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Gastrointestinal Bleeding Scintigraphy in the early 21st Century

Erin Grady, MD, FACNM[1]

[1]Section of Nuclear Medicine, Department of Radiology, Christiana Care Health System, Newark, DE

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Correspondence:

Erin Grady, MD, FACNM
Department of Radiology
Section of Nuclear Medicine
Christiana Care Health System
4755 Ogletown-Stanton Road
Newark, DE 19718
Fax: 302-733-6856
Email: egrady@christianacare.org

Running Title:

GIB Scintigraphy in the Early 21st Century

Learning Objectives:

On successful completion of this activity, participants should be able to describe: 1) diagnostic uses of gastrointestinal bleeding scintigraphy (GIBS); 2) proper methodology for performing GIBS; 3) the importance of correlative and hybrid imaging; 4) interpretive criteria to make a clinical diagnosis; 5) special considerations in pediatric GIBS; 6) imaging of Meckel's diverticula.

Abstract:

Gastrointestinal bleeding scintigraphy (GIBS) performed with ^{99m}Tc-labeled autologous erythrocytes or historically with ^{99m}Tc-sulfur colloid has been a clinically useful tool since the 1970s. This article reviews history of the techniques, the different methods of radiolabeling erythrocytes, an overview of the procedure along with useful indications, diagnostic accuracy and new techniques that one may find useful in their clinic including the use of single photon emission computed tomography/computed tomography (SPECT/CT) in the evaluation of gastrointestinal (GI) bleeding. A brief discussion of computed tomography angiography (CTA) evaluation for GI bleeding is also given. Causes of pediatric bleeding are discussed by age along with Meckel's diverticulum imaging.

Key words: GI bleeding scintigraphy or scan, radiolabeled red blood cells or erythrocytes, SPECT, SPECT/CT, CTA, pediatric GI bleeding by age, Meckel's diverticulum

GASTROINTESTINAL BLEEDING SCINTIGRAPHY

History

Alavi and colleagues at the University of Pennsylvania originally described evaluating gastrointestinal bleeding with scintigraphic methods using ^{99m}Tc sulfur colloid in 1977 (*1*). Miskowiak and colleagues at the University of Copenhagen described ^{99m}Tc human serum albumin for gastrointestinal (GI) bleeding in 1977 as well (*2*). Subsequently, Wizelberg and his colleagues at the Massachusetts General Hospital described diagnosing and localizing GI bleeding with ^{99m}Tc erythrocytes in 1979 (*3*). Other techniques for labeling red blood cells with greater efficiency ("*in vivtro*" and *in vitro* techniques described below) were developed later, but the practice of evaluating GI bleeding with scintigraphic techniques had already become established and utilized in clinical practice.

Background

GI bleeding is one of the major causes of death in the United States, with mortality ranging from 10-30% (*4*). In light of the significant mortality, timely diagnosis and evaluation are critical, as emergent intervention may be needed.

GI bleeding is divided into upper and lower GI bleeding. Upper GI bleeding originates up to the ligament of Treitz at the duodenal flexure. Upper GI bleeding affects 50 to 150 per 100,000 adults per year (*4*) and causes 20,000 deaths per year in the United States (*5*). Lower GI bleeding originates distal to the ligament of Treitz. Lower GI bleeding is fairly common, accounting for approximately 21% of GI bleeding overall (*6*), but is usually self-limited. The prevalence of lower GI bleeding increases by more than 200 times between the ages of 30 and 90 (*7*). Approximately 21 per 100,000 adults in the United States require hospitalization for lower GI bleeding annually (*4*). Upper and lower GI bleeding require different clinical approaches. A GI bleeding source can be difficult to distinguish clinically, although both entities have their usual signs. Upper GI bleeding generally presents with hematemesis (either red or coffee-ground emesis) or melena. Some melena however could be related to the ascending colon. Hematochesia is most often due to lower GI bleeding, but a brisk upper GI bleed could have a similar appearance. Non-invasive imaging and other tests assist the clinician in determining the appropriate treatment.

Scintigraphic GI bleeding scans are indicated for evaluation of overt gastrointestinal bleeding. Per the SNMMI guidelines for gastrointestinal bleeding scintigraphy, the goal of the exam is to determine whether or not the patient is actively bleeding, to localize the bleeding bowel segment and to estimate the rate of blood loss (*7*). All of these allow for treatment planning and risk stratification (*8*). The GI bleeding scintigraphy does best in the mid to lower GI tract. Occult bleeding identified by guaiac fecal occult testing is not an appropriate indication; the microscopic blood or slow bleeding which is intermittent and low volume identified in stool is below the detection limit of the scintigraphic imaging (*7*).

Technique

Prior to initiation of scanning, it is important to learn more about the patient and his/her symptoms. Understanding clinical descriptions of GI bleeding such as overt or occult GI bleeding are helpful in elucidating patient history from our clinical colleagues (Table 1) (*8*). Areas to explore include: whether the patient is stable enough to come down for imaging in the department, or if the study can be done portably with a portable scanner if available; clinical signs of GI bleeding; color of the bleeding; results of physical examination including results of rectal exam or nasogastric lavage, if performed; results of available prior imaging; results of endoscopy or colonoscopy. Good intravenous (IV) access is key; the patient should have 1 or 2 large bore IVs and fluid resuscitation products available on demand on entry to the nuclear medicine area. It is important to note if the patient has had any prior bowel/abdominal surgery and if the

surgery is recent. Recent barium evaluation is important to exclude as it may obscure findings when interpreting the GI bleeding scintigraphy (GIBS) (*7*). Knowing the patient's medications is helpful, especially when troubleshooting the cause of poor erythrocyte labeling. A list of medications and other substances contributing to poor labeling is available in Table 2 (*9-15*).

^{99m}Tc sulfur colloid has a short circulating half-life of 3 minutes and there is equally quick extraction of this tracer by the reticuloendothelial system (liver, spleen and bone marrow) (*11*). Imaging is generally performed for 20-30 minutes with ^{99m}Tc sulfur colloid. This decreases the opportunity to visualize the classically intermittent lower GI bleed. The high level of background activity in the liver and spleen can serve to obscure upper GI bleeding sources. For these reasons ^{99m}Tc erythrocytes have been found to be superior in multiple studies (*16-18)*. In other countries, ^{99m}Tc human serum albumin DTPA is used for the diagnosis of GI bleeding (*19*). All of these radiopharmaceuticals assist in "compartmental localization." With each of them we are imaging the vascular compartment, although some tracers stay in the vascular compartment longer than others.

