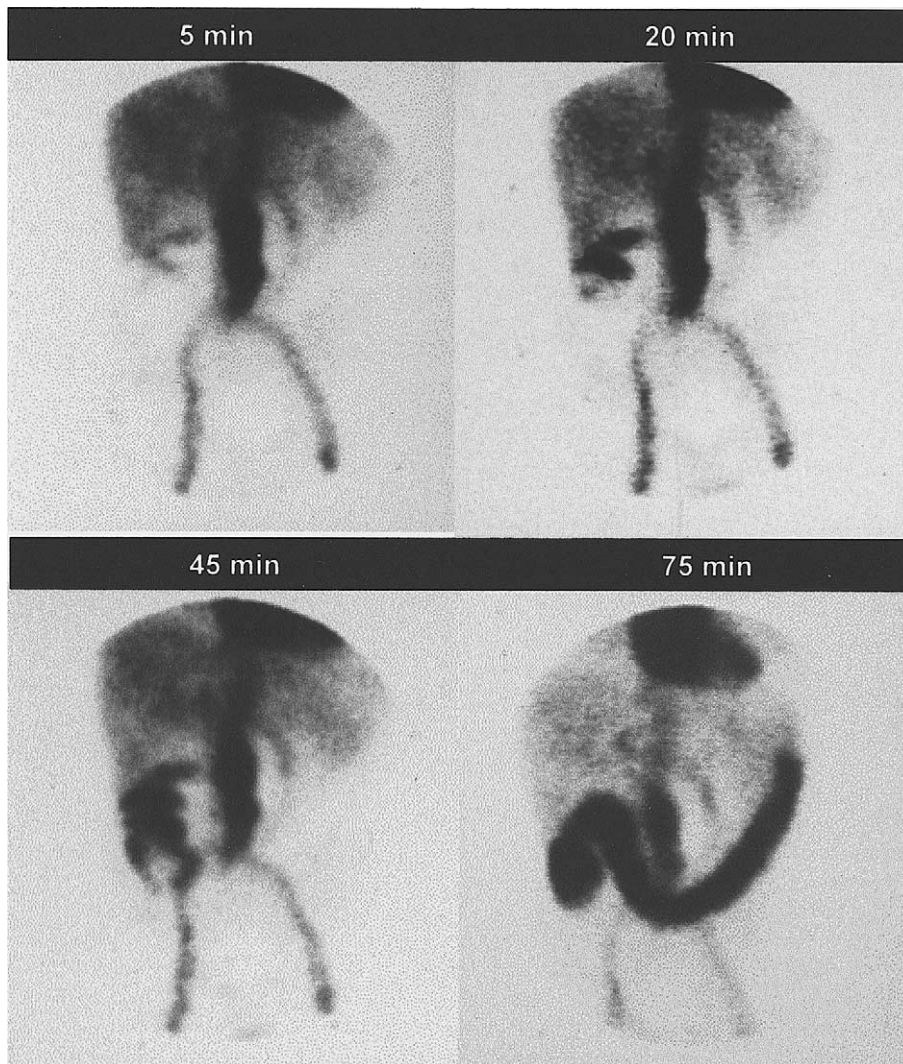
Fig 6. Red blood cell (RBC) study performed in a patient who presented with brisk rectal bleeding. The 5-minute image reveals a bleeding focus in the hepatic flexure region. Note that on subsequent frames, the blood progresses both antegrade, outlining the transverse colon, and retrograde, extending to the region of the cecum. Characteristics of large bowel bleeding in this patient include a peripheral location, and visualization of elongated and often haustrated regions of bowel that slowly change in appearance from frame to frame.

the liver, spleen, and bone marrow (Figs 3 and 4). More than just representing a curiosity, these abnormalities often help elucidate the underlying etiology of bleeding. Vascular or soft-tissue abnormalities, such as aneurysms, occlusions, or ectopic organs, may also alert the angiographer to modify the subsequent arteriographic approach. On rare occasions, we have observed static foci of abnormal uptake that were ultimately shown to be extravasated blood, which, for unknown reasons, did not move within the bowel lumen (Fig 11).[19] This diagnosis can only be made retrospectively, based on repeat

scintigraphy, and highlights the necessity and usefulness of repeat examination.

