Continuing Education

Scintigraphic Detection of Gastrointestinal Hemorrhage: Current Status

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This is the second in a series of four Continuing Education articles on imaging techniques. After studying this article the reader should be able to: 1) discuss why the detection of GI bleeding is clinically important; and 2) be aware of various imaging techniques and potential pitfalls.

Localization of the specific bleeding site in patients presenting with acute gastrointestinal (GI) hemorrhage remains a serious clinical problem. Alavi et al. (*1*) were the first to recognize a significant diagnostic role for scintigraphic imaging in localizing bleeding lesions. Their pioneering work, which was reported in 1977, stimulated extensive investigation to better define the proper role of scintigraphy in patients with GI hemorrhage. As a result, scintigraphy has emerged as the imaging modality of first choice for localizing bleeding sites in the lower GI tract. This paper is a selective review of the current status of radionuclide imaging in GI hemorrhage.

CLINICAL PERSPECTIVE

The clinical presentation, probable cause, and diagnostic evaluation of acute GI hemorrhage depend to a large extent on the location of the bleeding site. The GI tract is divided into two parts with the boundary being the ligament of Treitz at the junction of the duodenum and jejunum. The upper GI tract includes the esophagus, stomach, and duodenum. The lower GI tract includes all portions of the bowel distal to the ligament of Treitz (i.e., jejunum, ileum, and colon). Although scintigraphy may demonstrate bleeding sites in any portion of the GI tract, the major emphasis has been on the lower GI tract because of the clinical needs in this area.

Upper Gastrointestinal Hemorrhage

Bleeding above the ligament of Treitz is easily diagnosed and localized in 90% of patients by gastric aspiration and endoscopy. Major causes of bleeding in these patients are peptic ulcer, gastritis, esophagitis, esophageal varices, Mallory-Weiss syndrome, and tumors. Radionuclide imaging studies are generally not needed in upper GI bleeding because traditional endoscopic approaches are quite effective.

Lower Gastrointestinal Hemorrhage

The major causes of lower GI bleeding are diverticular disease, inflammatory bowel disease, tumors, and angiodysplasia (an acquired vascular malformation in the blood vessels of the bowel wall). In the pediatric and young adult population, Meckel's diverticulum is a common cause of bleeding. Sites of bleeding in the lower gastrointestinal tract, however, are often very difficult to localize not only during pre-operative diagnostic evaluation but also at surgery. This great diagnostic dilemma stems from both the long length and tortuosity of the lower GI tract as well as the typical intermittent pattern of blood loss in these patients. Another factor is the lack of a reliable clinical indicator capable of determining whether bleeding is active at any given time.

Patients with life threatening hemorrhaging who require emergency surgery will often become hypotensive and cease active bleeding before or during surgery, making it impossible to locate the specific origin of the bleeding during the operation. Thus, correct pre-operative localization of the bleeding site is essential for appropriate surgery. In the past, correct localization was impossible in many cases with traditional diagnostic approaches. In these cases, the surgeon was often forced to perform extensive blind bowel resections to control recurrent hemorrhage. As experience with scintigraphy increases, it seems to be evolving as clearly superior to other diagnostic modalities in pre-operative localization of lower GI bleeding sites (*2,3*).

Traditional Diagnostic Methods

Many of the traditional approaches listed in Table 1 have proven insensitive for detecting and localizing acute bleeding sites. Hematochezia, or passage of bloody stools, may continue for hours after cessation of active bleeding into the bowel

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TABLE 1. Traditional Diagnostic Methods

Stool: color, frequency, and guaiac test
Supine-Erect: blood pressure and pulse
Hematocrit and Hemoglobin
Proctoscopy and Colonoscopy
Barium Studies
Angiography

lumen. Although helpful in determining the magnitude of blood loss, neither orthostatic vascular response nor change in hematocrit provide any information about location. The emergent nature of lower tract bleeding usually precludes bowel cleansing, thus severly compromising colonoscopy and barium studies in the acute setting. In the past, angiography has been the major diagnostic tool for localizing bleeding sites. Angiography, however, requires active luminal bleeding and is often negative in intermittent bleeders or those with bleeding rates below 1.0 ml/min. In addition, angiography is uncomfortable, expensive, and has some risks. In many institutions, scintigraphy is used to screen for active bleeding before angiography (*4*), or it is actually used to completely bypass diagnostic angiography (*3*).