There are three ways to label erythrocytes. The first is known as the *in vivo* method. In this method, no blood is withdrawn from the patient. The patient initially has an intravenous injection of stannous pyrophosphate that is allowed to circulate for a few minutes. Pre-tinning is followed by intravenous injection of ^{99m}Tc pertechnetate. This technique is generally not preferred secondary to the lower labeling efficiency. Nonetheless, it is reserved for certain patients who will not receive blood products for religious reasons (*11*,*20)*.

The next method is the modified *in vivo* technique, also known as the "*invivtro*" method. This method starts out similar to the *in vivo* method with intravenous injection of stannous pyrophosphate. Blood is subsequently withdrawn from the patient and mixed with ^{99m}Tc pertechnetate. This method has a somewhat better labeling efficiency (*11,20*).

The final method is known as the *in vitro* method. In this technique, blood is initially withdrawn from the patient and a "cold kit" is used. This kit contains stannous pyrophosphate in addition to a few other components. ^{99m}Tc pertechnetate is added. The *in vitro* technique offers the best labeling efficiency which improves the target to background ratio and decreases the likelihood of free pertechnetate interfering with the interpretation of the exam. When removing and readministering blood products to a patient, care must be taken to ensure that the correct patient receives the radiolabeled blood products.

A summary of the erythrocyte labeling techniques is available in Table 3. All of the labeling methods have one thing in common: use of a redox reaction (Fig. 1) that results in labeling of the erythrocytes at the β-chain of the hemoglobin (*3*). In this redox reaction, $Tc^{7+}O_4^-$ is the oxidizing agent and the stannous ion (Sn^{2+}) is the reducing agent (*11,20*,*21*).

After labeling the patient's erythrocytes and readministering them to the patient, if required depending on the labeling technique, scintigraphic images of the patient's abdomen and pelvis are acquired dynamically with a 128^2 matrix. The dynamic images are performed for 10-20 seconds/frame with an optional initial angiographic phase performed for 1-3 seconds/frame (*7*). The dynamic images can be reframed or summed on an as needed basis to increase the information density per frame. Static images other than for troubleshooting (descried below) are not recommended, as cine visualization is key to interpretation (*22*). If a dual-head gamma camera is used for evaluation, acquiring the images with both camera heads could enhance visualization of a rectal bleed (7). The length of scanning time is not standardized, but should be for an adequate length of time to allow for bleeding. The reasoning behind this is that GI bleeding, particularly in the large bowel, can be intermittent. A time interval for imaging from

1-4 hours depending on camera availability is reasonable (*7*), although some studies indicate that the optimal timing would be 1-2 hours (*23,24*).

Normal Biodistribution & Interpretation

Normal biodistribution of ^{99m}Tc radiolabeled erythrocytes includes the cardiac blood pool, vascular structures, liver, spleen, penile circulation and usually mild activity in the kidneys and urinary bladder (Fig. 2).

Our scintigraphic exam will only be positive if the patient is actively bleeding at the time of imaging. In order to diagnose a GI bleed, there are four criteria that need to be met: the focus of extravascular activity should start in a region where there was no abnormal activity before, the focus should increase in intensity over time, the focus should move in either an anterograde or retrograde fashion and finally, the focus should conform to bowel (*11*). When identifying the site of bleeding, it is important to know the major feeding vessel. The major feeding vessels are determined embryologically: perfusing the foregut, midgut and hindgut. The portion of the foregut that is visualized on GIBS is the stomach through the second part of the duodenum and is perfused by the celiac trunk. Branches of the celiac trunk include the left gastric artery, common hepatic artery and splenic artery. The midgut is perfused by the superior mesenteric artery, from the duodenal papilla to through the majority of the transverse colon. Branches of the superior mesenteric artery include the inferior pancreaticoduodenal artery, intestinal arteries, ileocolic artery, right colic artery and middle colic artery. The hindgut is perfused by the inferior mesenteric artery, from the remaining transverse colon through the superior portion of the anal canal. Branches of the inferior mesenteric artery include the left colic artery, sigmoid branches and superior rectal artery (*11*,*25*). Examples of bleeding at these three major sites are illustrated (Figs. 3-5). Localizing the main arterial distribution is helpful when planning angiographic intervention. Variceal bleeding is also an important finding, but does not have an arterial source.

Some institutions perform delayed bleeding imaging which may not accurately localize the origin of bleeding unless the four criteria to identify a positive exam are seen on delayed dynamic imaging. Laboratory values of blood urea nitrogen (BUN) and creatinine (Cr) can be helpful as the BUN/Cr ratio of 25 or greater indicates a greater likelihood of a positive delayed image (*26*). There has been work suggesting a prognostic benefit to performing delayed bleeding imaging (*27*). Digital subtraction has been found to be helpful in the setting of delayed GIBS (*7*).

Pitfalls & Pearls

There are a number of potential false positive findings that can occur in the setting of GIBS. Red blood cells can localize in other locations other than a site of worrisome GI bleeding. Some of these entities include: splenosis, pancreatic pseudocysts, nonenteric bleeding/hematoma (*7*,*8*,*28*).

Other physiologic activity can occasionally confuse the interpreter; this activity is usually fixed. Previously reported sources of error include: renal activity from a morphologically normal kidney, renal transplant or horseshoe kidney; urinary bladder activity or contamination; a urinary diversion; dilated abdominal aorta; ischemic bowel; hepatic hemangioma; vascular collaterals such as caput medusa or dilated mesenteric veins; angiodysplasia; the left ovarian artery and gallbladder in patients with renal failure; penis; uterus; uterine leiomyoma (*7*,*20*).

If the patient has had recent bowel or other abdominal surgery, prominent activity can be seen related to normal hyperemia in the postoperative state. Inflammatory bowel diseases such as Crohn's disease, a diverticular abscess and hypervascular neoplasms may also make interpretation difficult (*7*,*20*).