After bleeding has been identified to occur in the colon, based on motion of the extravasated blood in the lumen, its location in either the small or large bowel should be determined. The small bowel is centrally located, and extravasated blood appears to progress rapidly distally through a series of small curvilinear segments on sequential imaging (Fig 5). In contrast, large bowel bleeding is generally peripheral in location and progresses in a more elongated pattern
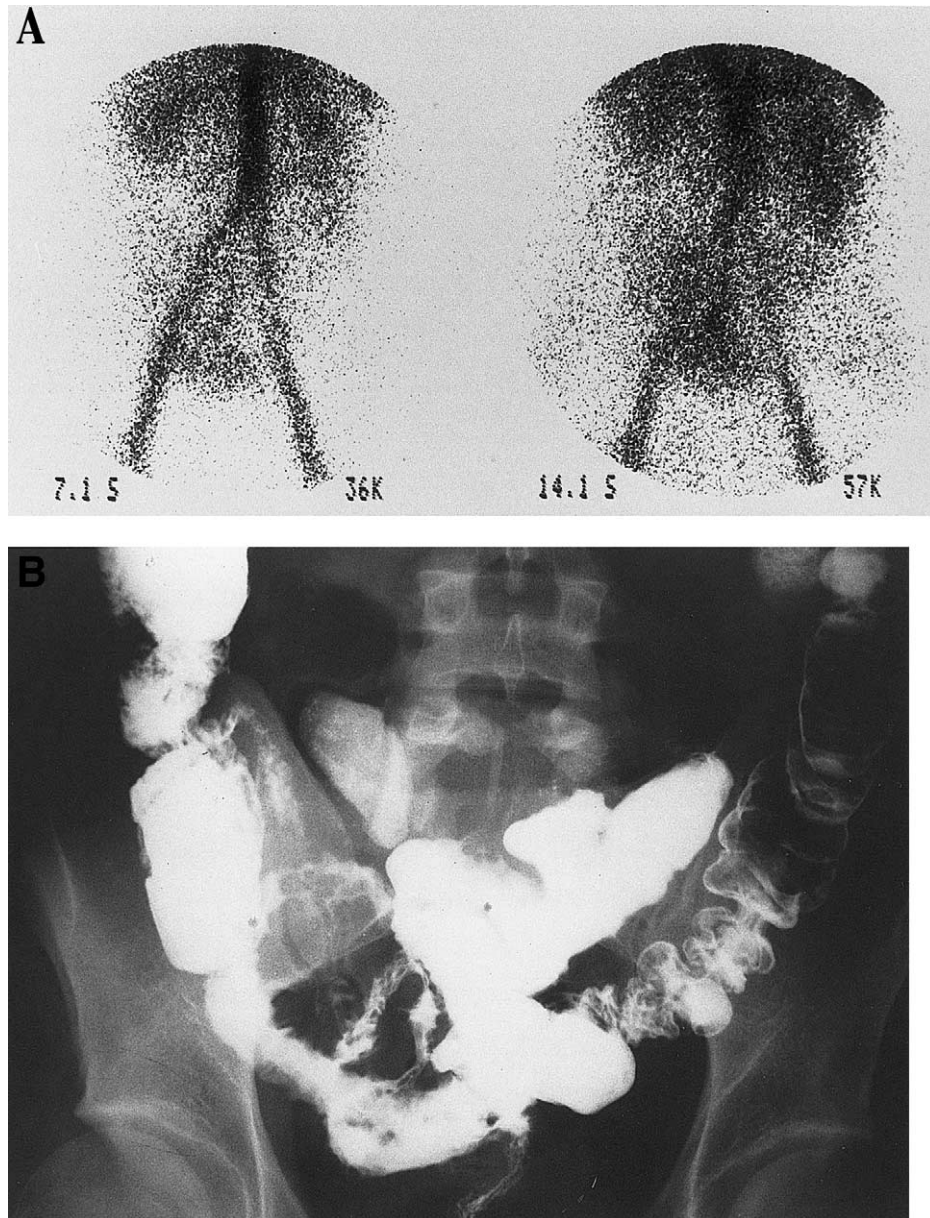
Fig 7. (A) Dynamic scintiscans of the abdomen in a 22-year-old man taken at 7-second intervals after injection of sulfur colloid (SC) show a blush of activity inferior to the aortic bifurcation that is similar in intensity to the iliac arteries. No extravasation was noted on the remainder of the study. **(B)** Correlative view from an upper gastrointestinal series and small bowel follow through examination performed on the same day shows marked deformity and irregularity of the distal ileum, consistent with Crohn disease. Reprinted with permission.[17]