SCINTIGRAPHIC APPROACHES

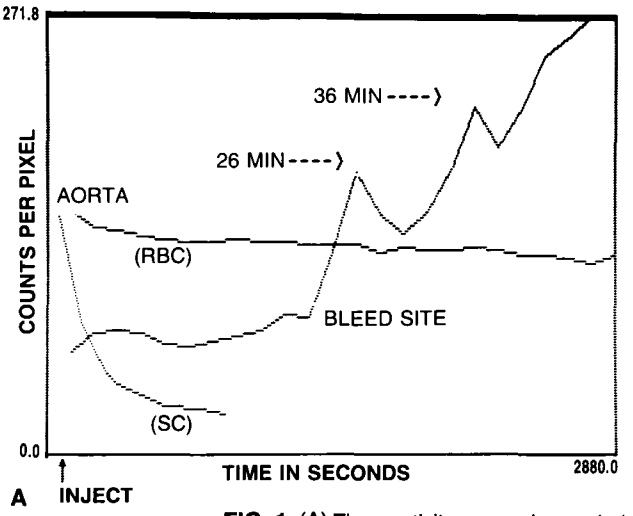
Since the early work of Alavi and his colleagues in demonstrating the theoretical basis and clinical superiority (over angiography) of scintigraphy using ^{99m}Tc-sulfur colloid, many investigators have reported success with ^{99m}Tc-red blood cells (RBCs). Both techniques depend on scintigraphic visualization of active bleeding into the bowel lumen while the radiotracer is blood borne. The major difference is the rate of radiotracer clearance from the blood.

Evidence of ^{99m}Tc-RBC Superiority

Clinical experience reported by a number of investigators (*2,5–11*) strongly supports the view that intermittent bleeding is the dominant feature in most patients with lower GI hemorrhage (Fig. 1). Diagnostic agents with short blood-pool duration show lower diagnostic sensitivity because they are frequently cleared before onset of the next bleeding episode. Thus, angiography (vascular $T_{½}$ < 30 sec) proved less sensitive than ^{99m}Tc-sulfur colloid (vascular $T_{½}$ = 3 min), which was in turn shown much less sensitive than ^{99m}Tc-RBC (vascular $T_{½}$ > 24 hr) for demonstrating bleeding sites which are so often intermittent. Clinical studies comparing ^{99m}Tc-sulfur colloid and ^{99m}Tc-RBC performed in tandem all report markedly better sensitivity for detecting bleeding with ^{99m}Tc-RBC (*5–11*). The largest series, a multi-institutional prospective study of 100 patients, reported a sensitivity of 93% for ^{99m}Tc-RBC and only 12% for ^{99m}Tc-sulfur colloid in detecting and localizing bleeding sites (*8*). Similar results were reported for other tandem series (*9–11*). In light of such poor relative sensitivity, ^{99m}Tc-sulfur colloid cannot be recommended for GI bleeding studies (Figs. 2 and 3). Using ^{99m}Tc-sulfur colloid and ^{99m}Tc-RBC in tandem fashion may offer no diagnostic advantage over the use of ^{99m}Tc-RBC alone. Furthermore, ^{99m}Tc-sulfur colloid adds radiation exposure and causes significant background interference in the liver and spleen regions that may obscure a bleeding site on the subsequent ^{99m}Tc-RBC study.

Role of the Meckel's Scan

The [^{99m}Tc]pertechnetate Meckel's scan differs fundamentally from other scintigraphic bleeding studies in that it does not demonstrate active bleeding, but rather shows the ectopic gastric mucosa usually present in bleeding Meckel's diver-



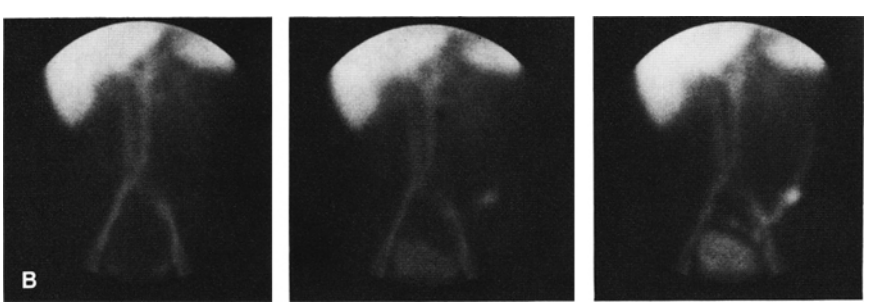


FIG. 1. (A) Time–activity curves demonstrate intermittent nature of lower GI bleeding. Regions over the aorta and bleeding site were used to monitor activity of tandemly administered ^{99m}Tc-sulfur colloid (SC) and red blood cells (RBCs). SC is rapidly cleared from the blood pool and none remains to demonstrate the first episode of intermittent bleeding at 26 min postinjection. RBCs remain in the vascular space and document the intermittent peaks of active bleeding. (B) Anterior abdominal images at 15, 25, and 40 min (left to right) after injection of ^{99m}Tc-RBCs show bleeding site in lower descending colon with bidirectional movement of lumenal activity. Diagnosis of a bleeding diverticulum at the site was confirmed at surgery.