Relying on all four criteria to diagnose a positive GI bleed will often clarify whether or not the patient has active GI bleeding or another process masquerading as bleeding. Performing static imaging in the lateral or oblique projection(s), single photon emission computed tomography (SPECT), single photon emission computed tomography/computed tomography (SPECT/CT) or correlating with a prior CT scan can also assist in clarifying the true etiology of certain findings. In particular, static images of the neck with attention to the thyroid and salivary glands are often taken to exclude the presence of free ^{99m}Tc pertechnetate if there is suspicion based on the GIBS of the abdomen/pelvis. It should be noted that patients treated with exogenous thyroid hormone, prior treatment with sodium iodide ^{131}I or thyroid suppression may not have thyroid visualization in spite of the presence of free pertechnetate. Similarly, salivary activity can be reduced by a host of medical conditions, medications or prior therapies (e.g. Sjögren's syndrome, Parkinson's disease, antihistamines, diuretics, antipsychotics, chemotherapy, prior surgical disruption, radiation therapy with external beam or with sodium iodide ^{131}I, etc.). Areas of free pertechnetate seen on scintigraphic images include: stomach, salivary glands, thyroid gland and the choroid plexus (*29*). A lateral image of the pelvis can be helpful to exclude the presence of a rectal bleed and clarify what may be only be physiologic penile activity.

Use of SPECT & SPECT/CT

In addition to clarifying unclear sites of radiolabeled erythrocytes, the use of SPECT or SPECT/CT has been employed to further define the location of the bleeding. This is a useful tool that may help with therapeutic planning, particularly if angiography or surgery is planned. When this technique is employed regularly, dynamic images are generally performed for 10 to 15-minute intervals and checked. When a suspicious focus of labeled erythrocytes is identified, then a SPECT or SPECT/CT can be performed (*30*). The SPECT/CT can be shortened to a 15-minute acquisition to arrive at a more rapid diagnosis (*7*). SPECT/CT has also been demonstrated to be helpful in localizing difficult bleeding sites (*31-35*). In particular, investigators have identified that SPECT or SPECT/CT can increase the sensitivity, specificity and enhance localization of bleeding sites (*30*). Accurate localization can help to streamline therapy for the patient and achieve an earlier therapeutic response. It should be noted that in the event of rapid intraluminal GI bleeding during the course of the SPECT/CT, localization could be impaired. Referencing the SNMMI procedure guidelines for SPECT/CT imaging is recommended (*36*).

Sensitivity of GIBS

The GIBS will detect a bleeding rate of 0.05-0.2 mL/minute (*3*,*37*). The sensitivity of GIBS is reported at 93% sensitivity and 95% specificity (*16,17*), although some other investigators cite lower rates (*38,39*). The variation in rates of sensitivity is likely related to the lack of gold standard, but it is clear that detection rates increase when the study is performed as intended: when the patient is actively bleeding.

There is research that indicates which characteristics of positive GIBS that can be predictive of positivity of a subsequent angiographic examination. Mehta and colleagues found that a positive GIBS within 12 minutes of scanning correlated with a positive angiogram (*40*). Chamarthy and colleagues found that early visualization of bleeding within the first frame of imaging correlated best with a positive angiogram (41). Prompt performance of GIBs, early time to positivity on the GIBS, relative intensity of activity and prompt performance of angiography subsequent to GIBS were found to lead to a positive angiogram by Lee and colleagues (*42*). Ng and colleagues found that "immediate" visualization of bleeding on GIBS, defined as 2 minutes or less, was associated with a positive angiogram (*43*). Gupta and colleagues also described that grading the intensity of bleeding may be helpful in predicting angiographic positivity (*44*). It is important for the best care to have the patient evaluated by angiography in a timely fashion after identifying a positive GI bleed.

GIBS for Surgical Planning

There are several articles that evaluate GIBS in the setting of surgical planning. These articles give a

mixed opinion on the efficacy of GIBS in the setting of surgical planning: some report it as effective sole means for surgical planning (*45,46*), others suggest that it is only useful as screening tool prior to angiography (*47*) and still others call it “useless” for surgical planning (*48*). Given this mixed opinion, it is uncertain how well this performs for surgical planning in all centers. Of note, none of these papers evaluated surgical planning with GIBS SPECT/CT. As we learned above, this technique enhances localization, sensitivity and specificity. In the future this could be a topic for further investigation.

Use of CTA versus GIBS

Some centers are starting to move away from the use of GIBS and are using computed tomography angiography (CTA) for evaluation of active GI bleeding. This technique is generally performed by doing 3 discrete CT scans of the abdomen and pelvis: a non-contrast CT (although some institutions do not perform the non-contrast phase), an arterial phase contrast-enhanced CT and a subsequent delayed phase CT. Water and hyperdense oral contrast are avoided. The slice thickness of these CTs is quite small on the order of 1-2 mm (*49*). When referencing appropriateness criteria for lower GI bleeding, both GIBS and CTA are ranked similarly for evaluating lower GI bleeding according to the American College of Radiology (ACR) (*50*).

While deciding whether GIBS or CTA is best is controversial, many have attributed the rapid adoption of CTA to several factors including: a faster diagnosis in patients who are clinically deteriorating (*51*), ability to delineate congenital and other vascular abnormalities that could affect the angiography approach (*52*), greater diagnostic accuracy (*53*) and relatively similar reported sensitivity of 0.3-1 mL of extravasated blood (*54*). Some drawbacks include higher cost and limited time of evaluation (*55*). Although the ACR Appropriateness Criteria rates the relative radiation level (RRL) of absorbed dose to the patient as the same for GIBS and CTA, the radiation dose to the patient is higher with CTA (Table 4) (*56*). The iodinated contrast load is also greater (there is no nephrotoxic aspect of GIBS), although with greater localization less contrast might be used on a more selective angiographic evaluation/intervention. Both false positives and false negatives can be seen in the setting of GIBS and CTA (*7*,*57*).

Pediatric GIBS considerations

GI bleeding in pediatric patients has a number of different etiologies that vary by location of the bleeding and by patient age. For upper GI bleeds, newborns to 1 month olds can have GI bleeding related to milk protein sensitivity, coagulopathy, stress gastritis or ulcer, vitamin K deficiency, swallowed maternal blood or vascular anomaly. Between the first and second month, stress gastritis or ulcer, acid-peptic disease, gastrointestinal duplications, gastric/esophageal varices, duodenal/gastric webs, bowel obstruction and vascular anomalies account for episodes of upper GI bleeding. In childhood and the adolescent period, acid-peptic disease, caustic ingestions, acid-peptic disease, bowel obstructions, Crohn’s disease, Dieulafoy lesions or Mallory-Weiss tears are the possible etiologies of upper GI bleeding (*58*).

