

# Nuclear Medicine in the Acute Clinical Setting: Indications, Imaging Findings, and Potential Pitfalls<sup>1</sup>

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## LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- List the clinical indications for nuclear medicine studies in the acute care setting.
- Recognize pertinent findings at nuclear imaging in patients with acute clinical manifestations.
- Identify potential technical and imaging pitfalls in nuclear imaging and ways of avoiding them.



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## TEACHING POINTS

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Nuclear medicine imaging provides valuable functional information that complements information obtained with anatomic imaging techniques in the evaluation of patients with specific acute clinical manifestations. Nuclear medicine studies are most often used in conjunction with other imaging modalities and as a problem-solving tool. Under certain circumstances a nuclear medicine study may be indicated as the first-line imaging modality, as in the case of renal scintigraphy for transplant dysfunction in the early postoperative period. Nuclear imaging may be preferred when a conventional first-line study is contraindicated or when it is important to minimize radiation exposure. The portability of nuclear imaging offers particular advantages for the evaluation of critically ill patients whose clinical condition is unstable and who cannot be safely transported out of the intensive care unit. The ability to visualize physiologic and pathophysiologic processes over relatively long time periods without adding to the patient's radiation exposure contributes to the high diagnostic sensitivity of several types of nuclear medicine studies. Viewing the acquired images in the cine mode adds to the value of these studies for diagnosing and characterizing dynamic abnormalities such as intermittent internal bleeding and bile or urine leakage. In this pictorial review, the spectrum of nuclear medicine studies commonly performed in the acute care setting is reviewed according to body systems and organs, with detailed descriptions of the indications, technical considerations, findings, and potential pitfalls of each type of study. Supplemental material available at <http://radiographics.rsna.org/lookup/suppl/doi:10.1148/rg.332125098/-/DC1>.

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**Abbreviations:** ATN = acute tubular necrosis, CSF = cerebrospinal fluid, ERCP = endoscopic retrograde cholangiopancreatography, GI = gastrointestinal, MAA = macroaggregates of human albumin, PIOPED = Prospective Investigation of Pulmonary Embolism Diagnosis, RBC = red blood cell, SPECT = single photon emission computed tomography

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## Introduction

Nuclear medicine can play an important role in diagnostic imaging performed for specific indications in the acute clinical setting. The functional information available with nuclear imaging often cannot be obtained from anatomic imaging with other modalities and can be used to make more accurate and confident diagnoses. A nuclear medicine study may be performed as the first-line imaging examination for some indications, as in the case of renal scintigraphy performed to determine the cause of transplant dysfunction. More often, nuclear imaging is used for problem solving in conjunction with other imaging modalities, such as hepatobiliary scintigraphy in a patient with equivocal findings at ultrasonography (US) performed for suspected acute cholecystitis. The ability to image normal physiologic and pathophysiologic processes over relatively long time intervals without increasing the patient's radiation exposure contributes to the high sensitivity of several nuclear medicine studies for the detection of abnormalities that have a dynamic component or occur intermittently, such as gastrointestinal (GI) tract bleeding. In some circumstances, such as when a different first-line imaging study is contraindicated or when it is important to minimize the patient's radiation exposure, nuclear imaging may be the preferred first-line modality. For example, ventilation-perfusion scintigraphy may be performed as the initial imaging examination for the detection of pulmonary embolism in a patient with an allergy to iodinated contrast agents or with severe renal impairment (1).

The spectrum of nuclear imaging studies commonly performed in adult patients in the acute clinical setting is described in this article according to the body system or organ being evaluated. The indications for, and specific uses of, each nuclear study are discussed to help readers correctly integrate nuclear medicine into the overall diagnostic imaging evaluation. Key technical considerations, imaging findings, and potential pitfalls of nuclear imaging studies are described in detail to facilitate their optimal use and accurate interpretation in the acute care setting. Further information about the techniques and protocols for many of these studies is available from the Web site of the Society of Nuclear Medicine and Molecular Imaging (2) and the published literature cited in the following sections.

## Hepatobiliary Scintigraphy

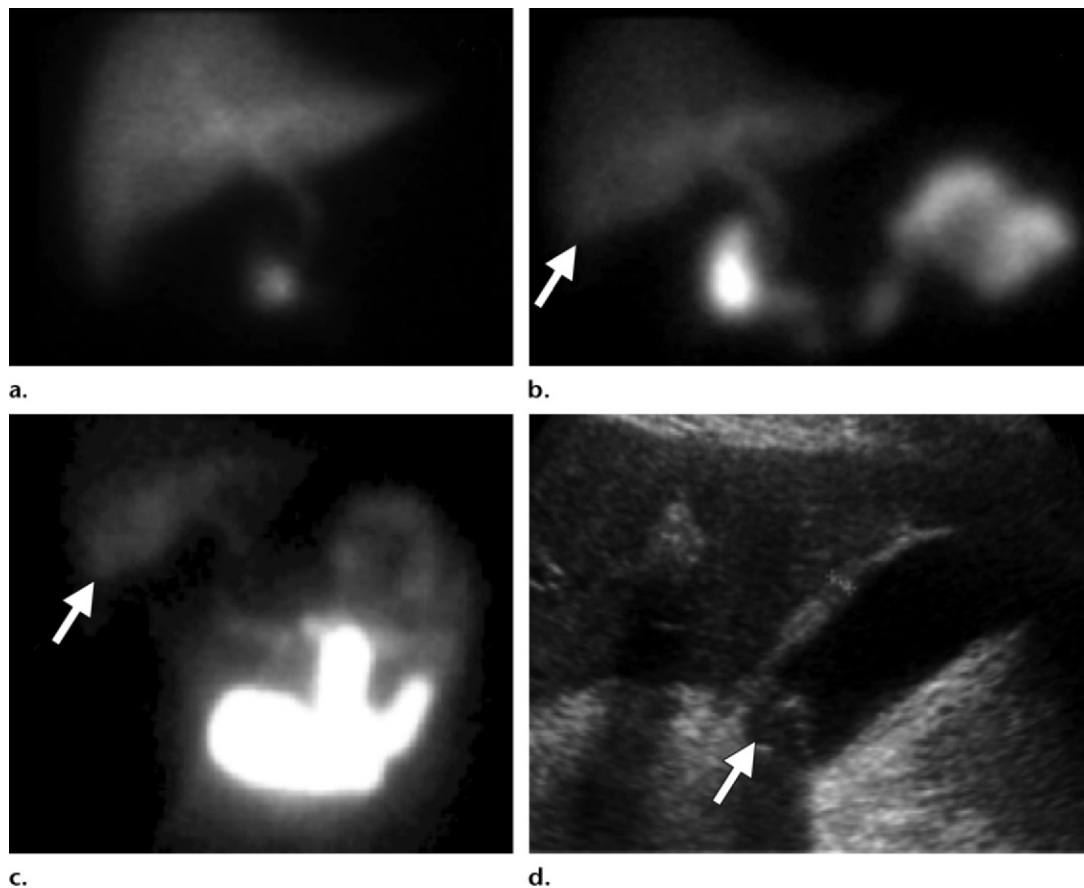
### Clinical Indications in the Acute Care Setting

Hepatobiliary scintigraphy is indicated predominantly for the diagnosis of acute cholecystitis. It may also be useful for diagnosing bile leaks, especially in the postoperative period. Common bile duct obstruction, although it is not typically considered an indication for this test, may be observed at hepatobiliary scintigraphy.

### Imaging Modalities and Radiopharmaceuticals

The accuracy of hepatobiliary scintigraphy for the detection of acute cholecystitis has been examined in many studies; in the largest of these, sensitivity and specificity of 98% and 100%, respectively, were found (3). In subsequent studies, the accuracy of hepatobiliary scintigraphy was compared with that of US, which has reported sensitivity ranging from 40% to 97% and specificity ranging from 64% to 100% (4–11). Despite the difference in accuracy between the two modalities, the first-line imaging study when the presence of acute gallbladder disease is suspected is often US, primarily because of its widespread availability, lack of ionizing radiation, and ability to depict other causes of acute abdominal pain. Many patients with acute cholecystitis may undergo initial computed tomography (CT) if the clinical manifestations are nonspecific or atypical. Hepatobiliary scintigraphy is often reserved for patients with indeterminate findings in other imaging studies.

When the presence of a bile leak is suspected in patients with acute abdominal pain, especially after cholecystectomy, hepatobiliary scintigraphy has proved useful (12). However, such patients often undergo an initial anatomic imaging study (most commonly CT) to allow the detection of perihepatic fluid collections; if CT shows a perihepatic fluid collection with characteristics of a biloma, then a functional evaluation with hepatobiliary scintigraphy may play a complementary role. If the presence of a common bile duct obstruction is suspected, initial US, endoscopic retrograde cholangiopancreatography (ERCP), or magnetic resonance (MR) cholangiopancreatography might be performed. The radiotracers most often used in hepatobiliary scintigraphy are the technetium 99m ( $^{99m}\text{Tc}$ )-labeled iminodiacetic acid analogs mebrofenin and disofenin.

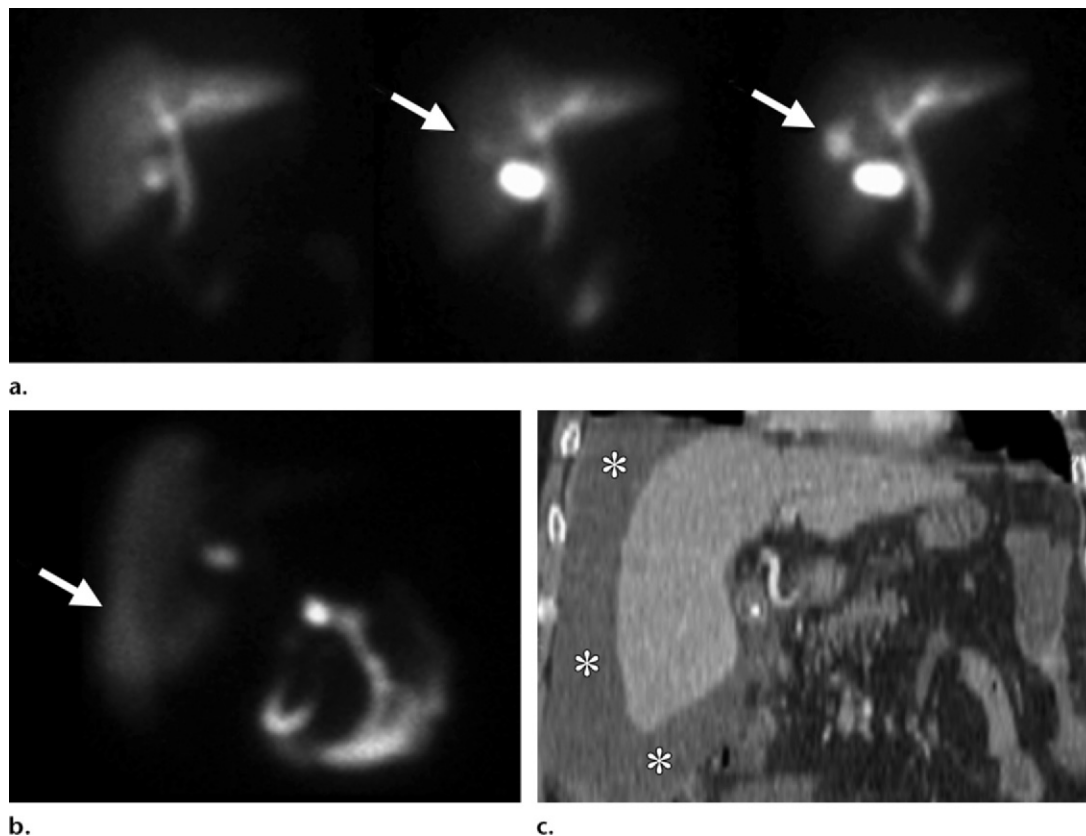


**Figure 1.** Acute cholecystitis in a 45-year-old man with severe epigastric pain. (**a–c**) Anterior images from hepatobiliary scintigraphy, obtained 15 minutes (**a**), 45 minutes (**b**), and 80 minutes (**c**) after the injection of  $^{99m}\text{Tc}$ -mebrofenin, show nonvisualization of the gallbladder. The hot rim sign (arrow in **b** and **c**), which is due to adjacent hepatic inflammation and decreased clearance of the radiotracer, was seen in all phases of imaging. (**d**) US image shows a stone impacted in the gallbladder neck (arrow) with thickening of the gallbladder wall.