on sequential imaging, often with visualization of well-defined haustrations (Fig 6). Finally, within the large or small bowel, the precise origin of bleeding should be determined based on identifying the geographic location of the chronologically initial site of bleeding visualized, rather than the most proximal site

of blood identified. This distinction is required due to the tendency of blood to move in a retrograde as well as an antegrade direction. If uncertainty exists, it can often be helpful to trace the motion of extravasated blood backwards with time to observe the first frame where abnormality is detected.[16] Occasionally, it can
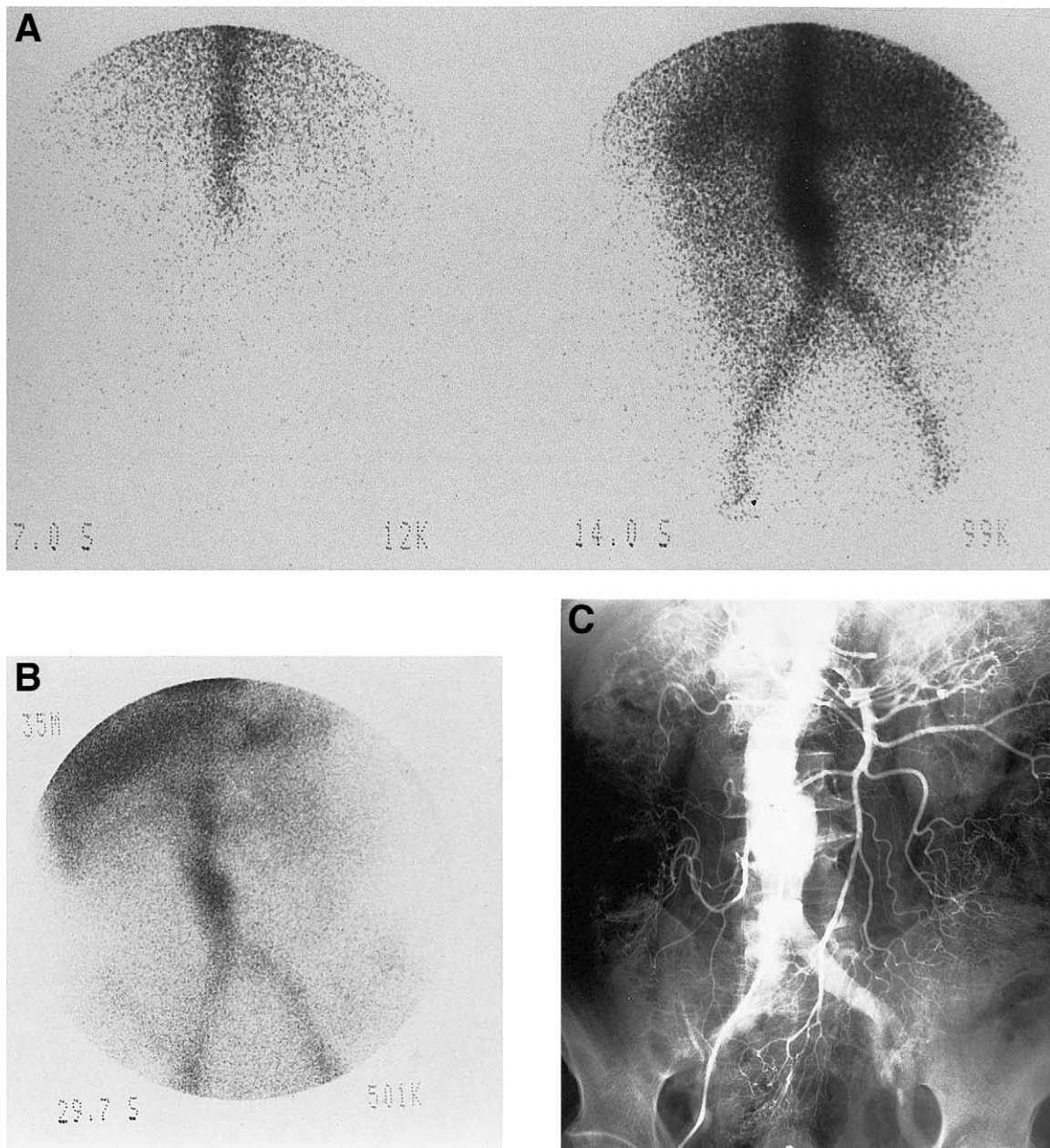
Fig 8. (A) Dynamic red blood cell (RBC) scintiscan of the abdomen shows ectasia of the mid-abdominal aorta, which is of importance to the angiographer before angiography. (B) Static RBC scintiscan of the same as Fig 8A. (C) This finding was confirmed on a aortographic contrast study performed to localize bleeding. Reprinted with permission.[17]