Lower GI bleeding has different etiologies by age. For newborns until 1 month of age, necrotizing enterocolitis, allergic proctocolitis, Hirschsprung disease, hemorrhagic disease of the newborn and malrotation with volvulus can be seen. In 1 month-2 year olds, an anal fissure, infectious colitis, allergic proctocolitis, Meckel’s diverticulum, Hirschsprung disease, intestinal duplication, lymphonodular hyperplasia and intussusception can cause lower GI bleeding. In 2-5 year old children, anal fissures, infectious colitis, polyps, Meckel’s diverticulum, Henoch-Schönlein purpura, hemolytic uremic syndrome and lymphonodular hyperplasia account for lower GI bleeding. In children older than 5 years, anal fissures, infectious colitis, polyps, inflammatory bowel disease and Henoch-Schönlein purpura (*58*) are causes of lower GI bleeding.

The recommended administered activity is based on the EANM Pediatric Dosage Card which uses a baseline activity of 56 MBq multiplied by a weight based factor and a minimum administered activity of 80 MBq (*7*,*59*). The imaging technique otherwise generally follows what is done for adult patients, as described above.

In addition to the broad differential diagnosis for both upper and lower GI bleeding in pediatric patients discussed above, it should be noted that because of the lower absorbed radiation dose, GIBS is preferred in the pediatric population and CTA should be avoided (*60*). If SPECT/CT is employed, the milliampere-seconds (mAs) settings should be appropriate for patient size and age (*34*).

MECKEL'S DIVERTICULUM IMAGING

Johan Friedrick Meckel first comprehensively described this diverticulum in 1809 (*26)*. Bleeding from a Meckel's diverticulum can potentially occur at any age, but is far more common in the pediatric age group. We recall the "rule of 2's" which relates to the Meckel's diverticulum: 2 feet from the end of the small intestine, 2 inches in length, 2% of the population, 2 times more common in males, presenting in the first 2 decades of life and often in the first 2 years. The most common congenital cause of a Meckel's diverticulum is failed closure of the omphalomesenteric duct, most commonly located in the distal ileum. Approximately 10-60% of these diverticula contain ectopic mucosa. A Meckel's diverticulum can contain either ectopic gastric, pancreatic or duodenal mucosa (*61*). Most commonly, the abnormal tissue is ectopic gastric mucosa. Irritation from the gastric acid and pepsin produced in an ectopic location will lead to bleeding (*62*). Other lesions with ectopic mucosa can include enteric duplications, gastrogenic cysts and duplication cysts (*63*).

In preparation for the exam, the patient should fast for 3-4 hours for best sensitivity, although this is not required (*64*). ^{99m}Tc pertechnetate is the radiopharmaceutical of choice as it localizes to gastric mucosa. This agent's mechanism of localization is via both the parietal cells and the mucin secreting cells of the gastric mucosa (*11*). A Meckel's scan assists in localizing the abnormal tissue in preparation for surgical removal. Per the North American Consensus Guidelines for pediatric radiopharmaceutical administered doses, the dosing of ^{99m}Tc pertechnetate is recommended at 1.85 MBq/kg, with a minimum of 9.25 MBq (*65*). There are a few "cold" pharmaceuticals that can be used to enhance the visualization of a Meckel's diverticulum (Table 5) (*11,61*).

Images are acquired dynamically with a frame rate of 30-60 seconds with a 128^2 matrix, lasting for a minimum of 30 minutes. Imaging for 60 minutes can be performed when clinical suspicion is high and the initial 30-minute images are negative (*61*).

Post-void images or a urinary catheter can be helpful should there be a diverticulum which is obscured by excreted activity in the urinary bladder. A dose of furosemide (1 mg/kg IV) may assist in clearing a prominent renal collecting system or ureter (*61*).

On imaging, a Meckel's diverticulum is identified as a focus of increasing intensity in the lower abdomen/upper pelvis. This focus should generally appear at the time of stomach visualization and increase in intensity as the stomach increases in intensity on the images (Fig. 6) (*11,20*).

Pitfalls in Meckel's Imaging

False positive results can occur from a number of clinical entities including intussusception, volvulus, abscess, appendicitis, neoplasm, angiodysplasia, Crohn's disease, ulcerative and other forms of colitis (*66-70*). For more information on GI and non-GI related causes of false positive results on Meckel's scans, see Table 6.

SPECT/CT has also been described as a troubleshooting technique in the setting of Meckel's diverticulum, excluding artifacts and assisting in surgical planning (*71*). Once again, use of SPECT/CT should be performed with the appropriate CT mAs for patient size and age (*34,61*).

CONCLUSION

Scintigraphic methods of imaging gastrointestinal bleeding remain an important method in Nuclear Medicine. Current techniques and interventions have been described. Prompt evaluation and direction of care is important in GI bleeding because it can be lethal in certain instances. Nuclear Medicine can contribute significantly to the management of these patients.

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Figure 1. Stannous reduction method (*3*).

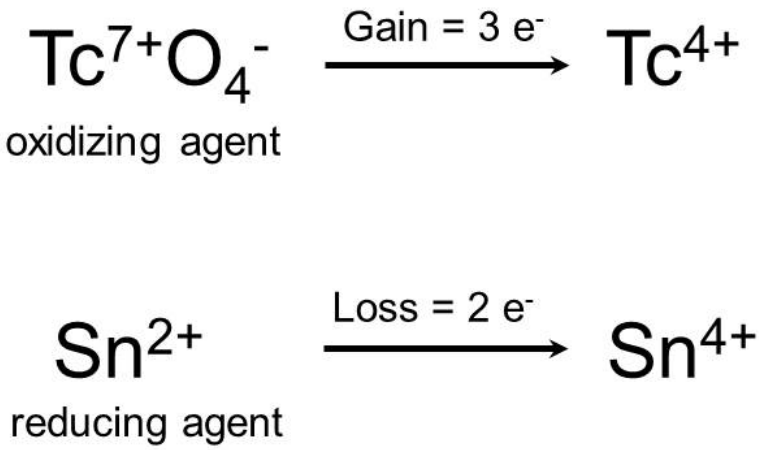

Figure 2. Normal biodistibution of ^{99m}Tc labeled erythrocytes. Heart (H), vascular structures (V), liver (L), spleen (S) and penis (P) are labeled. We see no intraluminal activity to suggest the presence of an active GI bleed.