### Scintigraphic Findings and Pitfalls

**Acute Cholecystitis.**—In most patients with acute cholecystitis, the cystic duct is obstructed by a stone, which prevents filling of the gallbladder by the radiotracer and results in nonvisualization of the gallbladder. In addition, the “hot rim sign,” or pericholecystic hepatic activity produced by increased accumulation of the radiotracer in the gallbladder fossa because of inflammation, may be seen (Fig 1; Movie 1 [online]). Radiotracer accumulation in the gallbladder fossa is typically associated with advanced or gangrenous cholecystitis and should not be mistaken for filling of the gallbladder lumen. The dilated cystic duct sign, which is produced by radiotracer activity in a short segment of the cystic duct proximal to an obstructing stone,

also has been described in the setting of acute cholecystitis (13). False-positive findings (eg, nonvisualization of the gallbladder) may result from recent food ingestion, prolonged fasting, total parenteral nutrition, hepatocellular dysfunction, or severe illness. False-negative findings (eg, activity in the gallbladder in the presence of cholecystitis, or regions of extra-cholecystic radiotracer accumulation mistaken for activity in the gallbladder) can occur in the presence of acalculous cholecystitis, with duodenal diverticula or biliary duplication cysts simulating the gallbladder (14). In patients who have been fasting for more than 24 hours and in patients who are receiving parenteral nutrition, the gallbladder may be full of sludge, which



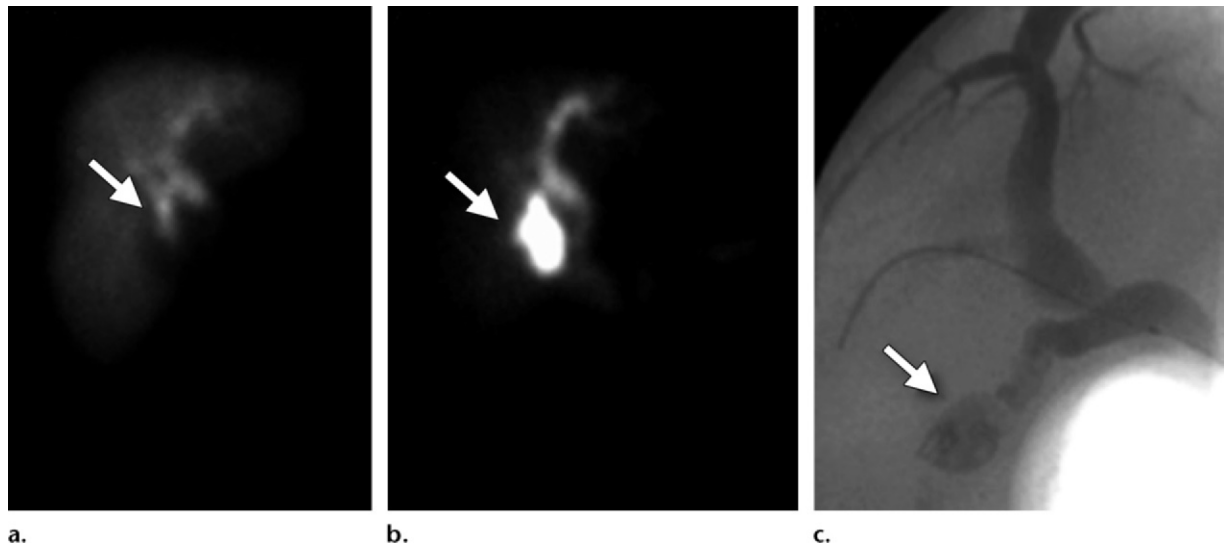
**Figure 2.** Perforated cholecystitis in a 45-year-old man with acute right abdominal pain. **(a)** Anterior images from hepatobiliary scintigraphy, obtained 35 minutes (left), 55 minutes (middle), and 60 minutes (right) after the injection of  $^{99m}\text{Tc}$ -mebrofenin, show activity in the gallbladder. A focal accumulation of the radiotracer (arrows) lateral to the gallbladder because of perforation was first seen at 55 minutes and had increased at 60 minutes. If the image acquisition had ended after the first 30 minutes, when the gallbladder was first visualized, the diagnosis of perforated cholecystitis would have been missed. **(b, c)** Anterior scintigraphic image acquired after a delay of 4 hours shows radiotracer activity in the perihepatic space around the lateral and inferior aspects of the liver (arrow in **b**), helping confirm that the perihepatic fluid seen on the coronal CT image (\* in **c**) is bile.

could prevent infilling by the radiotracer. An intravenous injection of cholecystikinin can be administered approximately 30 minutes before the radiotracer in order to prevent false-positive findings of acute cholecystitis.

**Perforated Cholecystitis.**—Perforated cholecystitis (either calculous or acalculous) is a rare but life-threatening condition. Delayed imaging is useful both to confirm nonfilling of the gallbladder in the setting of cystic duct obstruction and to look for complications such as biliary perforation, which may manifest as extrabiliary activity (Fig 2; Movie 2 [online]). **Premature discontinuation of cholescintigraphy in a patient with a biliary perforation or a bile leak may lead to a false-negative interpretation.** Radiotracer ac-

cumulations in the gallbladder fossa because of biliary perforation may be mistaken for activity within the gallbladder; however, delayed images or additional projections may help differentiate between these two locations of activity.

**Bile Leak.**—The detection and localization of bile leaks after surgery or trauma are crucial for the timely management of these complications. Delayed imaging, particularly of the right paracolic gutter, is important and often aids in the identification of bile leakage, which tends to accumulate in this dependent region. Scintigraphic images should be correlated with images obtained with other modalities for anatomic localization of abnormal accumulations of radiotracer activity. Single photon emission computed tomography (SPECT)/CT may be valuable for



**Figure 3.** Biliary leak from the cystic duct stump in a 63-year-old woman with abdominal pain after laparoscopic cholecystectomy. (**a, b**) Gradual accumulation of  $^{99m}\text{Tc}$ -mebrofenin in the gallbladder fossa is seen first on the anterior scintigraphic image obtained at 25 minutes (arrow in **a**) and has increased on the delayed anterior image obtained at 60 minutes (arrow in **b**) after the radiotracer injection. (**c**) ERCP image shows a similar distribution of the injected contrast agent (arrow), helping confirm the presence of a bile leak. When interpreting images from cholescintigraphy, familiarity with the clinical manifestations and surgical history is important because a bile leak in the gallbladder fossa might be mistaken for normal radiotracer accumulation in the gallbladder.

establishing the diagnosis of bile leak in cases in which the findings at planar scintigraphy are equivocal (15). Tracking of the radiotracer cephalad on delayed images may produce the appearance of a paradoxical increase in hepatic activity or an abnormal liver contour, findings that may contribute to a false-negative interpretation of the nuclear imaging study (Fig 3; Movie 3 [online]).

**Cholelithiasis.**—The patency of the common bile duct can be evaluated with hepatobiliary scintigraphy (Movie 4 [online]), although the modality is not a first-line imaging examination for this indication. Absence of radiotracer activity in the small bowel on delayed images is suggestive of biliary obstruction; however, partial obstruction of the common bile duct by stones may lead to false-negative findings. Rarely, large common duct stones may produce photopenic defects at scintigraphy.

## GI Tract Scintigraphy

### Clinical Indications in the Acute Care Setting

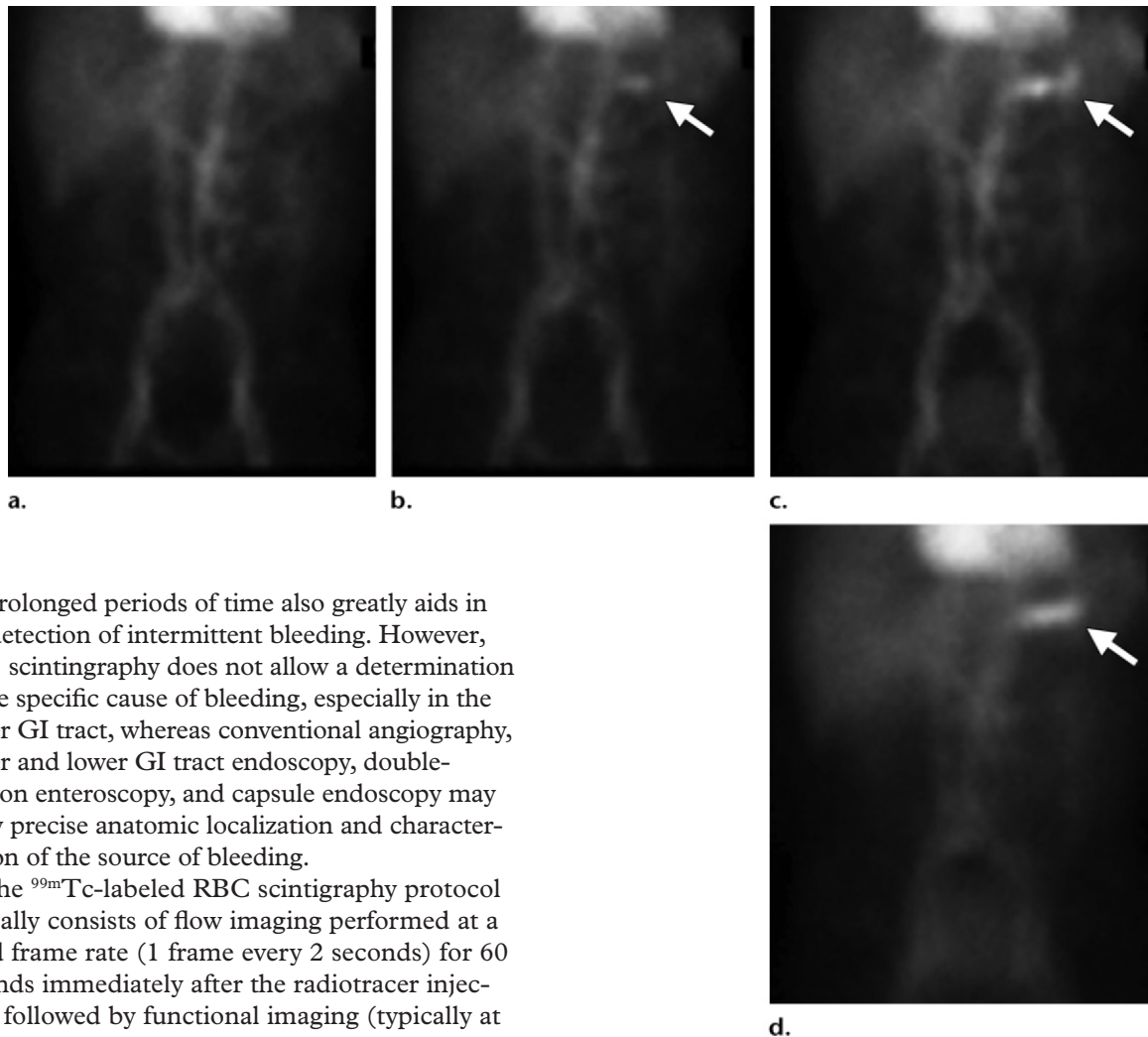
Scintigraphy of the GI tract is performed primarily in the setting of lower GI tract bleeding, to determine whether the rate of bleeding is sufficient to require urgent conventional (catheter-

based) angiography, endoscopy, or surgery. Patients in whom the site of bleeding is believed to be in the esophagus, stomach, or duodenum are typically evaluated first with upper GI tract endoscopy or nasogastric lavage. However, if upper GI tract bleeding is slow or the source cannot be identified at upper GI tract endoscopy, scintigraphy may be performed with  $^{99m}\text{Tc}$ -labeled autologous red blood cells (RBCs).  $^{99m}\text{Tc}$ -labeled RBC scintigraphy may help guide the management of bleeding by identifying a specific vascular territory (eg, celiac, superior mesenteric, or inferior mesenteric artery) as the source. It is also used occasionally for the detection of active bleeding in other sites, such as the thoracic cavity.