still remain difficult to identify with certainty whether an involved area of bowel is in the large or small colon. Investigators have instilled ^{99m}Tc-pentetic acid (DTPA)[20,21] or tap water[22] into the large colon via enema to define better its course, thereby helping localize the bleeding site.

O'Neill and coworkers have summarized the literature

concerning the accuracy of RBC bleeding studies (Table 3).[23] A rather large range of accuracy is attributed to technical differences, with suboptimal results associated with infrequent imaging and the use of delayed imaging to infer a bleeding source. Using optimal dynamic imaging techniques, excellent accuracy has been recorded.
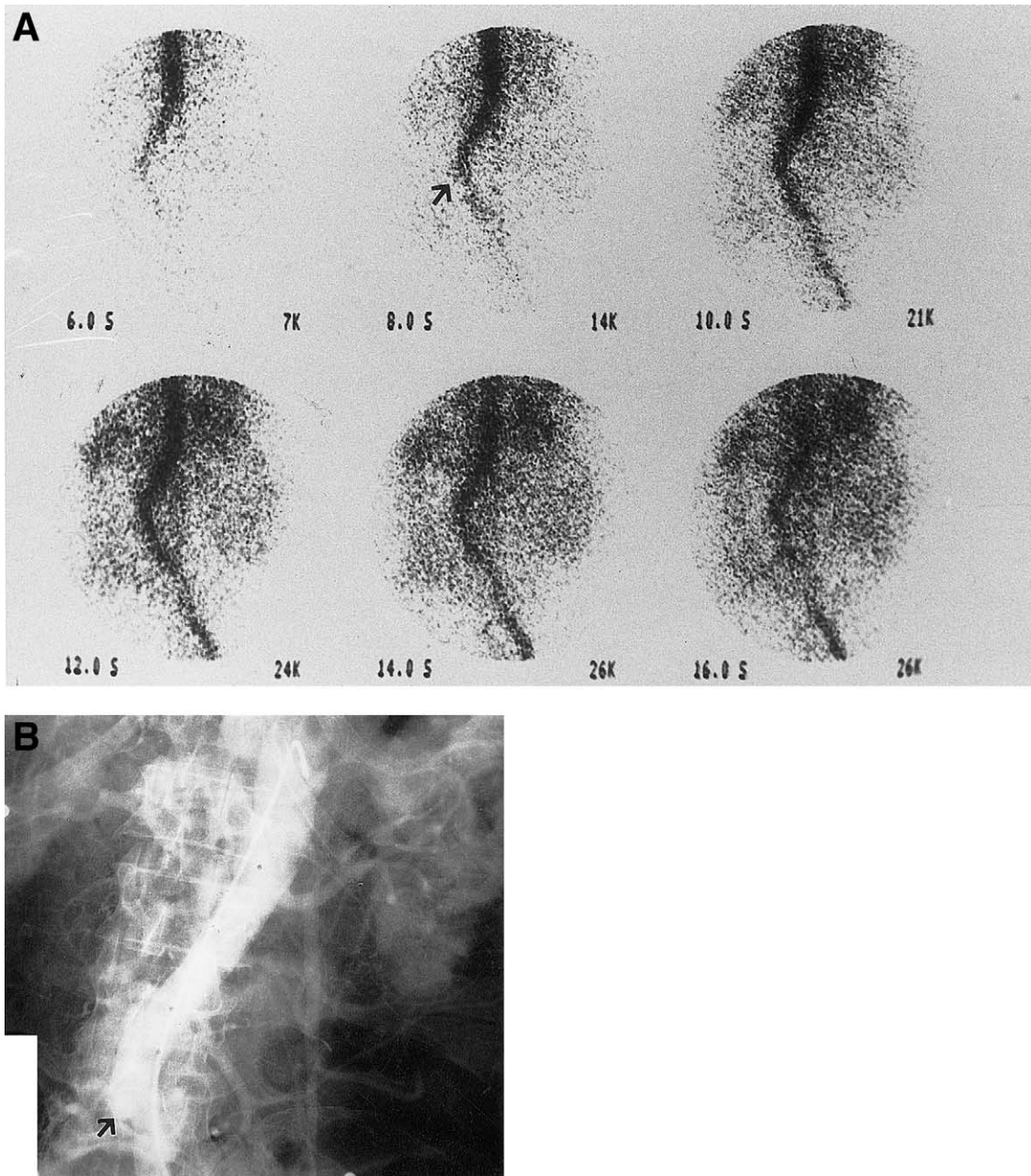
Fig 9. (A) Dynamic scintiscans of the abdomen in a 75-year-old patient acquired at 2-second intervals after the administration of 10 mCi of red blood cells (RBC) show moderate tortuosity of the abdominal aorta, with absent filling of the right common iliac artery (arrow). This finding is of importance to the angiographer for directing an angiographic approach other than the typical right femoral catheterization. (B) Abdominal aortogram obtained via a left femoral approach shows normal opacification of the left common iliac artery, with occlusion of the right common iliac artery (arrow). Reprinted with permission.[17]