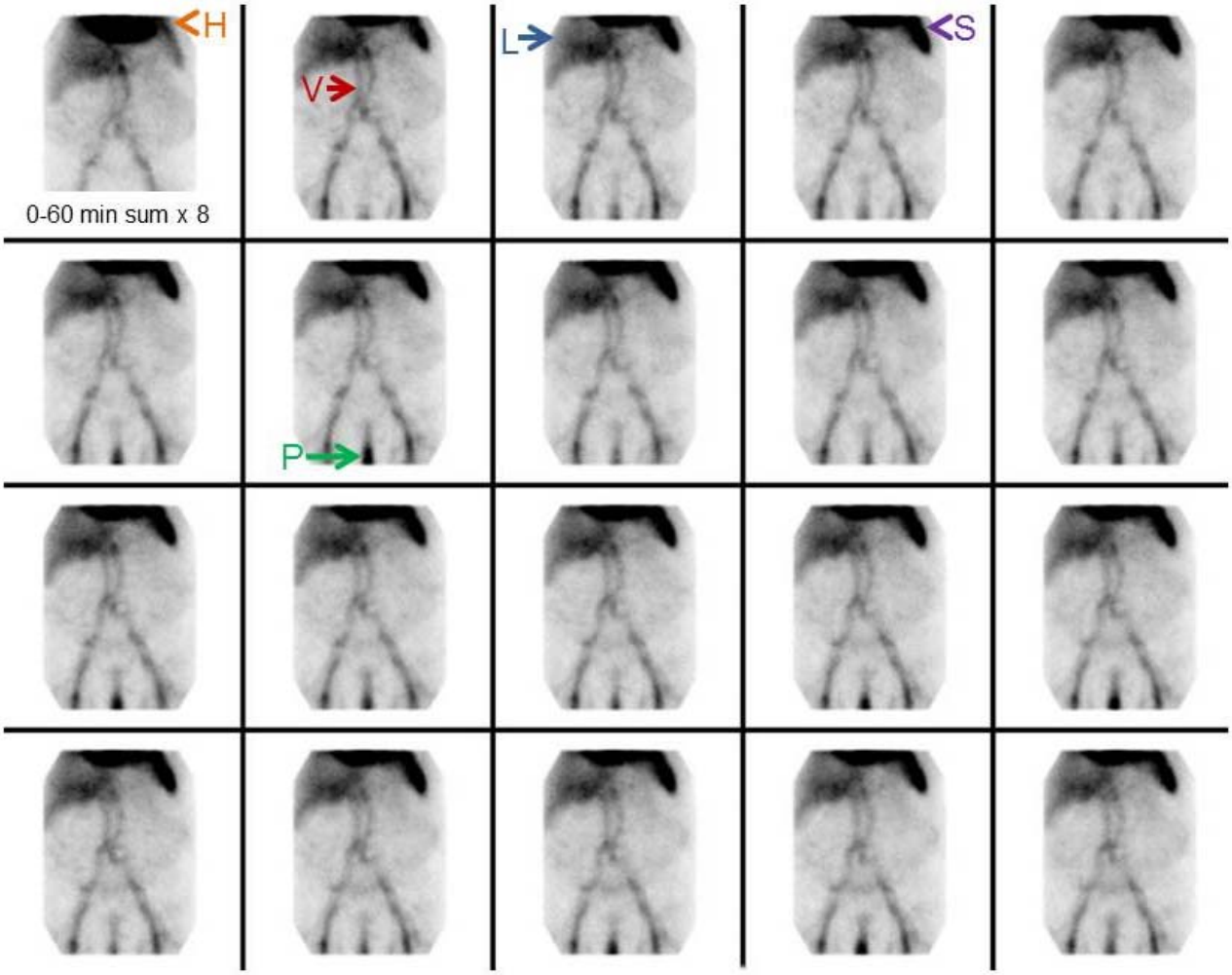

Figure 3. A focal area of increasing intensity is identified in the upper abdomen, moves in an anterograde fashion, conforms to bowel and has a distribution suspicious for a gastric bleed (red arrows). This is an example of bleeding originating from a branch of the celiac artery.