### Imaging Modalities and Radiopharmaceuticals

$^{99m}\text{Tc}$ -labeled RBC scintigraphy is the most sensitive imaging modality for detecting active bleeding, is noninvasive, and can depict both arterial and venous sources of bleeding (16). It is reported to have sufficient sensitivity to allow the detection of bleeding at rates of as little as 0.1 mL/min, whereas conventional angiography allows the detection of bleeding only at rates of 0.5 mL/min and above (16). The ability to image continuously

**Figure 4.** Hemorrhagic gastropathy in a 78-year-old man with epistaxis and melena. Anterior images from  $^{99m}\text{Tc}$ -labeled RBC scintigraphy, acquired at 5 minutes (a), 25 minutes (b), 65 minutes (c), and 85 minutes (d) after injection of the radiotracer, show a small amount of radiotracer accumulation (arrow) in the region of the stomach. The stationary position of this finding is suggestive of gastric bleeding rather than bleeding from the small bowel or colon, which typically moves rapidly because of peristalsis.



for prolonged periods of time also greatly aids in the detection of intermittent bleeding. However, RBC scintigraphy does not allow a determination of the specific cause of bleeding, especially in the upper GI tract, whereas conventional angiography, upper and lower GI tract endoscopy, double-balloon enteroscopy, and capsule endoscopy may allow precise anatomic localization and characterization of the source of bleeding.

The  $^{99m}\text{Tc}$ -labeled RBC scintigraphy protocol typically consists of flow imaging performed at a rapid frame rate (1 frame every 2 seconds) for 60 seconds immediately after the radiotracer injection, followed by functional imaging (typically at a rate of 1 frame per minute) for up to 90 minutes. Additional delayed static images in different projections can be acquired as needed. The study may be terminated earlier if bleeding is identified and its anatomic location can be determined.

### Scintigraphic Findings and Pitfalls

Scintigraphic findings of GI tract bleeding include intraluminal activity that increases progressively over time, and movement of the radiotracer during intraluminal transit. The latter finding is best depicted on cine images (17).

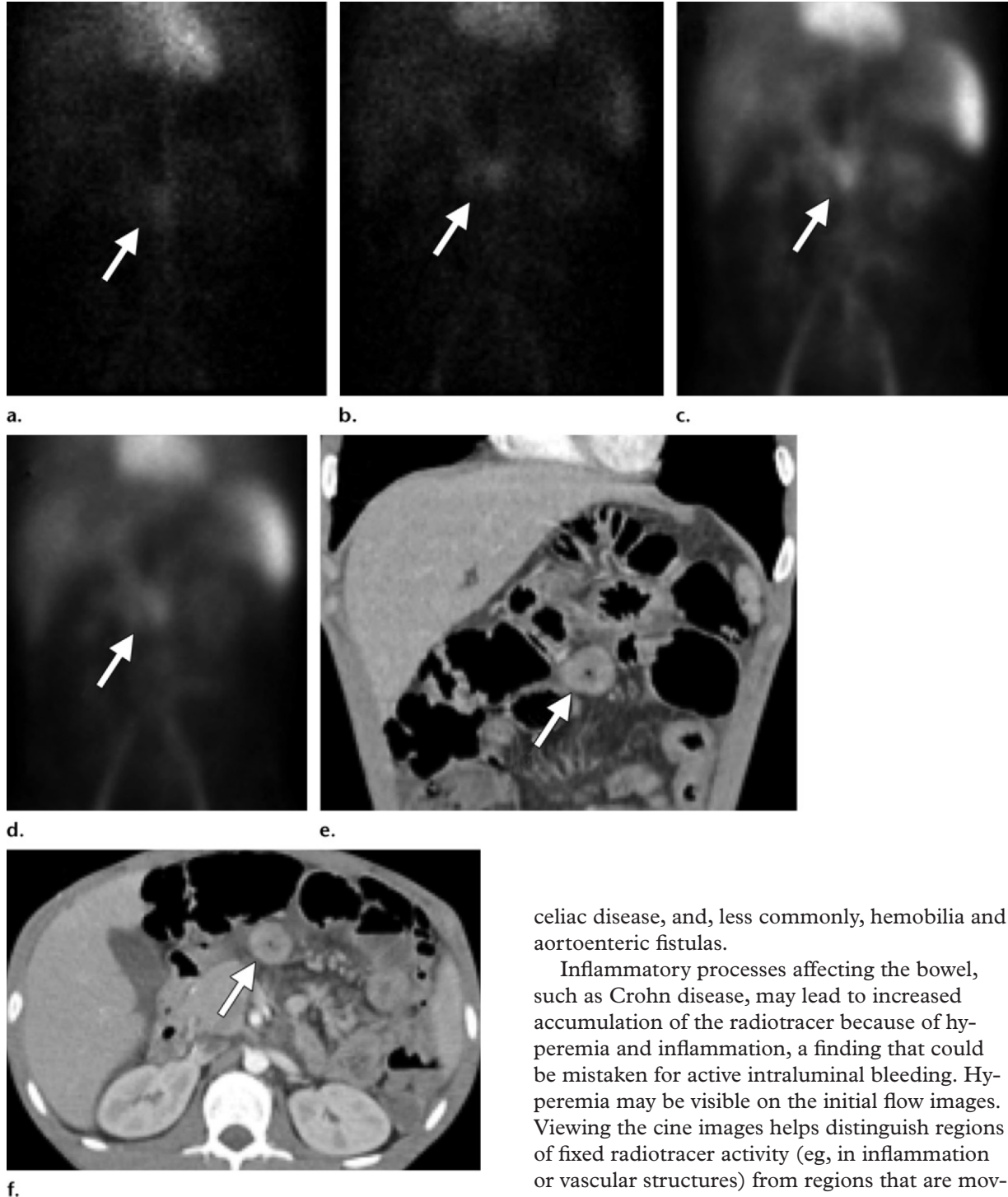
**Gastric Bleeding.**—The initial diagnostic test for upper GI tract bleeding typically involves either the sampling of gastric content through a nasogastric tube or upper GI tract endoscopy. However,  $^{99m}\text{Tc}$ -labeled RBC scintigraphy may reveal

the site of gastric bleeding (Fig 4; Movie 5 [online]). Causes of gastric bleeding include varices, peptic ulcers, angiectasia, and gastritis.

Inefficient RBC labeling may lead to false-positive findings because of the accumulation of free  $^{99m}\text{Tc}$  pertechnetate in the normal gastric mucosa. Less commonly, accumulated radiotracer in an accessory spleen or hepatic hemangioma overlapping with the stomach may simulate activity in the gastric lumen. In these instances, the absence of peristaltic motion helps differentiate radiotracer activity in solid organs from that in the GI tract.

**Small Bowel Bleeding.**—The small bowel is accessible with upper and lower GI tract endoscopy, double-balloon enteroscopy, and capsule endoscopy. In some cases,  $^{99m}\text{Tc}$ -labeled RBC scintigraphy can help detect and localize inter-

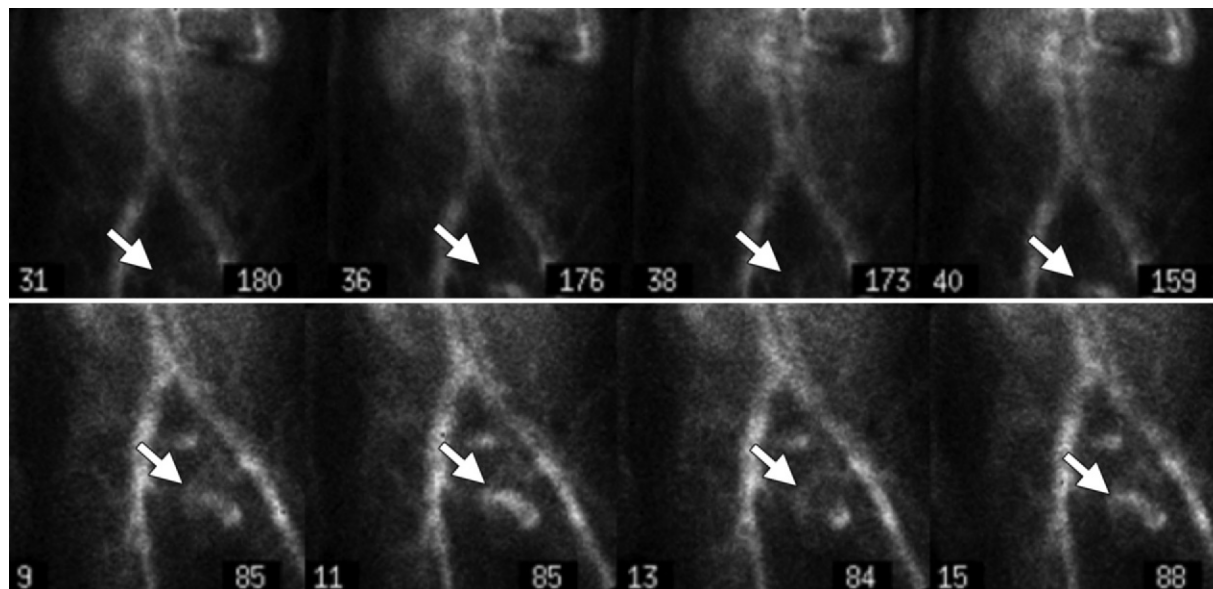
**Figure 5.** Inflamed bowel in an 18-year-old male patient with Crohn disease and GI tract bleeding. (**a–d**) Selected anterior images from  $^{99m}\text{Tc}$ -labeled RBC scintigraphy, acquired at 16 seconds (**a**) and 56 seconds (**b**) (during flow imaging) and at 10 minutes (**c**) and 60 minutes (**d**) (during functional imaging) after injection of the radiotracer, show a region of increased activity in the upper abdomen (arrow), a finding that does not move over time. The persistent radiotracer activity represents increased perfusion and hyperemia in an inflamed small bowel loop. (**e, f**) Coronal (**e**) and axial (**f**) CT images show the thickened wall of a small bowel loop in the upper abdomen (arrow), a feature that corresponds to the scintigraphic finding.



mittent small bowel bleeding. Causes of small bowel bleeding include tumors, Meckel diverticula, Dieulafoy lesions, angiectasia, Crohn disease,

celiac disease, and, less commonly, hemobilia and aortoenteric fistulas.

Inflammatory processes affecting the bowel, such as Crohn disease, may lead to increased accumulation of the radiotracer because of hyperemia and inflammation, a finding that could be mistaken for active intraluminal bleeding. Hyperemia may be visible on the initial flow images. Viewing the cine images helps distinguish regions of fixed radiotracer activity (eg, in inflammation or vascular structures) from regions that are moving because of peristalsis, which are typical scintigraphic features of GI tract bleeding (17) (Fig 5; Movie 6 [online]).



**Figure 6.** Normal penile uptake of the radiotracer at  $^{99m}\text{Tc}$ -labeled RBC scintigraphy in a 69-year-old man with non-ischemic cardiomyopathy and lower GI tract bleeding. Top row: Selected images obtained at the rate of 1 frame per minute show a region of increased activity at the lower edge of the field of view (arrows), a finding that appears and disappears on alternate images. To further evaluate this finding, the field of view was subsequently adjusted to include the pelvis. Activity is seen also in the left ventricular assist device in the upper left quadrant of the abdomen. Bottom row: Images obtained with the larger field of view show localized activity in the penis (arrows).

**Colonic Bleeding.**— $^{99m}\text{Tc}$ -labeled RBC scintigraphy is often the initial diagnostic test when the presence of active lower GI tract bleeding is suspected, and it can help guide therapy with endoscopy or angiography. Causes of colonic bleeding include diverticulosis, angiodysplasia, neoplasms, and internal hemorrhoids. When interpreting images from  $^{99m}\text{Tc}$ -labeled RBC scintigraphy, it is important to be aware that normal radiotracer activity in the penis (Fig 6; Movies 7, 8 [online]) or bladder may mimic rectal bleeding. **Activity in the urinary tract, especially the ureters and bladder, also may simulate radiotracer extravasation into the GI tract. Lateral or “tail-on-detector” views can be helpful to distinguish these normal structures from rectal bleeding.**

## Scintigraphy of the Native Kidney

### Clinical Indications in the Acute Care Setting

The most common indication for renal scintigraphy in the acute care setting is suspected urinary tract obstruction. Renal scintigraphy is particularly useful when interventions such as stent placement, percutaneous nephrostomy, or surgery are being considered. Urine leak and vascular compromise (eg, renal artery or renal vein thrombosis) are additional indications for this study.