Meckel's Diverticulae

Occasionally, gastrointestinal bleeding may be caused by Meckel's diverticulae, remnants of the omphalomesenteric duct (Fig 12).[37] The majority of Meckel's diverticulae that bleed have the presence of ectopic gastric mucosa, which concentrates [99m]Tc-
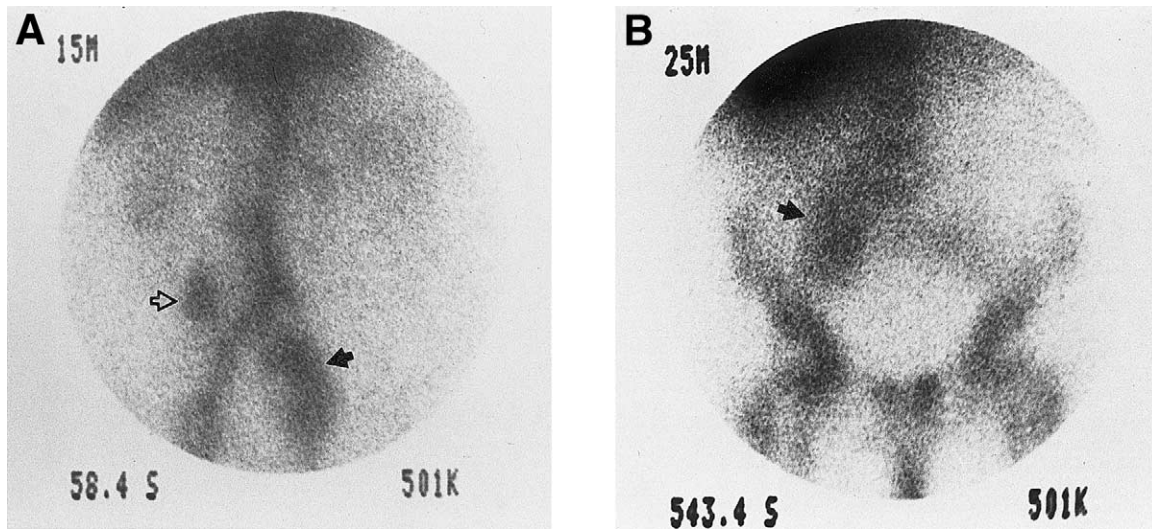
Fig 10. (A) Pelvic kidney apparent on a red blood cell (RBC) study (solid arrow). (B) Pelvic kidney seen on sulfur colloid (SC) study (solid arrow). A sigmoid bleed is also seen (open arrow). RBC study reprinted with permission.[18]