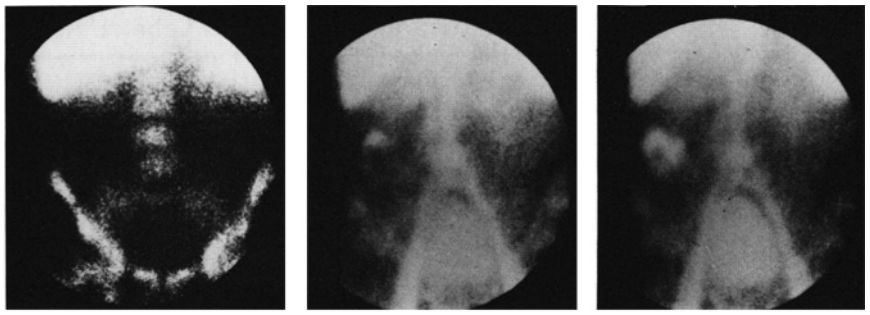


FIG. 2. Example of tandem ^{99m}Tc-sulfur colloid and ^{99m}Tc-RBC studies. The SC image at 20 min postinjection is negative. The RBC study became positive in the right upper quadrant at 55 min (middle) and shows progressive bleeding at 80 min (right). Note: Activity in urinary bladder is normal. Angiodysplasia of the ascending colon just below the hepatic flexure was confirmed as the bleeding site at surgery.

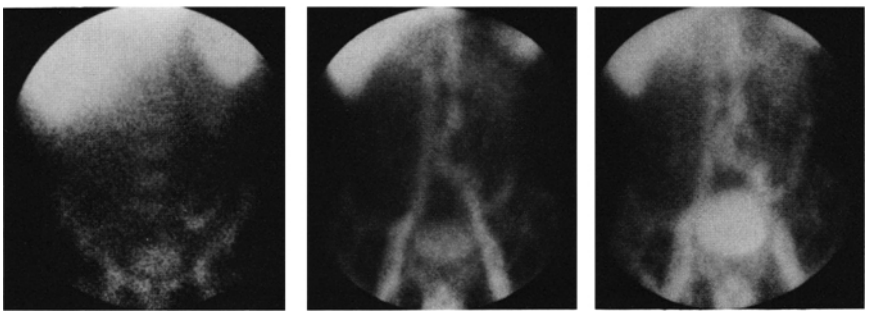


FIG. 3. Tandem study with sigmoid colon bleeding site demonstrated by both ^{99m}Tc-sulfur colloid and ^{99m}Tc-RBCs. Anterior view at 15 min following SC administration is on left. Technetium-99m-RBC images at 25 min (middle) and 80 min (right) clearly show the bleeding lesion.

ticulae. This study is usually done in children and young adults with lower GI bleeding episodes. A positive study showing concentration of pertechnetate by the ectopic gastric mucosa (Fig. 4) provides strong presumptive evidence that peptic ulceration in the Meckel's is the source of bleeding in the pediatric patient. Overall sensitivity and specificity in 226 reported patients with surgical confirmation of 85% and 95%, respectively, indicates the important continuing role of this study technique (*12,13*). Proposed drug and hormone enhancement schemes which might further improve sensitivity are outlined in Table 2.

Active bleeding is not necessary and may actually be detrimental to diagnosing a Meckel's by causing rapid washout of secreted pertechnetate from the lumen. The Meckel's study is best performed as part of the follow-up diagnostic evaluation in patients who have ceased active bleeding. If the patient is actively bleeding, a ^{99m}Tc-RBC study should be done to attempt localization of the site.

PATIENT SELECTION

Ideally, scintigraphy should only be performed on patients with a significant amount of lower GI hemorrhage who are bleeding actively at the time of the study.

Patients with an extremely low rate of blood loss will present with chronic anemia and guaiac positive stools. These are not good indications for this study, and such patients are almost invariably negative. They should be studied only as a last resort after negative endoscopy and barium studies have been completed.

In general, ^{99m}Tc-RBC scintigraphy should be limited to patients whose bleeding rates make them potential surgical candidates. These patients generally present with hemato-

TABLE 2. Hormone/Drug Enhanced Meckel's Study

Hormone/Drug	Dose	Desired Action
Pentagastrin	6 μg/kg	Increased [^{99m}Tc]pertechnetate uptake
Cimetidine	300 mg/day	Block [^{99m}Tc]pertechnetate release
Glucagon	50 μg/kg	Decreased lumen motility

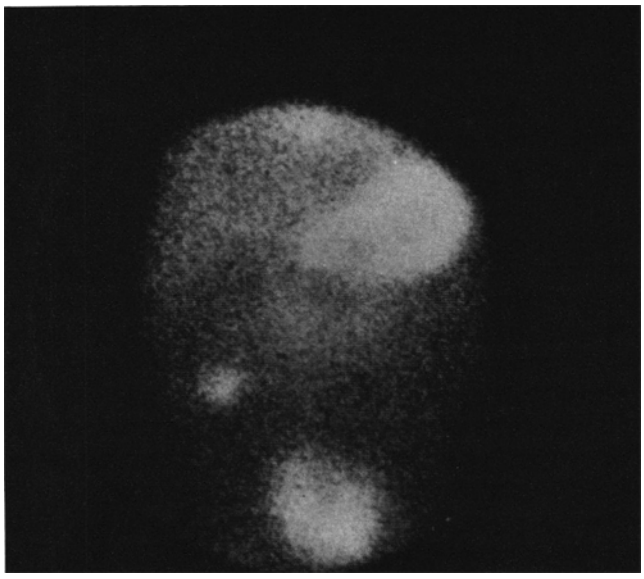


FIG. 4. Anterior view 30 min after i.v. [^{99m}Tc]pertechnetate illustrates typical finding of Meckel's diverticulum in the right lower quadrant.