### Imaging Modalities and Radiopharmaceuticals

US is frequently the first imaging modality used to evaluate the urinary system. It is readily available, can be performed at the patient's bedside, does not require the administration of a contrast agent, and does not involve the use of ionizing radiation. Doppler US is helpful if vascular complications are suspected. Nonenhanced CT is indicated as the first-line imaging modality for the detection of obstructing renal and ureteral stones (18).

Renal scintigraphy is usually performed to assess the functional significance of dilatation observed in the renal collecting system at imaging with other modalities, such as US or CT. Diuretic renal scintigraphy is often used to help differentiate obstructed from nonobstructed chronically dilated collecting systems and/or ureters, particularly in patients with a history of surgery or obstruction. The radiotracer most commonly used for this purpose is  $^{99m}\text{Tc}$  mertiatide (ie,  $^{99m}\text{Tc}$ -MAG<sub>3</sub>), a tubular agent. Because  $^{99m}\text{Tc}$  mertiatide is cleared primarily by active secretion in the proximal tubules with only minimal glomerular filtration,  $^{99m}\text{Tc}$  mertiatide clearance can serve as a surrogate measure for effective renal plasma flow.  $^{99m}\text{Tc}$  pentetic acid (ie,  $^{99m}\text{Tc}$ -DTPA) is a glomerular agent that may be used only in patients with normal or mildly impaired renal function because its extraction from plasma by the kidney depends directly on the glomerular filtration rate. The renal clearance of  $^{99m}\text{Tc}$  pentetic



acid filtered by the renal glomeruli closely approximates the glomerular filtration rate (19–22).

MR imaging is rarely performed in the initial workup for common acute clinical indications but may be used for problem solving or when CT is contraindicated in patients in whom the presence of urinary tract obstruction is suspected.

### Scintigraphic Findings and Pitfalls

In the setting of urinary tract obstruction, the time-activity curve generated from diuretic renal scintigraphy shows decreased radiotracer activity (decreased perfusion) in the affected kidney during the angiographic phase and delayed cortical concentration (delayed uptake) before the diuretic is administered. Delayed clearance of activity is seen after the diuretic is administered, with half-time of more than 20 minutes. Failed clearance of the radiotracer from the kidney after the administration of furosemide is suggestive of high-grade obstruction. In some cases of high-grade obstruction, no excretion of the radiotracer into the renal collecting system is seen. Common causes of false-positive findings of urinary system obstruction include attenuated effectiveness of furosemide, severe dilatation of a nonobstructed collecting system with a resultant reservoir effect, poor hydration, and high filling pressure of the bladder (20).

A urine leak is seen as extravasation of the radiotracer outside the expected anatomic boundaries of the collecting system or ureter. In the presence of a forniceal rupture of the obstructed system, radiotracer tracking is often seen along the ureter in the retroperitoneal space or in the paracolic gutter. In the presence of a urine leak that is due to disruption of a surgical anastomosis, radiotracer activity may be seen either in the peritoneal cavity (delineating the contour of the bowel loops) or in the retroperitoneal cavity, depending on the location of the leak. Knowledge of the postoperative anatomy is important, and the acquisition of additional views (eg, anterior images in patients in whom the presence of an anastomotic leak is suspected after ileal conduit reconstruction surgery) may be useful.

Acute compromise of the renal artery or vein of a native kidney typically causes markedly decreased or absent perfusion at renal scintigraphy. It is frequently impossible to reliably distinguish these two vascular abnormalities from each other or differentiate them from a chronically nonfunctioning kidney on the basis of findings at scintigraphy alone. In the acute phase of renal vein thrombosis, the kidney may be edematous, with decreased perfusion, delayed radiotracer uptake and excretion, and retention of  $^{99m}\text{Tc}$  mertiatide. Retention of  $^{99m}\text{Tc}$  pentetic acid also has been

described in the setting of segmental acute renal vein thrombosis (21).

Acute tubular necrosis (ATN), also known as acute vasomotor nephropathy, may be seen at renal scintigraphy in native kidneys. ATN typically affects both kidneys and has a multifaceted etiology that includes ischemic injury, contrast material-induced nephropathy, and nephrotoxic effects of drug therapy. Renal perfusion is typically relatively well maintained in comparison with the reduced renal excretion of the radiotracer into the collecting systems unless ATN is severe, in which case both perfusion and excretion may be markedly decreased.

## Renal Transplant Scintigraphy

### Clinical Indications in the Acute Care Setting

Renal transplant scintigraphy is usually performed to evaluate graft dysfunction in the first few days or first few weeks after surgery, but it also may be performed in patients who experience an acute deterioration of renal function months after successful transplantation. The nuclear imaging study can be helpful for distinguishing patients with conditions requiring surgical management (eg, vascular compromise or ureteral obstruction affecting the transplant) from those with renal transplant complications that can be managed conservatively or with medical therapy (eg, ATN or acute rejection). Common clinical manifestations of graft dysfunction are an elevated creatinine level, decreased urine output, or both. Fever, pain, and swelling may occur in the presence of acute rejection.

The most common complications in the early postoperative period have either a medical or a surgical cause. Because they manifest within relatively predictable time frames, the timing of their occurrence relative to the transplantation procedure may be helpful for their differentiation. In addition, a comparison of renal scintigraphic images obtained after the manifestation of graft dysfunction with images obtained at baseline postoperative renal scintigraphy may help narrow the differential diagnosis. The most common medical complication is ATN related to ischemic injury to the graft; ATN occurs more often in cadaveric transplants than in transplants from living donors. Acute rejection is another common medical complication that may be observed at renal scintigraphy. Other immune-mediated or immunosuppressive therapy-related manifestations of renal transplant dysfunction develop more slowly and are not described here.

Ureteral obstruction, vascular compromise, and urine leak are surgical complications that can be detected at renal scintigraphy. Perirenal collections such as abscesses, hematomas, and lymphoceles are usually diagnosed clinically or with US, but those that cause extrinsic obstruction of the ureter or extrinsic mass effect on the bladder also may be seen at renal scintigraphy.

### Imaging Modalities and Radiopharmaceuticals

The selection of a first-line imaging modality for evaluating a renal transplant depends on the differential diagnosis. If the presence of ATN is suspected, renal transplant scintigraphy is typically the first-line modality.  $^{99m}\text{Tc}$  mertiatide is the preferred radiopharmaceutical for renal transplant scintigraphy because it is secreted by the renal tubules and because uptake occurs even in the setting of impaired glomerular filtration. Most patients experience some degree of renal transplant dysfunction after transplantation surgery, and if the dysfunction is severe (eg, the serum creatinine level is greater than 6 mg/dL), the diagnostic value of the nuclear study may be limited because of poor radiotracer uptake and/or excretion. The uptake of  $^{99m}\text{Tc}$  pentetic acid, which depends on the glomerular filtration rate, is likely to be decreased in patients with a serum creatinine level of more than 2.5 mg/dL; thus, this radiotracer is less useful than  $^{99m}\text{Tc}$  mertiatide in this clinical setting.

Renal Doppler US is the first-line imaging examination for the detection of vascular compromise or postoperative fluid collections, although renal scintigraphy may play a complementary role in those settings. CT and MR imaging are useful for evaluating the entire abdomen and pelvis and provide valuable details about the transplant and adjacent anatomic structures; however, the use of a contrast agent may be contraindicated in patients with poor renal function, who may have a high risk for contrast media-induced nephropathy or nephrogenic systemic fibrosis.

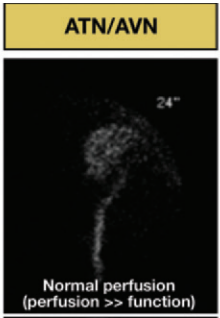
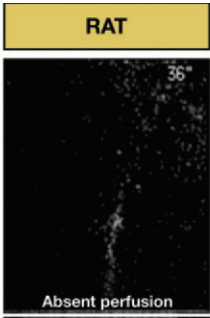
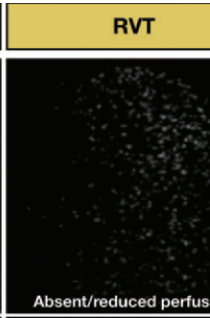
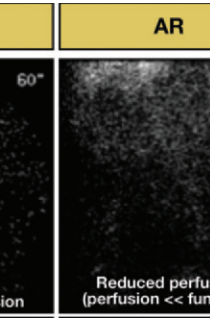
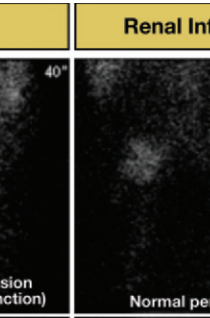
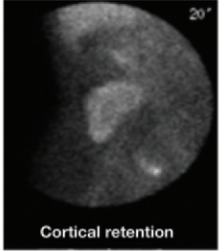
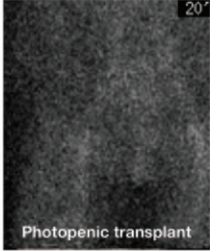
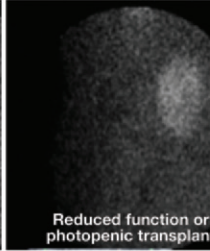
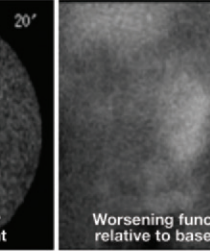
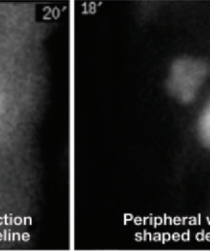
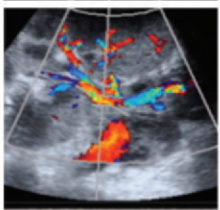
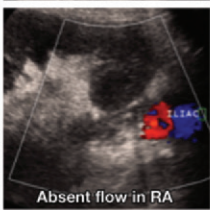
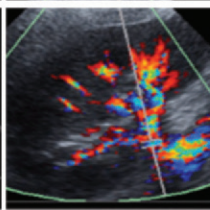
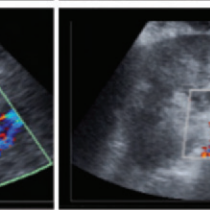
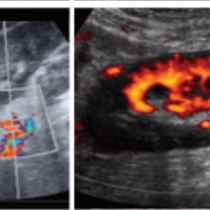
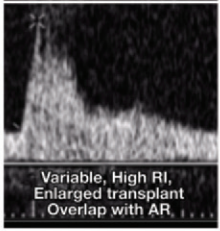

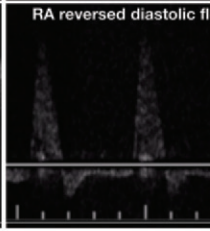
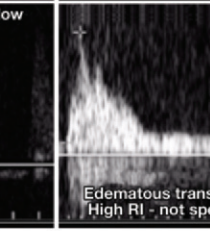
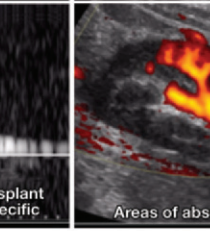
### Scintigraphic Findings and Pitfalls

Knowledge about the surgical approach used in transplantation, the type of ureteral anastomosis, and the type and number of vascular anastomoses (depending on whether the donor had one renal artery or multiple renal arteries) is important when interpreting scintigraphic studies of renal transplants. Familiarity with the appearances of common causes of graft dysfunction is also helpful.

Scintigraphic hallmarks of ATN include relative preservation of renal perfusion during the angiographic phase, with gradual accumulation of the radiotracer in the renal parenchyma because urinary excretion is minimal or absent (Fig 7; Movie 9 [online]). In ATN, unlike acute rejection, perfusion is typically better than function in the renal transplant. The timing of onset also may help differentiate the two entities: Acute rejection typically occurs from 1 week to a few months after transplantation, whereas ATN usually occurs in the first few days after transplantation and spontaneously resolves over the following days or weeks. However, in severe cases of ATN, both decreased perfusion and reduced radiotracer uptake may be seen at scintigraphy, a pattern that precludes definitive diagnosis and implies a poor prognosis. Repeat renal scintigraphy may be necessary to determine whether ATN has resolved. If a follow-up study demonstrates spontaneous resolution of ATN but a subsequent follow-up study shows an abrupt decrease in perfusion and function, acute rejection is a likely cause (22,23).