pertechnetate (TcO_4^-).[38,39] Typically, 370 MBq (10 mCi) of TcO_4^- are administered, and sequential, anterior abdominal images are obtained over the course of 30 to 60 minutes. Activity appearing in the right lower quadrant of the abdomen, with a similar timing of visualization as the
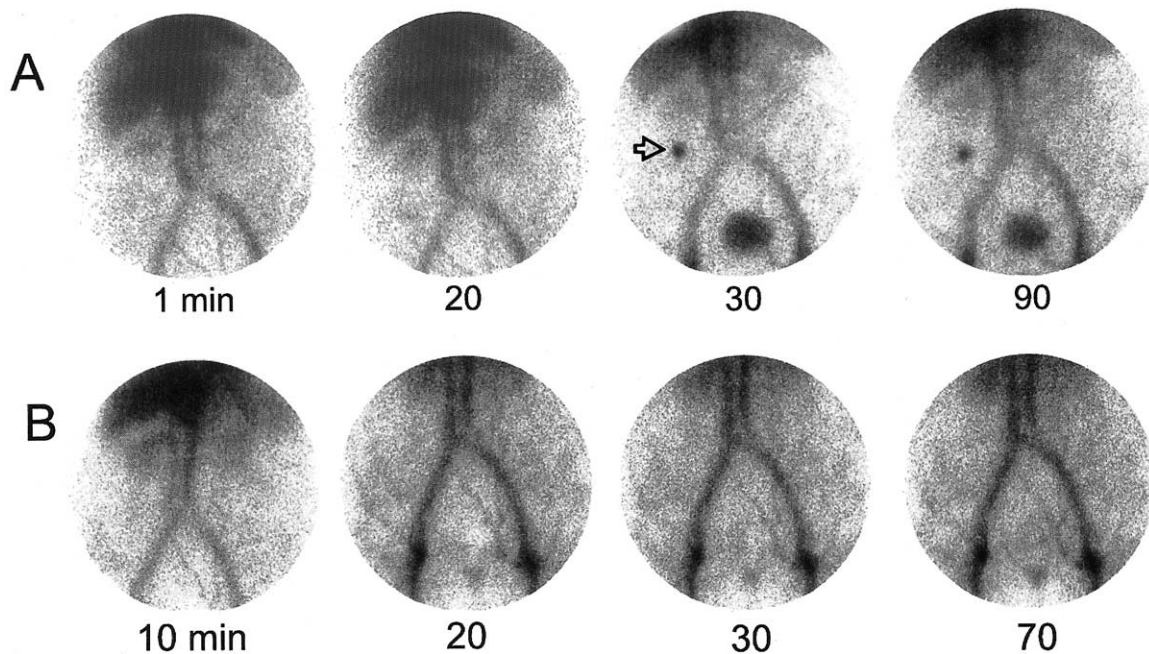

Fig 11. Acute gastrointestinal bleeding developed in a 70-year-old woman hospitalized for acute pulmonary edema. (A) Following unremarkable upper and lower gastrointestinal endoscopy and upper gastrointestinal series, red blood cell (RBC) bleeding scintigraphy showed a stationary focus of activity that appeared in the right-lower quadrant of the abdomen after 30 minutes but did not move or significantly intensify with time through 90 minutes. Angiography showed a vascular ectasia of the cecum in this region, presumed to be the cause of the bleeding. (B) RBC bleeding scan was electively repeated 2 weeks later once the patient was stable and no longer visualized the region of abnormality. Postulated mechanisms for this unusual finding include intramural bleeding, adherent clot, or possibly aperistaltic ischemic bowel. Reprinted with permission.[19]

Table 3. Correct Localization of Gastrointestinal Bleeding Identified by ^{99m}Tc-RBC Scintigraphy*