chezia and blood volume changes requiring transfusion. In these patients, the major question concerns when to initiate the study, since it is highly desirable to administer ^{99m}Tc-RBC during a bout of active lumenal bleeding.

Unfortunately, there are no perfect clinical indications of bleeding activity that can be used to trigger study onset. We reviewed our experience in 1983 and found two clinical factors which helped to select patients most likely to have active bleeding. Orthostatic blood pressure changes were present in 86% of patients with positive scintigraphy and in only 27% of those with negative results (Student's t-test, $p < 0.01$). The mean transfusion requirement was 6.9 units packed RBCs in positive cases compared to 1.5 units packed RBCs in negative cases ($p < 0.001$). Patients who are bleeding actively by these criteria are studied as soon as possible. They have a higher probability of a positive study during the early sequential imaging phase of the ^{99m}Tc-RBC study, when localization of the site is most accurate. Patients without orthostatic changes often have stopped bleeding or are only positive on delay views.

Differences in patient selection criteria may well explain the significant difference in average delay time to a positive study reported by various authors (*4,8,14*). Patient selection criteria are best developed in close coordination with the referring clinicians and probably should be reviewed periodically in the light of study results at a particular institution.

RBC LABELING CONSIDERATIONS

Three methods have been utilized to label RBCs with ^{99m}Tc: in vivo method, in vitro method, and the modified in vivo method. All three methods require the addition of a reducing agent, usually stannous ion, to the RBCs prior to adding [^{99m}Tc]pertechnetate. This process is sometimes called "pretinning" the red blood cells. Although ^{99m}Tc attaches to the beta chain of the hemoglobin molecule, the same location as ^{51}Cr, it requires proper intracellular concentration of the tin reducing agent for labeling to occur.

Other blood-pool radiopharmaceuticals such as ^{111}In-RBC and ^{99m}Tc-albumin have been used for GI bleeding studies but have not demonstrated any clinical superiority to ^{99m}Tc-RBCs.

In Vivo Method

In this method all circulating RBCs are pre-tinned by i.v. administration of a reconstituted cold pyrophosphate kit containing 1 mg of stannous ion (*15*). However, when [^{99m}Tc]pertechnetate is administered 30 min later, a significant portion remains available for concentration by the salivary glands and gastric mucosa. The subsequent bowel activity often leads to diagnostic confusion, making this method of RBC labeling unacceptable for GI bleeding studies.

In Vitro Method

A simple kit to label erythrocytes was developed at the Brookhaven National Laboratory a decade ago (*16,17*), and it is now available* on an extended IND Phase III unlimited basis for routine clinical use. The in vitro approach provides a consistently superior label for GI bleeding studies because quality control testing and additional washing steps can remove any unbound ^{99m}Tc. This is the ideal tracer and provides consistent image and study quality for bleed localization (*4,18,19*). The steps required for in vitro red cell labeling according to our own modification of the Brookhaven kit are listed in Table 3. This procedure requires ~ 30 min, including the quality control steps.

TABLE 3. Preparation of In Vitro Labeled RBCs*

1. Add 7 ml of patient whole blood to kit vial which contains:
   100 units sodium heparin
   3.7 mg sodium citrate dihydrate
   5.54 mg dextrose anhydrous
   1.5 μg tin as stannous ion
   NaOH for pH adjustment
2. Centrifuge vial contents at 800 G for 10 min.
3. Remove plasma and add 50 mCi [^{99m}Tc]pertechnetate to the packed cells. Mix and incubate for 10 min.
4. Perform quality control to determine percent cellular labeling:
   Remove 0.5 ml of labeled RBC solution and combine with 1.5 ml normal saline in test tube.
   Measure total activity in tube, then centrifuge and remove supernatant and count RBC activity.
   Express as % of total.

*Letterman Army Medical Center Technique (*7*).

Modified In Vivo Method

This modification of the in vivo technique provides improved labeling efficiency by allowing ~ 10 min incubation of pretinned erythrocytes with [^{99m}Tc]pertechnetate in the i.v. apparatus (*4,20*). This is the most commonly used method and is preferred whenever in vitro labeling cannot be done, because it reduces the amount of free pertechnetate interference. This method is outlined in Table 4.