Ureteral obstruction commonly occurs at the site of ureterovesical anastomosis because of edema, ischemia, or technical complications in the early postoperative period. The scintigraphic findings of ureteral obstruction in a renal transplant are essentially the same as those described for native kidneys in the preceding section (see "Scintigraphy of the Native Kidney"). At later intervals after transplantation, the grafted donor ureter, being part of the renal transplant, may be involved in acute rejection. An immune response involving the ureter may result in ischemic changes and fibrosis leading to obstructive stenosis or ureteral fistula and urine leak (24).

Urine leak is a relatively rare complication that may occur within the first few weeks after transplant surgery, either because of dehiscence at the ureterovesicular anastomosis or because of distal ureteral necrosis. Urine leaks elsewhere in the collecting system are usually related to ischemic insult from graft harvesting, impaired vascular supply, or graft rejection (22). Radiotracer leakage from the collecting system or ureter may accumulate in intra- or extraperitoneal sites, depending on whether the peritoneum was disrupted during surgery (Movie 10 [online]). A urinoma may be seen as a photopenic region adjacent to the kidney and may or may not be filled by the radiotracer over time. If no radiotracer activity is seen in a urinoma, that feature is indistinguishable from a perinephric hema-

	ATN/AVN	RAT	RVT	AR	Renal Infarcts
Renal Scintigraphy	 24" Normal perfusion (perfusion >> function)	 36" Absent perfusion	 60" Absent/reduced perfusion	 40" Reduced perfusion (perfusion << function)	 24" Normal perfusion
	 20" Cortical retention	 20" Photopenic transplant	 20" Reduced function or photopenic transplant	 20" Worsening function relative to baseline	 18" Peripheral wedge-shaped defects
Renal US	 Variable, High RI, Enlarged transplant, Overlap with AR	 Absent flow in RA	 RA reversed diastolic flow	 Edematous transplant, High RI - not specific	 Areas of absent flow
		 RA intraluminal echoes			
Comments	The timing of onset helps differentiate ATN/AVN from acute rejection. Decreased flow in severe ATN/AVN may mimic obstruction.	RAT cannot be reliably distinguished from RVT at renal scintigraphy; US is helpful for narrowing the differential diagnosis.	RVT cannot be reliably distinguished from RAT at renal scintigraphy; US is helpful for narrowing the differential diagnosis.	Late-stage AR may mimic toxic effects of immunosuppressive therapy. Graft dysfunction after spontaneous resolution of ATN is suggestive of AR.	Renal segmental infarcts may occur in association with other medical or surgical complications and may lead to graft dysfunction.

**Figure 7.** Early complications of renal transplantation. Images from renal scintigraphy (first row: angiographic phase; second row: functional phase) and images and spectral Doppler waveforms from renal US (third and fourth rows) in various patients show findings of ATN or acute vasomotor nephropathy (AVN, first column), renal artery thrombosis (RAT, second column), renal vein thrombosis (RVT, third column), acute rejection (AR, fourth column), and renal infarction (fifth column). The scintigraphic and US images depicting each complication were acquired on the same day or only a few days apart and in the same patient, with the exception of the renal artery thrombosis images, which are from different patients. RA = renal artery, RI = resistance index.

toma or lymphocele. Delayed images obtained with the surgical drain or drainage bag in the periphery of the field of view may be helpful for detecting a slow urine leak.

Vicarious hepatobiliary excretion represents a small part of <sup>99m</sup>Tc mertiatide excretion in patients with normal kidney function but is increased in patients with urinary tract obstruction or renal dysfunction. Radiopharmaceutical impurities also

may lead to hepatobiliary activity (25). Radio-tracer activity in the biliary system and GI tract may be seen on delayed images and should not be confused with a urine leak.

Scintigraphic findings of vascular compromise (ie, thrombosis of either the renal vein or the renal artery) in the early postoperative period

are nonspecific (Fig 7). Renal artery stenosis is encountered in the late postoperative period and is not discussed in this article. In the presence of renal artery thrombosis, which is a rare postoperative complication, there is no perfusion to the kidney during the angiographic phase, and a photopenic region is seen in the anatomic location of the renal transplant, which is outlined by high background radiotracer activity, findings that are indicative of the absence of renal function (Movie 11 [online]). Because a renal transplant (unlike a native kidney) has no draining collateral vessels, renal vein thrombosis in the transplant causes reduced or absent perfusion and reduced function, with markedly reduced uptake and no excretion of the radiotracer (Movie 12 [online]), whereas the native kidney affected by renal vein thrombosis may demonstrate retention of activity over time.

**For the imaging evaluation of renal transplants, scintigraphy alone does not allow reliable differentiation between arterial and venous compromise, and renal Doppler US may be useful for this purpose.** The finding of a filling defect in the renal vein on gray-scale US images is considered diagnostic of renal vein thrombosis, but such a defect might go undetected if the entire length of the renal vein is not visualized. A Doppler US finding of reversed diastolic flow in the renal artery supports the diagnosis of renal vein thrombosis but is not specific; it also may be seen in the presence of acute rejection. Absence of flow in a sonographically visualized renal artery and absence of flow in the kidney hilum and parenchyma are diagnostic findings of renal artery thrombosis (22).

Segmental infarction shares a common etiology and time frame with renal artery thrombosis and may also manifest clinically as graft dysfunction (23). Anatomic lesions such as an atheroma in the renal artery, surgical trauma, and the suturing technique used all may cause thromboembolism at the level of the segmental arteries, especially in the setting of hypercoagulability (26). Renal infarcts may appear as peripheral wedge-shaped defects with no radiotracer activity in all phases of renal transplant scintigraphy (Fig 7; Movie 13 [online]).

Acute rejection typically manifests at renal transplant scintigraphy as decreased graft perfusion, reduced graft function, and high background

radiotracer activity; however, this pattern is diagnostically nonspecific (Fig 7; Movie 14 [online]). The time frame within which the deterioration of function occurs can help distinguish acute rejection from entities such as vascular compromise and ATN: Although any of these entities may occur in the immediate postoperative period, acute rejection typically occurs from 1 week to a few months after transplantation, whereas ATN and vascular compromise occur earlier, typically within the 1st week after transplantation (22).

## Myocardial Perfusion Scintigraphy

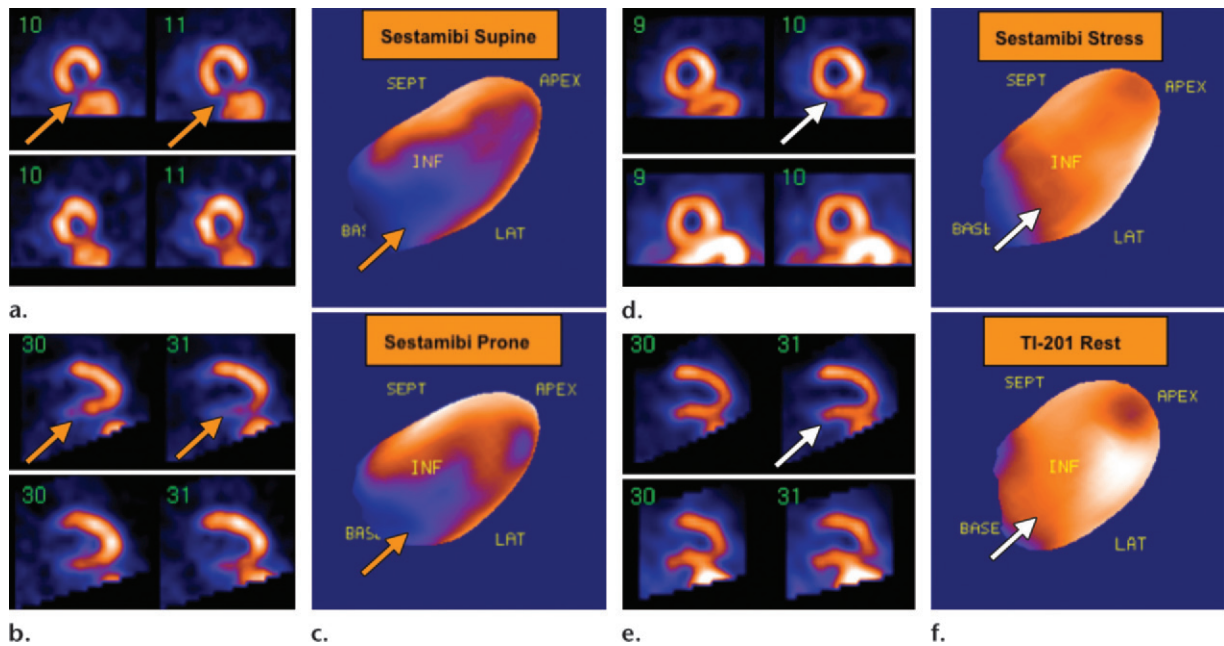
### Clinical Indications in the Acute Care Setting

Myocardial perfusion scintigraphy may be performed in patients with acute chest pain to allow the detection of myocardial ischemia and infarction. Rest-only myocardial perfusion scintigraphy has been shown to have a sensitivity of 93% and a negative predictive value of 99% for the detection of infarction in the setting of acute angina (27).

### Imaging Modalities and Radiopharmaceuticals

The imaging modality used for myocardial perfusion imaging in a patient with acute coronary syndrome depends largely on the level of clinical suspicion that myocardial ischemia or infarction is present. Patients with a high likelihood of myocardial ischemia or infarction, as determined on the basis of electrocardiographic findings, serum myocardial enzyme levels, or both, often undergo immediate angiography. Myocardial perfusion imaging with electrocardiographically gated SPECT is frequently performed in patients for whom there is a moderate likelihood that angina is the cause of acute chest pain. In patients for whom there is little or no suspicion that an acute coronary syndrome is present, coronary CT angiography is used with increasing frequency to interrogate the coronary artery anatomy. Myocardial perfusion scintigraphy has been shown to be a useful predictor of outcome in patients presenting to the emergency department with typical angina and either normal or equivocal electrocardiographic findings (28).

Radiopharmaceuticals used for myocardial perfusion scintigraphy include  $^{99m}\text{Tc}$  sestamibi (ie,  $^{99m}\text{Tc}$ -MIBI),  $^{99m}\text{Tc}$  tetrofosmin, and thallium 201 ( $^{201}\text{Tl}$ ) chloride.



**Figure 8.** Myocardial perfusion abnormality in a 51-year-old man with acute chest pain. The  $^{99m}\text{Tc}$  sestamibi injection for a pain-rest perfusion study was administered while the patient was in the emergency department and experiencing severe chest pain. (a–c) Selected short-axis images (a), vertical long-axis images (b), and polar maps (c) obtained with the patient supine (top) and prone (bottom) during pain-rest perfusion scintigraphy show a large, moderately severe perfusion abnormality in the inferior left ventricular wall (orange arrows). (d–f) Selected short-axis images (d), vertical long-axis images (e), and polar maps (f) from a previous myocardial perfusion study performed with  $^{99m}\text{Tc}$  sestamibi during stress (top) and with  $^{201}\text{Tl}$  chloride while the patient was at rest (bottom) show no myocardial perfusion abnormality in the inferior wall (white arrows). These findings indicate that the perfusion abnormality in a–c is new. *INF* = inferior, *LAT* = lateral, *SEPT* = septum.

### Scintigraphic Findings and Pitfalls

Myocardial perfusion scintigraphy in a patient with acute chest pain typically includes the acquisition of nonstress (rest) images only. The radiotracer must be injected while the patient is experiencing acute chest pain. A radiotracer injection administered after chest pain has resolved can result in false-negative findings.

However, rest myocardial perfusion images alone do not allow reliable differentiation of ischemia from infarction. Potential pitfalls at image interpretation include breast attenuation affecting the anterior myocardial wall in women and diaphragmatic attenuation affecting the inferior myocardial wall (typically in men), findings that may simulate perfusion defects. Diaphragmatic attenuation can be differentiated from a myocardial perfusion defect by repeating the study with the patient positioned prone, which should lead to an increase in measured activity in the inferior wall if the apparent defect was due to diaphragmatic attenuation (Fig 8). If the patient cannot

tolerate a SPECT examination (eg, because of unstable clinical status or extreme obesity), planar images may be obtained. If no abnormality is seen at rest-only scintigraphy, a subsequent rest-stress study may be performed when the patient's acute symptoms have resolved.