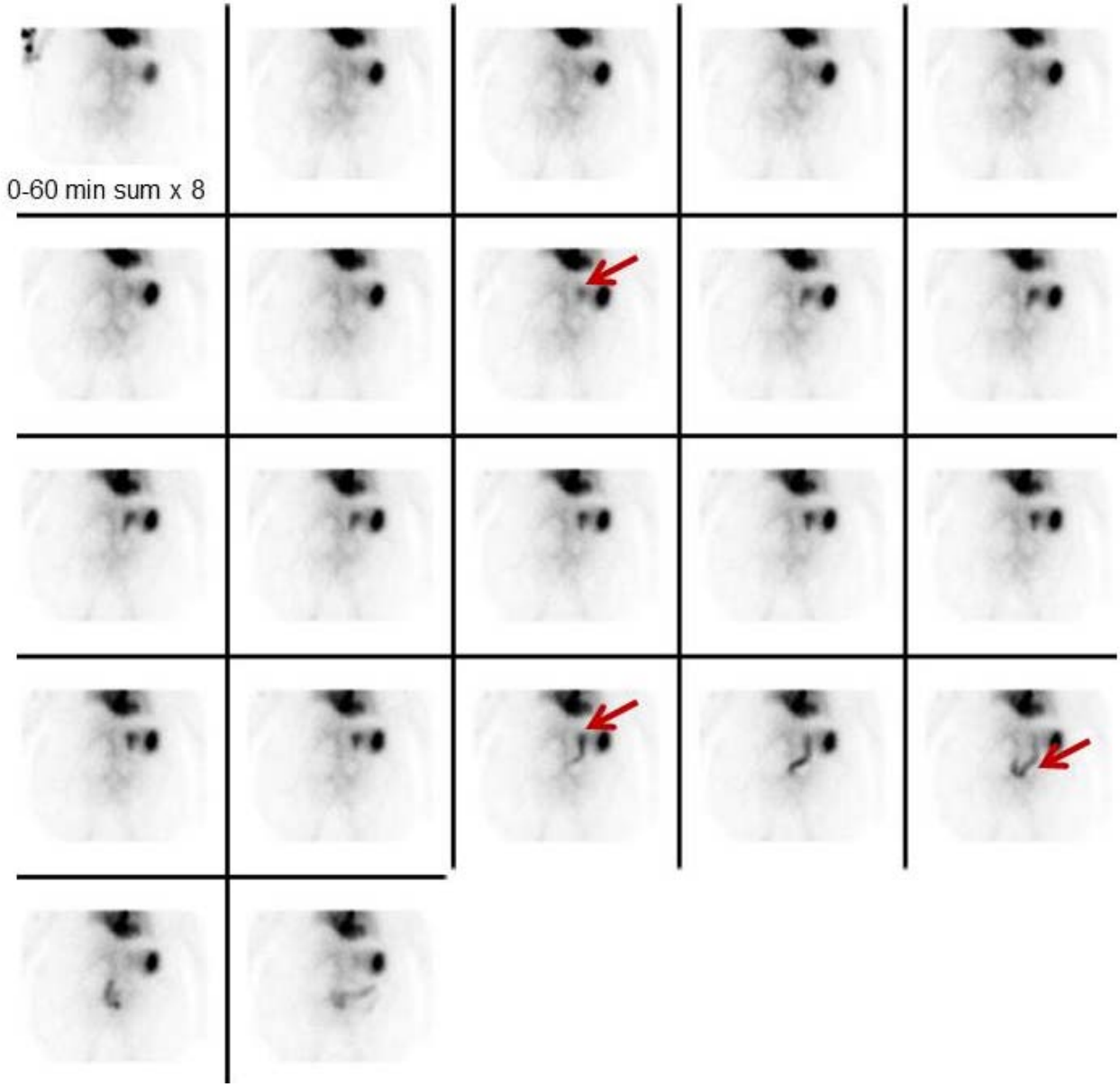

Figure 4. A focus of increasing intensity is identified in the lower abdomen at the midline (red arrows), there is anterograde and retrograde movement conforming to bowel lumen. As the focus crosses midline several times, this is most compatible with a small bowel bleed. This is an example of bleeding originating from a branch of the superior mesenteric artery.

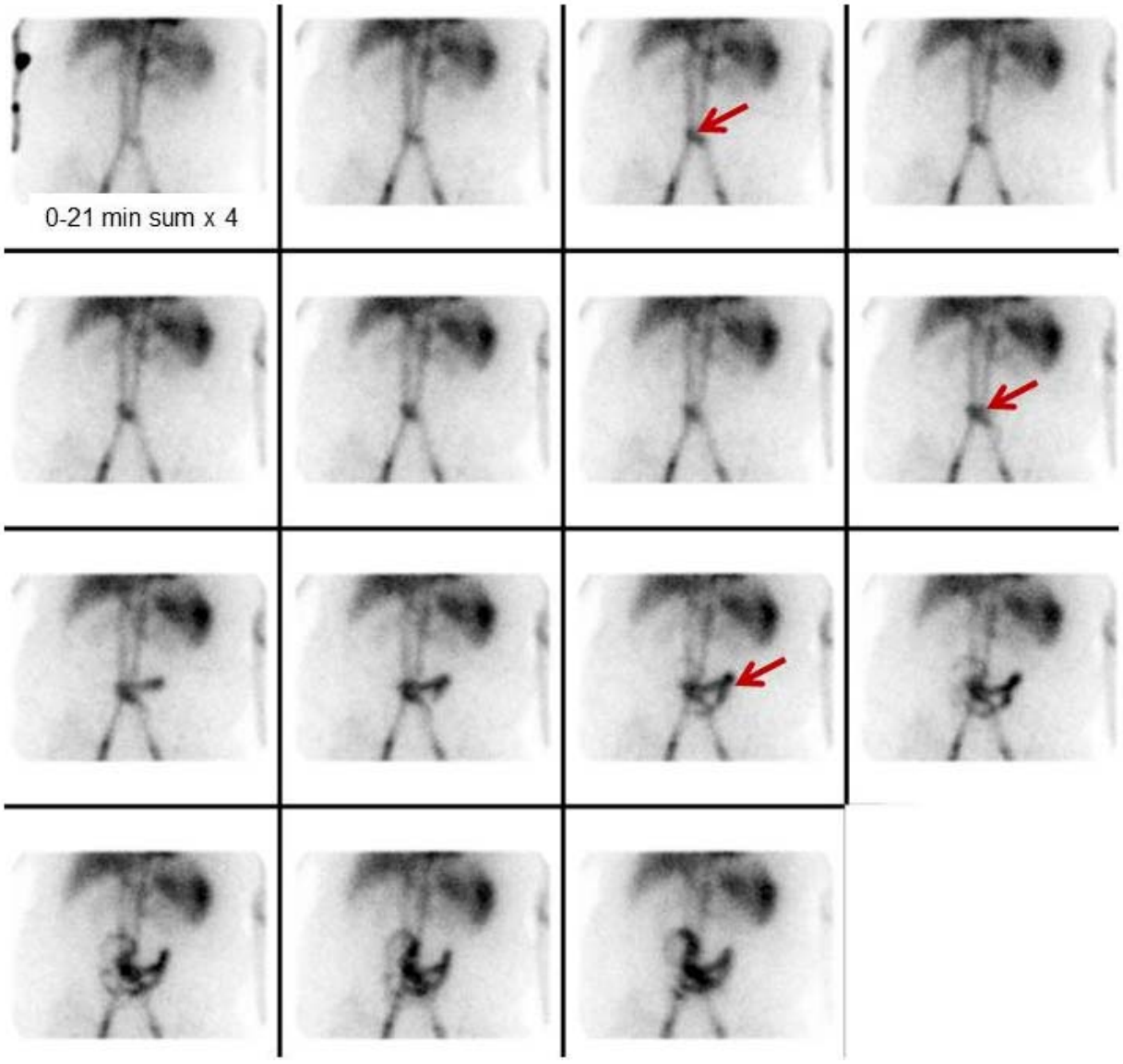

Figure 5. A focus of increasing intensity is identified in the left upper quadrant with anterograde movement and given its distribution in the periphery of the abdomen (red arrows) is typical of a large bowel bleed originating in the descending colon. This is an example of bleeding originating from a branch of the inferior mesenteric artery.