Investigator	Year	No. Scans	% Positive	% Correct
O'Neill et al[23]	2000	26	96	88
Suzman et al[24]	1996	224	51	96
Orechhia et al[25]	1985	76	34	94
Emslie et al[26]	1996	75	28	88
Leitman et al[27]	1989	28	43	86
Bearn et al[28]	1992	23	78	82
Dusold et al[29]	1994	74	59	75
Rantis et al[30]	1995	80	47	73
Van Geelen et al[31]	1994	42	57	69
Nicholson et al[32]	1989	43	72	67
Hunter and Pezim[33]	1990	203	26	58
Bentley and Richardson[34]	1991	182	60	52
Garofalo and Abdu[35]	1997	161	49	19
Voeller et al[36]	1991	111	22	0

*Reprinted with permission.[23]

orthotopic gastric mucosa of the stomach, is considered highly suspicious for Meckel's diverticulae. To increase yield, the patient can be pretreated with cimetidine, which is postulated to decrease the release of radiotracer by gastric mucosa and, thereby, increase lesion to background ratios (Fig 12).[40]

CONCLUSION

Radionuclide scintigraphy for detection of gastrointestinal bleeding leverages nuclear medicine's ability to monitor physiologic and pathologic process in a noninvasive manner. Proper performance and interpretation of images depend on a sound understanding of the principles of the examination, which we have reviewed here.
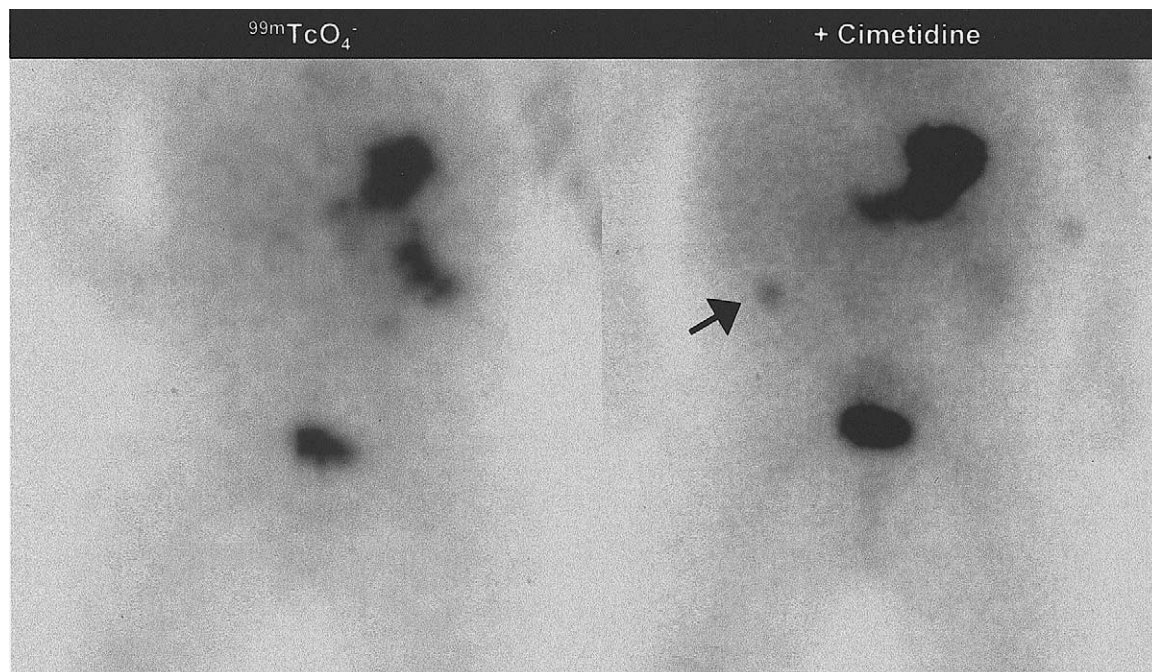

Fig 12. Single, representative 40-minute images from a pertechnetate study (left panel) failed to detect ectopic gastric mucosa in a 7-month-old girl with gastrointestinal hemorrhage (left panel). The patient had been placed on cimetidine for an insufficient 3 hours before the study. After an additional day of cimetidine treatment, the study was repeated (right panel). Corresponding 40-minute image reveals a well-defined focus of pertechnetate uptake in the right lower quadrant of the abdomen (arrow), in a location typical for Meckel's diverticulae.

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