### Lung Scintigraphy

#### Clinical Indications in the Acute Care Setting

The most common indication for lung ventilation-perfusion scintigraphy in the acute care setting is the clinical suspicion that pulmonary embolism is present. Evaluation of perfusion in lung transplants immediately after transplantation may be indicated to exclude compromise of the venous anastomosis and can be performed with scintigraphy while the patient is still in the intensive care unit (29).

## Imaging Modalities and Radiopharmaceuticals

Pulmonary CT angiography is currently the first-line imaging modality for the diagnosis of pulmonary embolism in most patients and can be combined with pelvic and lower-extremity CT venography to allow the detection of deep vein thrombosis. CT is widely available and typically can be performed with no special preparations. The sensitivity and specificity of pulmonary CT angiography performed with a multidetector CT scanner are greater than 95% (30).

Ventilation-perfusion scintigraphy may be performed as the initial imaging examination if pulmonary CT angiography is contraindicated because the patient has an allergy to iodinated contrast media, renal insufficiency, or morbid obesity exceeding the weight limits of the CT scanner or if the patient cannot be moved to the imaging suite (1).

Venous compression US is often used to detect deep vein thrombosis in the extremities but cannot be used to diagnose pulmonary embolism. MR angiography, although it is appealing because of the lack of ionizing radiation, is not routinely used in the diagnosis of pulmonary embolism but may be used as an adjunct for problem solving or as an alternative in patients for whom pulmonary CT angiography is contraindicated. Conventional pulmonary angiography, long considered the reference standard for the diagnosis of pulmonary embolism, is no longer frequently used since less invasive imaging modalities with high sensitivity have become available.

An injection of  $^{99m}\text{Tc}$ -labeled macroaggregates of human albumin (MAA) is used for perfusion scintigraphy, and xenon 133 ( $^{133}\text{Xe}$ ) gas or a  $^{99m}\text{Tc}$ -pentetic acid aerosol is used for ventilation scintigraphy. Generator-produced krypton 81m gas and an aerosol containing  $^{99m}\text{Tc}$ -labeled ultrafine carbon particles (Technegas; Cyclopharm,

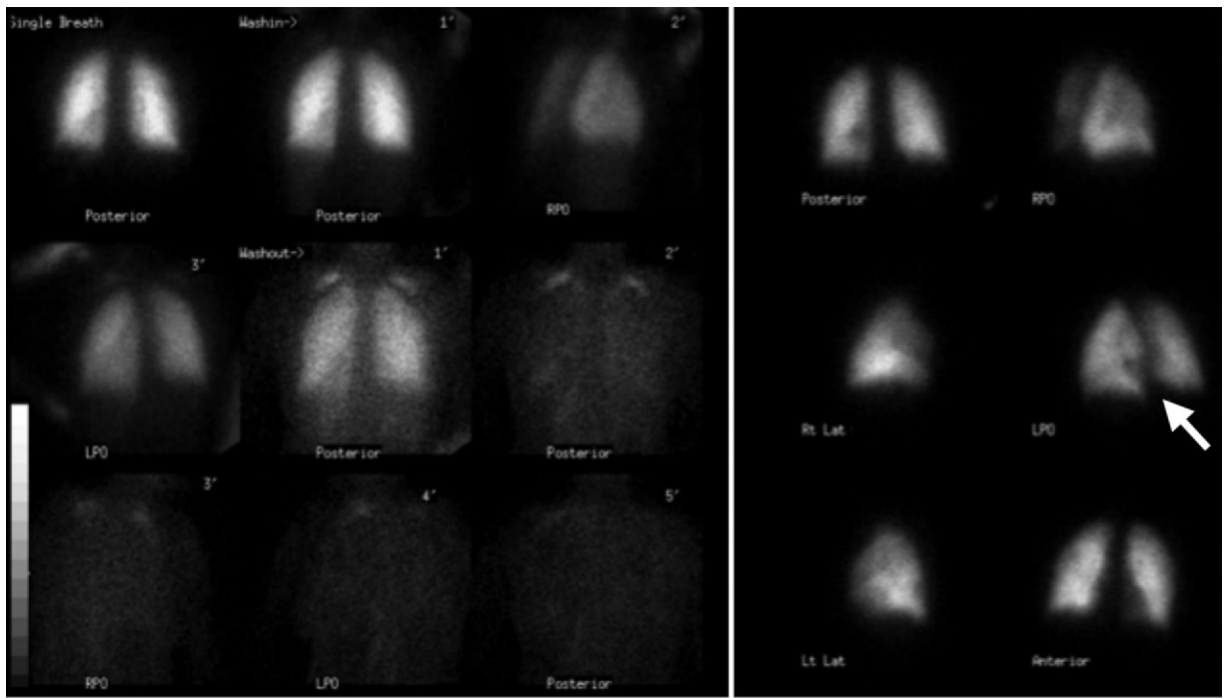
Lucas Heights, Australia) also have been used for ventilation scintigraphy, but the aerosol is not yet approved for use in the United States.

## Scintigraphic Findings and Pitfalls

Various guidelines have been developed for interpreting ventilation-perfusion nuclear imaging studies. These include the modified PLOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) and Biello criteria (31–33). The results of ventilation-perfusion scintigraphy are reported as the probability or likelihood that pulmonary embolism is present on the basis of the imaging study. To obtain the posttest probability, the probability on the basis of scintigraphic findings is integrated with the pretest probability, which is based on patient-specific data and determined by prediction rules.

The diagnostic strategy underlying the use of ventilation-perfusion scintigraphy in the workup for pulmonary embolism is based on Bayesian analysis (35), which postulates that for a reasonably sensitive and specific test, the lower the pretest probability, the more likely it is that a positive test result will be false, and the higher the pretest probability, the more likely it is that a negative test result will be false. During the interpretation of ventilation-perfusion studies, a likelihood ratio or test probability for the presence of pulmonary embolism is determined. This ratio is integrated with the pretest probability, which is based on prediction rules, with those used most often in clinical practice being the Wells score, Geneva model, PERC (Pulmonary Embolism Rule-out Criteria), and PISAPED (Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis) criteria. Concordant results are likely to be true results, meaning that no further workup is needed for the diagnosis of acute pulmonary embolism. Discordant results usually mandate further workup, which may include pulmonary CT angiography, venous compression US, or D-dimer assay alone or in combination (Fig 9), depending on the diagnostic algorithm used.

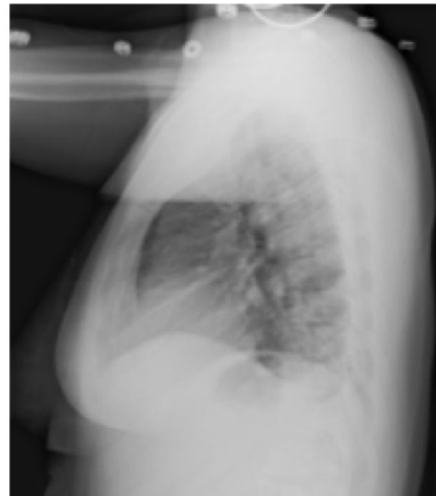
**Figure 9.** (a) Images from  $^{133}\text{Xe}$  ventilation (left) and  $^{99m}\text{Tc}$ -MAA perfusion (right) scintigraphy in a 26-year-old woman with worsening right-sided chest pain 8 weeks postpartum demonstrate a moderate-sized wedge-shaped mismatched perfusion-ventilation defect in the posterior segment of the lower lobe of the left lung (arrow), a finding that arouses the suspicion that pulmonary embolism is present. Blunting of the right posterior costophrenic angle is also seen. *LPO* = left posterior oblique view, *Lt Lat* = left lateral view, *RPO* = right posterior oblique view, *Rt Lat* = right lateral view. (b, c) Posteroanterior (b) and lateral (c) chest radiographs show clear lungs with blunting of the right posterior costophrenic angle. These findings, according to the modified PLOPED and Biello criteria, indicate an intermediate probability of the presence of pulmonary embolism and usually mandate further workup. (d, e) Axial (d) and oblique sagittal (e) images from pulmonary CT angiography show a filling defect in the segmental pulmonary artery that supplies the posterior left lower lobe (arrow).



a.



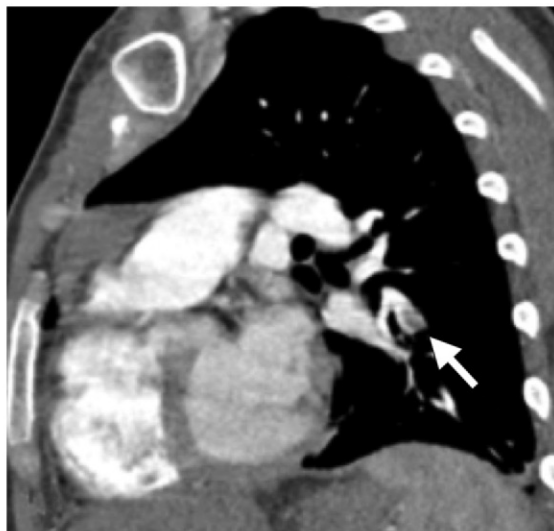
b.



c.



d.



e.

The hallmark of pulmonary embolism is the presence of segmental perfusion defects that are either moderate in size (affecting 26%–75% of the lung segment) or large (affecting more than 75% of the lung segment) and that are combined with normal ventilation, a pattern described as a ventilation-perfusion mismatch. In a patient with pulmonary embolism, multiple segmental arterial territories in both lungs are typically affected by ventilation-perfusion mismatches. Pulmonary infarction, which may be seen in the setting of pulmonary embolism, can lead to a triple-match defect, a region of absent or decreased ventilation and perfusion corresponding to airspace opacity on chest radiographs or CT images. Primary ventilatory abnormalities often lead to matched perfusion defects because of reflexive vasoconstriction, a pattern that should not arouse the suspicion that pulmonary embolism is present unless corresponding radiographic abnormalities are seen. Likewise, abnormalities that are characterized by better perfusion than ventilation, a pattern described as reverse mismatch, are suggestive of a nonthromboembolic cause.

Chest radiographic findings are included in the ventilation-perfusion interpretative criteria, and chest radiography should be performed in temporal proximity to ventilation-perfusion scintigraphy (34). The degree of vessel occlusion (complete versus partial) and the size of the occluded vessel may affect the appearance of the perfusion abnormality. Partial vessel occlusion may lead to only mildly decreased perfusion of the vascular territory, a nonspecific finding (34).

Assessment of the quality of the study is crucial. Injection of too few  $^{99m}\text{Tc}$ -MAA particles (fewer than 70,000) can lead to inadequate imaging because of the quantum mottle effect caused by statistical fluctuation of the imaged photons. The perfusion images then may have a grainy appearance that mimics small perfusion defects.

**When the ventilation portion of a pulmonary ventilation-perfusion study is performed with an aerosol, the count rate of the  $^{99m}\text{Tc}$ -MAA activity (measured as counts per minute) in the perfusion portion of the study must be at least four times the count rate of the activity in the ventilation portion of the study. Verification of the count rates allows the detection of an inadequate number of injected  $^{99m}\text{Tc}$ -MAA particles, which may be indicative of extravasation of the injected radiopharmaceutical.**

#### Teaching Point

Recognition of patterns of scintigraphic findings that characterize nonthromboembolic diseases is important, as these abnormalities may be the cause of the patient's symptoms. A pattern of reverse mismatch, in which the ventilatory abnormality (eg, absent or minimal activity on wash-in images, with or without retention of activity on wash-out images) is worse than the perfusion abnormality, can be seen in the presence of mucus plugging of the airways (Fig 10) or atelectasis. This pattern is associated with a functional right-to-left (ie, venous-to-systemic) shunt in the pulmonary circulation, which may cause or contribute to hypoxemia. Matched perfusion and ventilation abnormalities can be seen in chronic obstructive pulmonary disease and asthma exacerbation, which may be alternative diagnoses in patients with dyspnea and hypoxia. Microemboli that occlude the far distal pulmonary arteries affect perfusion at the periphery of the lung segments, causing them to have a prominent appearance on perfusion images. This imaging appearance may be produced by fatty emboli, amniotic fluid emboli, or tumor cell emboli (36).