Special Labeling Problems

Use of acid citrate-dextrose (ACD) instead of heparin in the modified in vivo labeling technique has been shown to improve binding efficiency and decrease renal and bladder activity related to excretion of ^{99m}Tc-heparin complexes (*21*). It is also important to avoid using the initial eluate from long growth-time generators, since ^{99}Tc (the decay product of ^{99m}Tc) acts as a competitive inhibitor of eluted ^{99m}Tc in all types of erythrocyte labeling. The first elution should be discarded and a rapid second elution used whenever the generator ingrowth time is over 24 hr. Patients with low hematocrits seem to require longer incubation times than 10 min for the modified in vivo labeling method. Removal of the incubating syringe for optional centrifugation and washing can be done to assure high labeling efficiency (*22*).

IMAGING TECHNIQUES

The imaging technique utilized for GI bleeding studies is critically important to a successful outcome. The technique must be designed to answer the main clinical question: Where is the bleeding site located? The answer to this question is vital to guiding diagnostic or interventional angiography or for

TABLE 4. Method for Modified In Vivo Labeling of RBCs*

1. Reconstitute the contents of one vial of pyrophosphate containing 1 mg of stannous chloride with 1 ml saline and inject the patient.
2. Insert a butterfly infusion set into the patient's peripheral vein 15–20 min later. Attach a 3-way stopcock to the butterfly set and flush line with a heparin solution containing 10 units per ml (100 units in 10 ml normal saline) attached to one arm of the stopcock.
3. Withdraw blood to clear heparin from catheter into a discard syringe. Then withdraw 3 ml of whole blood through the heparinized catheter into a shielded syringe containing 20–25 mCi of [^{99m}Tc]pertechnetate. Invert gently several times.
4. Flush the catheter using the dilute heparin solution to prevent clotting.
5. Incubate the RBCs and pertechnetate in the shielded syringe for at least 10 min with occasional gentle mixing every minute.
6. **Optional:** Remove syringe and centrifuge, discard plasma, and wash cells in normal saline. This step will reduce the amount of ^{99m}Tc not bound to the RBCs.
7. Inject ^{99m}Tc-RBCs through catheter.
8. Remove injection apparatus and dispose in radioactive waste.
9. **Optional technique for using ACD solution instead of heparin:** Keep line open with normal saline drip instead of heparin solution. Add 1 ml ACD solution to shielded syringe containing [^{99m}Tc]pertechnetate. After clearing line, draw 5 ml whole blood into shielded syringe and proceed as above (*21*).

*Adopted from Massachusettes General Hospital's technique (*14*).

directing surgical resection of the bleeding bowel segment. Important technique considerations are outlined in Table 5.

Early Study Technique

A scintigraphic technique must be designed to overcome the localization problems stemming from intermittent lumenal bleeding and bidirectional movement of blood activity in the bowel lumen. This is best accomplished by either continuous dynamic imaging or by using frequent sequential images.

TABLE 5. Technetium-99m-RBC GI Bleeding Study Techniques

Early Study Technique
LFOV high-resolution system best
Bolus flow study
Continuous computer imaging
Individualize early study duration
Delayed Imaging Options
Restart sequential imaging
Initiate new study
Special Techniques
Dynamic computer display
^{99m}Tc-DTPA enema
^{99m}Tc-DISHIDA for small bowel anatomy
Pre- and post-defecation images
Bedpan image
Drug interventions
Ancillary Study Information
Red cell mass
LVEF as pre-op screen

Blood in the bowel lumen may move significant distances in both directions within 5–15 min of a bleeding episode. If images are obtained at 20–30-min intervals, there is potential for significant localization error. Imaging should be started at the time of injecting ^{99m}Tc-RBCs to assure correct localization of early bleeding. Dynamic flow studies of bolus arrival may prove helpful in identifying certain vascular lesions and artifacts. The highest resolution system should be used to help distinguish bleeding from the vascular background activity, which provides helpful localization landmarks. Studies are conducted best with a large field-of-view camera, but they can be performed with a mobile camera using a diverging collimator.

The duration of the early imaging study should be as long as practically possible until a bleeding episode is visualized. Sequential computer acquisition as a dynamic study for cinematic playback has been extremely useful for localizing intermittent bleeding sites. In a large multi-institutional study (*8*), 83% of all patients with continued bleeding were visualized during a 90-min computer acquisition (Fig. 5). However, several other series (*4,14*) report that a majority of patients became positive only several hours after administering ^{99m}Tc-RBCs. This difference in timing is probably related to local variation in patient selection and diagnostic workup and emphasizes the need to individualize study duration for a particular institution.