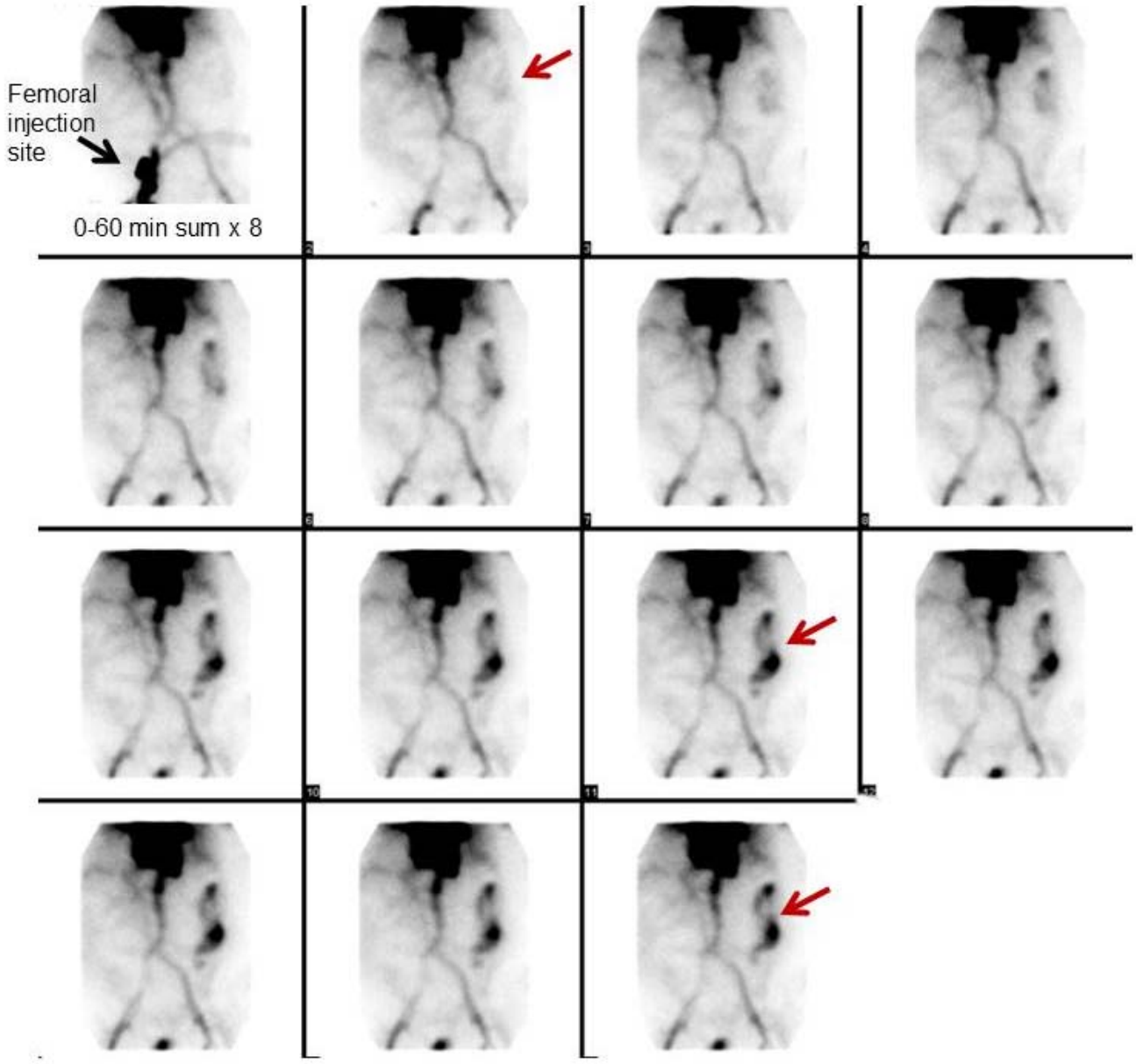

Figure 6. Typical imaging appearance of a Meckel's diverticulum. Note that the focus increases in intensity over time similar to the level of gastric uptake.