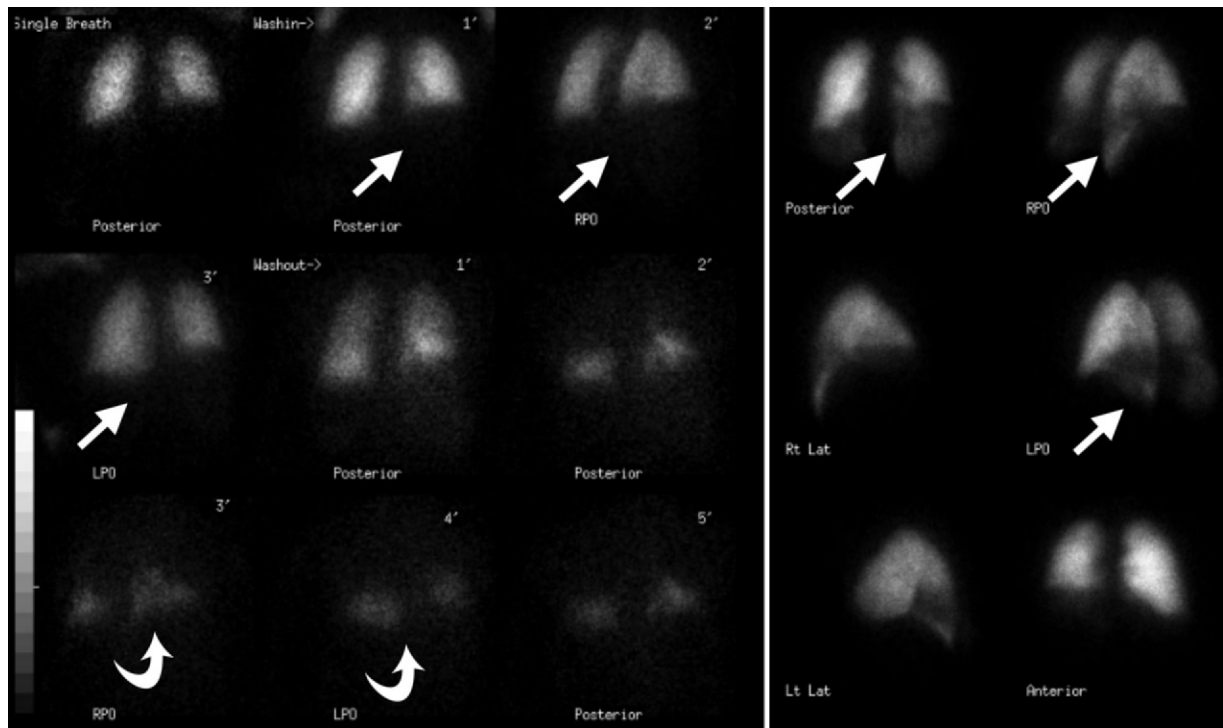
### Central Nervous System Scintigraphy

Although most brain imaging studies for acute indications are performed with CT or MR imaging, nuclear imaging can be useful for the evaluation of cerebral perfusion and cerebrospinal fluid (CSF) shunt patency. Cerebral perfusion scintigraphy may be performed as an adjunct test to demonstrate the presence or absence of effective cerebral perfusion in patients being evaluated for brain death. CSF shunt scintigraphy is a minimally invasive method for assessing flow through shunt devices to assess their patency and detect shunt malfunctions.

### Brain Scintigraphy for Cerebral Perfusion Assessment

**Clinical Indications in the Acute Care Setting.**—Scintigraphic assessment of cerebral perfusion may be performed as an ancillary test in the evaluation of patients for brain death (37–40). Typical clinical scenarios for this study include (a) evalu-





**Figure 10.** Ventilation-perfusion scintigraphy demonstrates a reverse mismatch in a 64-year-old woman with hypoxia and dyspnea after hernia repair. Image series from  $^{133}\text{Xe}$  ventilation (left) and  $^{99\text{m}}\text{Tc}$ -MAA perfusion (right) scintigraphy shows markedly decreased activity in the lower lobes of both lungs (straight arrows), findings more pronounced on ventilation images than on perfusion images. Retention of  $^{133}\text{Xe}$  is seen in both lung bases during washout (curved arrows at left). *LPO* = left posterior oblique view, *Lt Lat* = left lateral view, *RPO* = right posterior oblique view, *Rt Lat* = right lateral view.

ation of brain death before patients' organs are harvested for donation; (b) evaluation of cerebral perfusion in patients with conditions such as hypothermia and drug intoxication, which can interfere with clinical and electroencephalographic assessments of brain activity; and (c) evaluation of patients in whom brain death may be the result of criminal activity.

Lack of cerebral perfusion occurs because of the elevation of intracranial pressure above systemic arterial pressures in the setting of brain edema. It is important to remember that the absence of effective cerebral perfusion at planar scintigraphy performed with  $^{99\text{m}}\text{Tc}$  pentetic acid does not equate with brain death: Blood flow to the brainstem cannot be adequately assessed with  $^{99\text{m}}\text{Tc}$  pentetic acid. Furthermore, patients who lack effective cerebral perfusion may not meet the clinical criteria for a diagnosis of brain death (37). However, several studies have shown that a lack of effective cerebral perfusion is associated with a poor prognosis (39).

#### **Imaging Modalities and Radiopharmaceuticals.**

Several imaging modalities are useful for assessing cerebral perfusion. Because it is accurate, portable, and relatively straightforward, cerebral perfusion scintigraphy is typically the first-line test for cerebral perfusion assessment in patients being evaluated for brain death.  $^{99\text{m}}\text{Tc}$  pentetic acid is a hydrophilic agent used in planar scintigraphy. Lipophilic radiotracers that are used in cerebral SPECT include  $^{99\text{m}}\text{Tc}$  bicisate (ie,  $^{99\text{m}}\text{Tc}$ -ECD) and  $^{99\text{m}}\text{Tc}$  exametazime (ie,  $^{99\text{m}}\text{Tc}$ -HMPAO).

A major disadvantage common to most other imaging modalities used to evaluate cerebral perfusion is the need for transport of the patient from the intensive care unit to the imaging suite, a labor-intensive process that may not be feasible if the patient is in unstable condition. Digital subtraction angiography allows the assessment of brain perfusion via the anterior and posterior circulation but requires the insertion of a catheter

and injection of a contrast medium. The results of some studies indicate that CT and MR imaging may be useful for assessing cerebral perfusion, but diagnostic accuracy with these techniques has not yet been demonstrated in large patient populations (39). Transcranial Doppler US can be used to assess cerebral perfusion and can be performed in the intensive care unit; however, the sensitivity of US for this indication is variable (38), and a lack of visible flow in the intracranial arteries may be due to an inadequate acoustic window instead of the absence of flow.

**Scintigraphic Findings and Pitfalls.**—Findings that are indicative of no effective cerebral perfusion include a lack of activity in the distribution of the anterior and middle cerebral arteries during the angiographic phase and in the superior sagittal sinus immediately after the first pass of the radiotracer. For studies performed with  $^{99m}\text{Tc}$  pentetic acid, no radiotracer activity or only faint activity in the superior sagittal sinus on static images is indicative of the absence of effective cerebral perfusion if the initial angiographic phase images show no cerebral perfusion. On delayed images obtained with  $^{99m}\text{Tc}$  bismate or  $^{99m}\text{Tc}$  exametazime, both of which are retained in perfused brain tissue, an absence of radiotracer activity in the cerebrum is also indicative of a lack of effective perfusion (Fig 11).

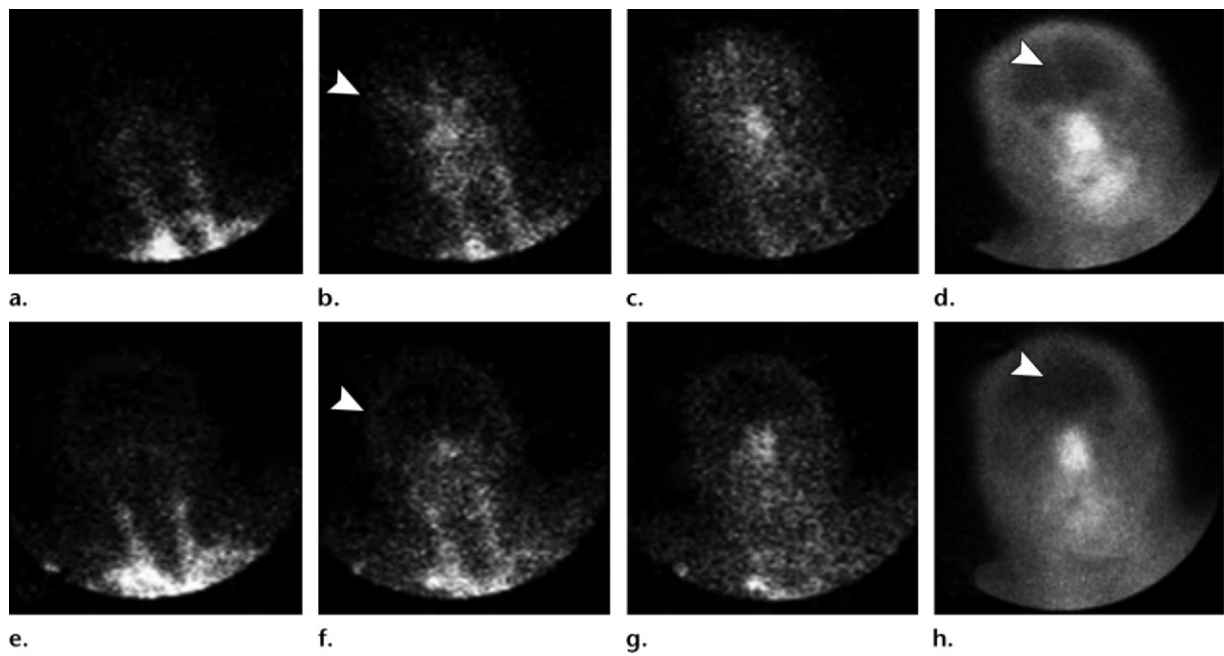
Several technical considerations are important for accurate scintigraphic evaluation of brain perfusion. **The initial injected bolus must be clearly visualized in transit through the common carotid arteries during the angiographic portion of the study to achieve a technically adequate study.** Foci of activity in the soft tissues of the face (eg, “hot nose”) and scalp may be mistaken for focal activity in the brain, particularly if these tissues are hyperemic because of trauma or surgery. Although  $^{99m}\text{Tc}$  bismate and  $^{99m}\text{Tc}$  exametazime are normally trapped in viable perfused brain tissue and the absence of activity in the brain on delayed images is suggestive of a lack of effective

cerebral perfusion, a review of angiographic phase images is critical to avoid misdiagnoses due to a lack of trapping because of radiopharmaceutical instability, extravasation of the radiotracer during its injection, or use of an inappropriate radiopharmaceutical. There are rare reports of observations of intracranial perfusion in patients with extensive liquefactive necrosis of the brain, in children with incompletely ossified skulls, and in adults with open head injuries, presumably because the resultant decreases in intracranial pressure allowed continuous flow through the intracranial arteries (37,41,42). There is currently no clear evidence indicating that these lipophilic agents allow improved diagnostic accuracy. Studies performed with  $^{99m}\text{Tc}$  pentetic acid can be repeated in close succession if the patient’s clinical condition changes. However, activity from  $^{99m}\text{Tc}$  bismate and  $^{99m}\text{Tc}$  exametazime is retained in the brain for a prolonged period and is likely to confound repeat studies performed too soon after the first administration of one of those agents.

### CSF Shunt Scintigraphy

**Clinical Indications in the Acute Care Setting.**—Scintigraphic assessment of CSF shunt patency is typically performed in the acute care setting when there are clinical reasons for suspecting that the shunt is malfunctioning (43,44). Initial clinical manifestations may be relatively nonspecific and may include headache, lethargy, and difficulty concentrating. The most common shunt systems are ventriculoperitoneal and ventriculoatrial shunts, although other configurations (eg, ventriculopleural, lumboperitoneal) may be encountered. Obstruction is the most common cause of CSF shunt malfunction, and obstructions most often occur in the shunt catheter. CSF scintigraphy is typically performed when there are clinical grounds for suspecting that the catheter system is obstructed.