Delayed Study Technique

When bleeding is not visualized during the early continuous imaging study, delayed images should be obtained at time intervals consistent with clinical requirements. Usually, delayed views may be obtained up to 24 hr with a single ^{99m}Tc-RBC dose. If lumenal activity is seen on a delayed view, sequential imaging should be restarted with either the same dose or a

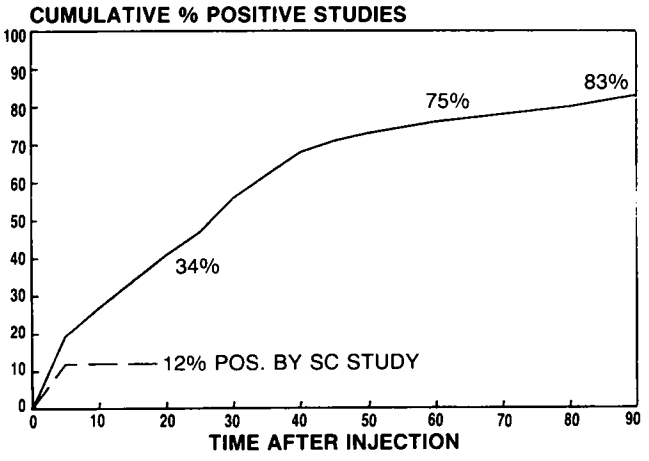


FIG. 5. Time-to-positive scintigraphic result of 41 confirmed bleeders. Graph illustrates relationship between detected positive cases and duration of continuous imaging phase of ^{99m}Tc-RBC bleeding study. In this series (*8*), only 17% of confirmed bleeders become positive after 90 min. If the continuous imaging was stopped at 60 min, an additional 8% of the cases would have been missed. Note that even at 20 min, ^{99m}Tc-RBCs demonstrated 34% of bleeding sites, whereas ^{99m}Tc-sulfur colloid only showed 12%.

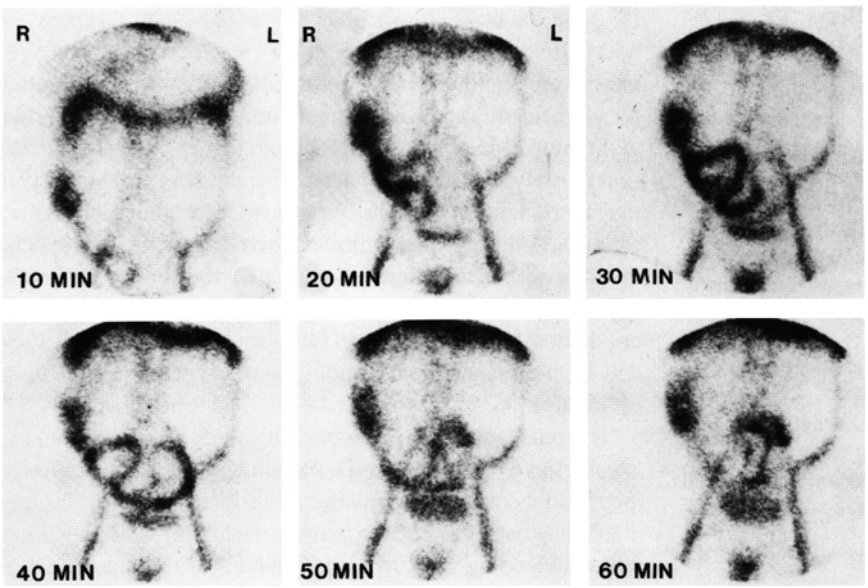


FIG. 6. Delayed image (upper left view) 24 hr after administering ^{99m}Tc-RBCs shows activity throughout the colon and terminal ileum. After repositioning, sequential 10-min images are restarted utilizing the original dose and demonstrate onset of active bleeding in the region of the terminal ileum and cecum. A leiomyoma of the terminal ileum was found at surgery. Reprinted with permission (*23*).

new dose of ^{99m}Tc-RBC in order to confirm the correct location of the bleeding site. This is particularly true when several hours have elapsed between images. Figure 6 is an excellent example of the use of renewed sequential imaging to confirm a bleeding location after delayed views revealed almost pancolonic distribution of activity (*23*). Lumenal activity on a delayed view has been dubbed the "nuclear guaiac" test because this merely demonstrates that bleeding has occurred sometime in the imaging interval but does not reliably localize the bleeding site (Fig. 7).