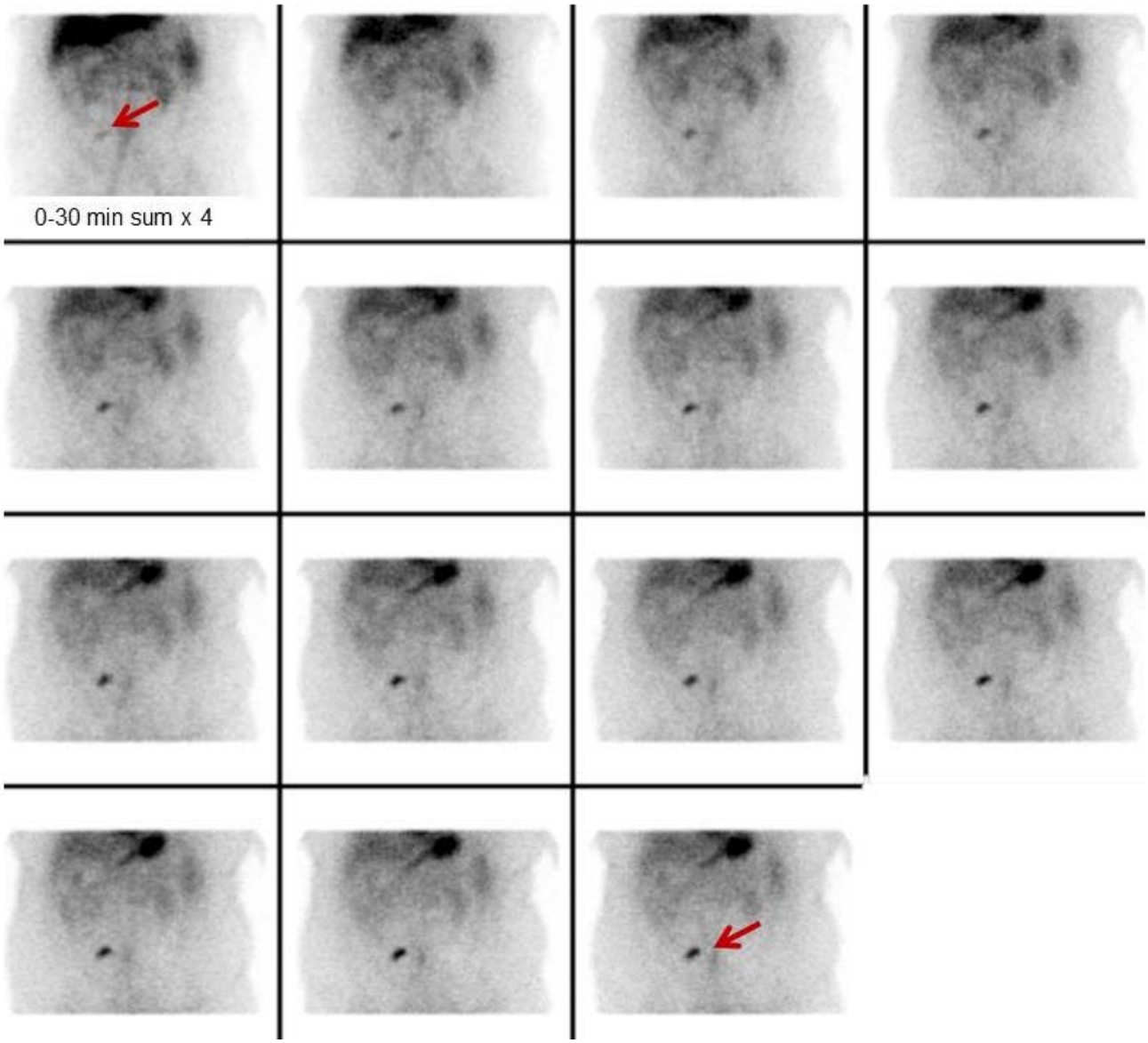

Table 1. GI bleeding definitions (*8*).

Term	**Definition**
Overt GI Bleeding	Also known as acute GI bleeding. This type of GI bleeding is visible in the form of hematemesis, melena or hematochesia.
Occult GI Bleeding	Also known as chronic GI bleeding. This type of bleeding is not apparent to the patient and presents as a positive fecal occult blood test or anemia.
Obscure GI Bleeding	Recurrent bleeding of uncertain source following or despite upper and/or lower endoscopy.
Hematemesis	The vomiting of blood.
Melena	Dark, tarry/sticky feces containing partially digested blood.
Hematochesia	The passage of fresh blood per anus, usually in or within stools.

Table 2. Medications, other substances & conditions interfering with erythrocyte radiolabeling, leading to free ^{99m}Tc pertechnetate (*9-15*).

Medication	**Mechanism of disrupted erythrocyte labeling**
Methyldopa	Oxidation of stannous ion; decreasing reduction
Hydralazine	Oxidation of stannous ion; decreasing reduction
Quinine	Possible antibody to RBCs
Doxorubicin	Lowers labeling efficiency in proportion to concentration of drug
Iodinated contrast media	Decreases stannous reduction; altered Tc-99m binding
Chocolate	Unknown
Tobacco	Relates to reactive oxygen species present; oxidation of the stannous ion, possible damage to the RBC plasma membrane and/or possible chelating action on the stannous and/or pertechnetate ions
Heparin	Forms complexes with ^{99m}Tc pertechnetate in the presence of stannous ion, causing renal excretion
Too much or too little stannous ion	Altered reduction of ^{99m}Tc pertechnetate
Recent blood transfusion	Unknown
Sickled red blood cells	Abnormal hemoglobin structure reduces labeling

Table 3. Methods of labeling erythrocytes with ^{99m}Tc and labeling efficiency (*3,11,20,21*).

Method	**Description & considerations**	**Labeling efficiency**
In vivo	The patient is injected with stannous pyrophosphate 1 mg IV, circulating for 20 minutes. This is followed by an intravenous injection of 555-1110 MBq ^{99m}Tc pertechnetate. This technique is generally not recommended secondary to its low labeling efficiency, but is reserved for patients who will not receive blood products for religious reasons.	75-80%
Modified in vivo (aka "in vivtro")	The patient is injected with stannous pyrophosphate 1 mg IV, circulating for 20 minutes. A vial of blood is then mixed with 555-1110 MBq of ^{99m}Tc pertechnetate. This is allowed to incubate for 10 minutes before intravenous injection into the patient.	85-90%
In vitro	A vial of blood is withdrawn from the patient that is added to the vial containing stannous pyrophosphate. After 5 minutes, the first vial "A" is added which contains sodium hypochlorite to destroy the extracellular Sn^{2+}. The citrate buffer ("B") is then added. ^{99m}Tc pertechnetate 555-1110 MBq is added and incubates before intravenously administering to the patient.	≥97%

Table 4. Comparison of whole body absorbed radiation dose evaluated by GIBS vs. CTA (*56*).

Technique	**Radiation dose (mSv)**
Pediatric GIBS with 80-784 MBq ^{99m}Tc RBCs	0.559-5.488
Adult GIBS with 555-1110 MBq ^{99m}Tc RBCs	3.885-7.77
CTA protocoled for GI bleeding without initial unenhanced CT phase	18.2
CTA protocoled for GI bleeding with initial unenhanced CT phase	27.3

Table 5. Pharmaceuticals that augment visualization of a Meckel's diverticulum (*11*,*58*).

Pharmaceutical	**Dosing/timing**	**Effect**
Cimetidine (other H_2 blockers like famotidine or ranitidine or a proton pump inhibitor can also be used, but have different dosing)	20 mg/kg/day PO x 2 days in children or 10-20 mg/kg/day x 2 days in neonates	Inhibits release of ^{99m}Tc pertechnetate by intraluminal cells, thus increasing and prolonging uptake
Glucagon	50 mcg/kg IV 10 minutes after administration of ^{99m}Tc pertechnetate	Slightly reduces gastric activity of ^{99m}Tc pertechnetate and suppresses peristaltic activity
Pentagastrin (no longer recommended in the United States secondary to side effects)	6 µg/kg SQ 20-30 minutes prior to ^{99m}Tc pertechnetate administration	Increases gastric mucosal uptake of ^{99m}Tc pertechnetate, thus increasing the target to background ratio

Table 6. False positive results on a Meckel's scan (*11*,*58*).

GI-Related False Positives	**Non-GI Related False Positives**
Peptic ulcer	Hydronephrosis
Barrett's esophagus	Aneurysm of abdominal vessel
Retained gastric antrum	Calyceal diverticulum
Duplication cyst of the ileum	Anterior sacral meningeomyelocele
Small bowel obstruction	Hemangioma
Appendicitis	Lymphoma
Intussusception	Ectopic kidney
Inflammatory bowel diseases such as Crohn's disease or ulcerative colitis	Recent laproscopic surgery (hyperemia at periumbilical port site
Carciniod of the small bowel	
Volvulus	
Small bowel bleeding not related to Meckel's	