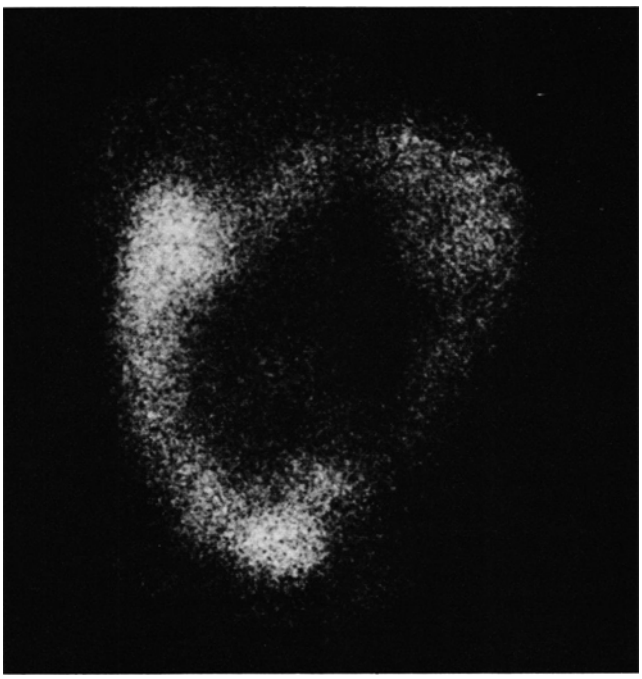


FIG. 7. The "nuclear guaiac" test is a term applied to delayed images with pan-colonic activity. This 24-hr ^{99m}Tc-RBC image alone merely proves that interval bleeding occurred but gives little information about the location of the bleeding lesion. In this case, the source was subsequently shown to be a bleeding diverticulum in the splenic flexure.

Special Techniques

A number of special techniques have been suggested to assist in defining the anatomic bleeding site in those cases where the location is not obvious from activity moving through the bowel lumen.

When it is unclear whether a bleeding site is located in the small bowel or colon, these structures can be outlined scintigraphically by administering either i.v. ^{99m}Tc-DISHIDA or oral ^{99m}Tc-sulfur colloid to visualize the small bowel, or a ^{99m}Tc-DTPA enema for colon visualization (*24*). These maneuvers should not be attempted until routine images are complete because their interference activity will make it impossible to further evaluate for active bleeding activity (Fig. 8).

When there is confusion between a suspected bleeding site in the sigmoid colon as opposed to the possibility of small bowel or dependent transverse colon, pre- and post-defecation images as well as a bedpan image can provide conclusive sigmoid localization (Fig. 9).

Theoretically, certain drug interventions have the potential to enhance ^{99m}Tc-RBC bleeding scintigraphy results. Glucagon may be used to slow rapid bowel transit and thus allow increased accumulation of tracer at the bleeding site. Cholecystokinin, on the other hand, can be used to stimulate bowel peristalsis when movement of a bleeding focus might define the location.

Methods designed to stimulate renewed bleeding during sequential imaging must be done with proper medical precautions. Bleeding may be renewed by merely raising the patient's blood pressure by fluid replacement and pressor agents. Another more risky form of bleeding provocation entails administering heparin (10,000 units by i.v. bolus with 1,000 units i.v. per hr) to patients with chronic oozing (*25*). This must be

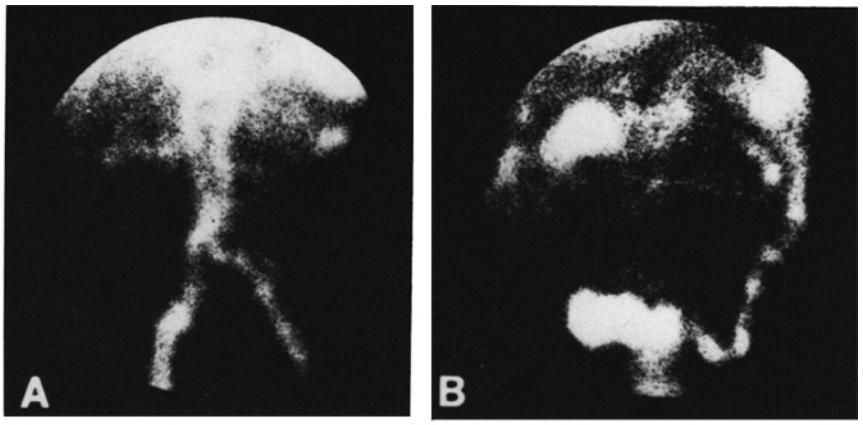


FIG. 8. Utility of the ^{99m}Tc-DTPA enema in proving that left upper quadrant extravasation (A) is actually within a lumen separate from the colon, which is outlined in (B) with the enema. Small bowel bleeding site was subsequently proven surgically. Reprinted with permission (*24*).

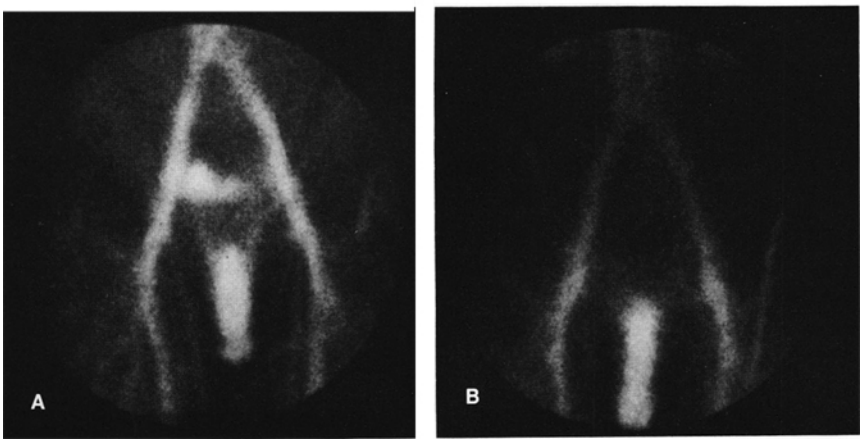


FIG. 9. Pre- and post-defecation images (A and B, respectively) clearly show that activity in lower abdomen was in the rectosigmoid. Notice the significant artifact caused by the (flaccid) penile blood pool. This should not be confused with a rectal bleeding site. (Courtesy Dr. Michael Hartshorne, Brooke Army Medical Center.)

TABLE 6. Technetium-99m-RBC GI Bleed Imaging Artifacts

Urine Activity Artifacts	Blood-Pool Activity Artifacts
Bladder artifact	Penile blood flow
Foley catheter pattern	Mesenteric varices
Renal outflow dilation/obstruction	Aneurysm or AVM
	Uterus blood pool
	Tumor blood pool

done under careful monitoring in order to immediately reverse the anticoagulant effect when bleeding is seen.

Ancillary information such as calculation of red cell mass and left ventricular ejection fraction is readily available from the same dose of ^{99m}Tc-RBC. This type of information could be helpful in monitoring transfusion requirements and could be used for pre-operative cardiac screening.

INTERPRETATION PITFALLS

Normal variations and common artifacts that can be confused with bleeding sites are listed in Table 6. Each of these structures has identifiable characteristics. Vascular lesions will show no change in location or relative intensity over time (Fig. 10). Artifacts caused by urinary excretion are readily identified in most cases. Confusion between recto-sigmoid bleeding and urinary bladder activity can usually be resolved by pre- and post-defecation views, and penile activity can be identified by moving the penis and re-imaging.

SUMMARY

Scintigraphic detection using ^{99m}Tc-RBCs is now commonly accepted as the best initial diagnostic test in patients with lower GI hemorrhage. With proper patient selection, attention to technical details, and avoidance of potential pitfalls, this study has provided diagnostic sensitivity, specificity, and overall accuracy in the mid-90% range at a number of institutions (*8*). Since this test is often pivotal in surgical or interventional decisions, it should be available on an emergency basis.

ACKNOWLEDGMENT

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

FOOTNOTE

*Cadema Medical Products, Inc., Middletown, NY

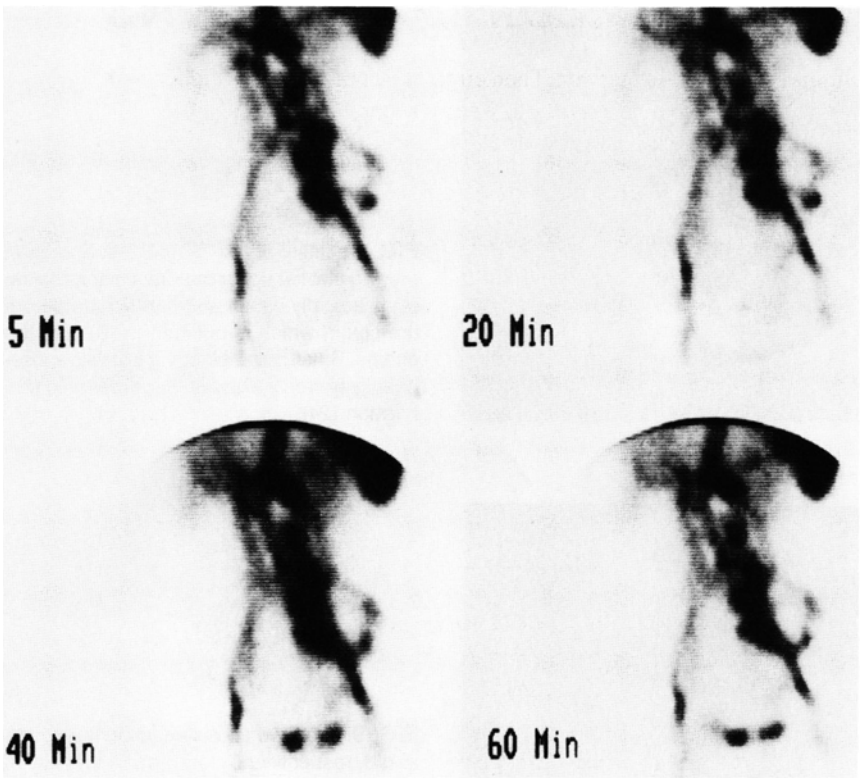


FIG. 10. Artifact caused by mesenteric varices in a patient with cirrhosis and suspected lower GI bleeding. Such blood-pool artifacts do not change appearance throughout the study. The typical pattern of a Foley catheter artifact is also seen on the 40- and 60-min images. Radioactive urine pools around the catheter bulb, which is a central cold defect. This activity may change throughout the study because of variable catheter drainage and should not be confused with a bleeding site.

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