**Imaging Modalities and Radiopharmaceuticals.**—The initial imaging evaluation for suspected CSF shunt malfunction is typically a



**Figure 11.** Evaluation of cerebral perfusion at  $^{99m}\text{Tc}$ -pentetic acid scintigraphy in an 18-year-old male patient who was ejected from a car. (**a–d**) Selected anterior images from an initial perfusion study show flow in the common carotid arteries and external carotid arteries (**a**), middle cerebral arteries (arrowhead in **b**), and brain capillaries (**c**). Activity is seen in the superior sagittal sinus on both the dynamic image (**c**) and the static image (arrowhead in **d**). (**e–h**) Corresponding images from a repeat study performed a few hours later show flow in the common carotid arteries and external carotid arteries (**e**), but not the middle cerebral arteries (arrowhead in **f**) or the brain capillaries (**g**). No activity is seen in the superior sagittal sinus on the dynamic image (**g**) or the static image (arrowhead in **h**). Findings in **e–h** indicate a lack of effective cerebral perfusion.

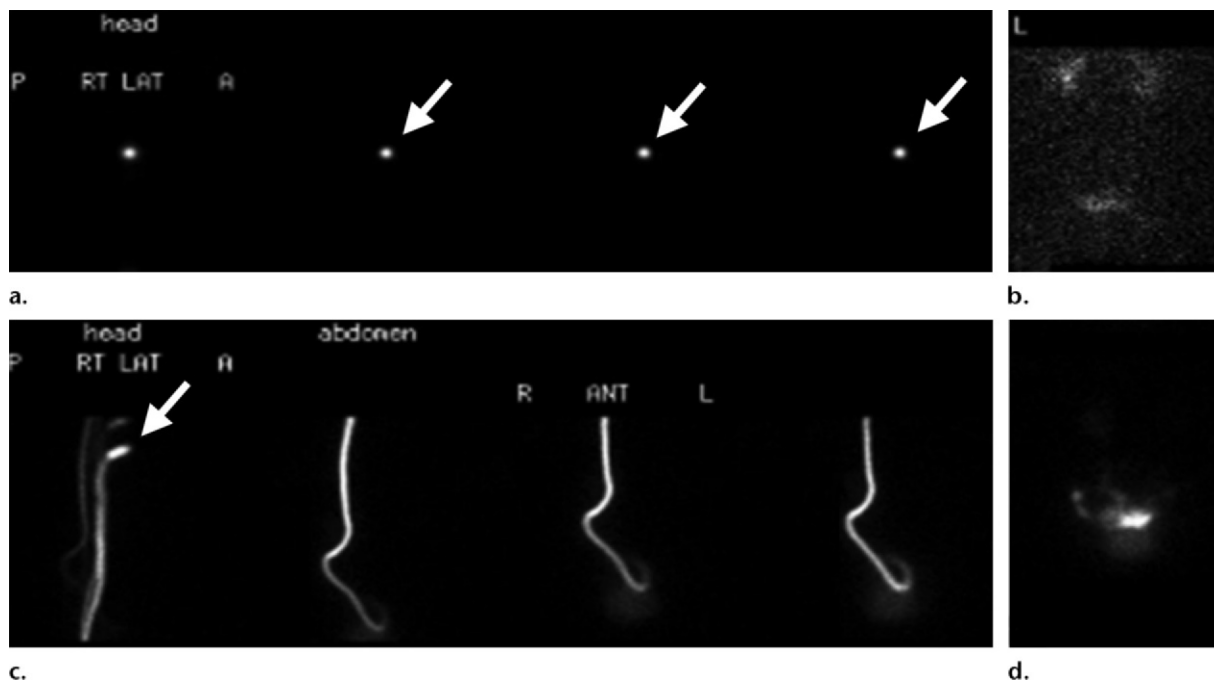
series of radiographs (shunt series) to evaluate the entire course of the shunt catheter system for disconnections or discontinuities. Many patients with an acute onset of signs of possible CSF shunt malfunction are evaluated with nonenhanced head CT. Although a finding of interval ventricular enlargement supports the diagnosis of shunt obstruction, ventriculomegaly and hydrocephalus may not be present.

Preservative-free  $^{99m}\text{Tc}$  pentetic acid and  $^{99m}\text{Tc}$  pertechnetate are the radiopharmaceuticals preferred for use in CSF shunt scintigraphy.

#### **Scintigraphic Imaging Findings and Pitfalls.—**

Shunt patency can be established by observing spontaneous flow of the radiotracer from the injection site to the distal end of the shunt catheter,

with evidence of transit of the radiotracer out of the distal catheter tip. In normal studies, this pattern of flow is typically observed 10–15 minutes after the radiotracer injection. For ventriculoatrial shunts, the shunt catheter should be visualized to the level of the right atrium, and activity should be seen in the kidneys and bladder after the radiotracer reaches the heart and enters the systemic circulation. For ventriculoperitoneal shunts, free spillage of activity into the peritoneal cavity should be visualized to exclude an obstruction or localized fluid collection at the distal shunt tip. Repositioning the patient several times in the right and left decubitus positions may be useful to demonstrate free movement of activity in the peritoneal cavity.



**Figure 12.** Evaluation of CSF shunt patency at  $^{99m}\text{Tc}$ -pentetic acid scintigraphy in a 30-year-old woman with a headache after shunt placement to treat a myelomeningocele. **(a)** Selected right lateral images show persistent focal activity at the injection site (arrows), a finding that represents soft-tissue infiltration by the radiotracer. Lack of visualization of the distal limb of the shunt could be mistakenly interpreted as evidence of shunt obstruction. **(b)** Additional anterior image of the abdomen shows activity in the kidneys and bladder, a finding produced by absorption of the radiotracer infiltrate from soft tissue into the circulation. **(c)** Selected right lateral and anterior images from a repeat study performed 1½ hours later show radiotracer activity at the injection site (arrow) and rapidly ensuing visualization of the distal limb of the shunt. **(d)** Anterior image of the abdomen shows free flow of the radiotracer in the peritoneal cavity. *A* = anterior side, *ANT* = anterior view, *L* = left side, *P* = posterior side, *R* = right side, *RT LAT* = right lateral view.

Failure to observe the transit of radiotracer activity through the shunt system despite upright positioning of the patient and pumping of the shunt reservoir is suggestive of shunt obstruction. However, false-positive findings of shunt obstruction can occur if the radiotracer is injected into the soft tissues adjacent to the shunt system (Fig 12) (43). Misinterpretation can be avoided by observing radiotracer activity in the renal collecting systems and bladder despite a lack of radiotracer transit through the shunt catheter. Delayed but complete transit of activity through the shunt system is more difficult to interpret and may be

due to partial obstruction of the shunt system, a decreased driving pressure for CSF flow, or shunt valves set to open at inappropriately high pressures. Withdrawal of CSF before or during the radiotracer injection also may simulate obstruction by decreasing the CSF pressure in the shunt system below the pressure required to trigger valve opening.

### Conclusion

The use of nuclear imaging studies for selected acute clinical indications provides valuable diagnostic information that often has important implications for patient management. The functional information from nuclear imaging studies

complements the anatomic information obtained with standard modalities such as US, CT, and MR imaging. Awareness of appropriate indications for nuclear imaging studies as well as the limitations and potential pitfalls of such studies in the acute clinical setting is necessary for optimal image acquisition and interpretation.

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## References

- Bettmann MA, Baginski SG, White RD, et al. ACR Appropriateness Criteria® acute chest pain—suspected pulmonary embolism. *J Thorac Imaging* 2012;27(2):W28–W31.
- Society of Nuclear Medicine practice guidelines. <http://interactive.snm.org/index.cfm?PageID=772>. Accessed July 26, 2012.
- Weissmann HS, Frank MS, Bernstein LH, Freeman LM. Rapid and accurate diagnosis of acute cholecystitis with 99mTc-HIDA cholescintigraphy. *AJR Am J Roentgenol* 1979;132(4):523–528.
- Freitas JE, Mirkes SH, Fink-Bennett DM, Bree RL. Suspected acute cholecystitis: comparison of hepatobiliary scintigraphy versus ultrasonography. *Clin Nucl Med* 1982;7(8):364–367.
- Zeman RK, Burrell MI, Cahow CE, Caride V. Diagnostic utility of cholescintigraphy and ultrasonography in acute cholecystitis. *Am J Surg* 1981;141(4):446–451.
- Mauro MA, McCartney WH, Melmed JR. Hepatobiliary scanning with 99mTc-PIPIDA in acute cholecystitis. *Radiology* 1982;142(1):193–197.
- Samuels BI, Freitas JE, Bree RL, Schwab RE, Heller ST. A comparison of radionuclide hepatobiliary imaging and real-time ultrasound for the detection of acute cholecystitis. *Radiology* 1983;147(1):207–210.
- Ralls PW, Colletti PM, Halls JM, Siemsen JK. Prospective evaluation of 99mTc-IDA cholescintigraphy and gray-scale ultrasound in the diagnosis of acute cholecystitis. *Radiology* 1982;144(2):369–371.
- Worthen NJ, Uszler JM, Funamura JL. Cholecystitis: prospective evaluation of sonography and 99mTc-HIDA cholescintigraphy. *AJR Am J Roentgenol* 1981;137(5):973–978.
- Shuman WP, Mack LA, Rudd TG, Rogers JV, Gibbs P. Evaluation of acute right upper quadrant pain: sonography and 99mTc-PIPIDA cholescintigraphy. *AJR Am J Roentgenol* 1982;139(1):61–64.
- Chatziioannou SN, Moore WH, Ford PV, Dhekne RD. Hepatobiliary scintigraphy is superior to abdominal ultrasonography in suspected acute cholecystitis. *Surgery* 2000;127(6):609–613.
- Walker AT, Shapiro AW, Brooks DC, Braver JM, Tumeh SS. Bile duct disruption and biloma after laparoscopic cholecystectomy: imaging evaluation. *AJR Am J Roentgenol* 1992;158(4):785–789.
- Coleman RE, Freitas JE, Fink-Bennett D, Bree RL. The dilated cystic duct sign: a potential cause of false-negative cholescintigraphy. *Clin Nucl Med* 1984;9(3):134–136.
- Mettler FA, Guiberteau MJ. Hepatobiliary imaging. In: *Essentials of nuclear medicine imaging*. 6th ed. Philadelphia, Pa: Elsevier Saunders, 2012; 237–270.
- Tian Yue K, Pin Lin K, Goh Soon Whatt A. Imaging postoperative bile leaks and assessing integrity of biliary-enteric anastomoses with fusion HIDA SPECT/CT scintigraphy. *Clin Nucl Med* 2010;35(11):875–878.
- Graça BM, Freire PA, Brito JB, Ilharco JM, Carvalho VM, Caseiro-Alves F. Gastroenterologic and radiologic approach to obscure gastrointestinal bleeding: how, why, and when? *RadioGraphics* 2010;30(1):235–252.
- Zuckier LS. Acute gastrointestinal bleeding. *Semin Nucl Med* 2003;33(4):297–311.
- Coursey CA, Casalino DD, Remer EM, et al. American College of Radiology ACR Appropriateness Criteria: acute onset flank pain—suspicion of stone disease. <http://www.acr.org/Quality-Safety/Appropriateness-Criteria/Diagnostic>. Accessed July 26, 2012.
- Scheff AM, Fletcher JW, Bowman RR, et al. ACR-SPR practice guideline for the performance of adult and pediatric renal scintigraphy. <http://www.acr.org/Quality-Safety/Standards-Guidelines/Practice-Guidelines-by-Modality/Nuclear-Medicine>. Accessed July 26, 2012.
- Mettler FA, Guiberteau MJ. Genitourinary system and adrenal glands. In: *Essentials of nuclear medicine imaging*. 6th ed. Philadelphia, Pa: Elsevier Saunders, 2012; 315–344.
- Quigley JM, Druy EM, Rich JI. Acute renal vein thrombosis with a diagnostic renal scintigram. *AJR Am J Roentgenol* 1981;137(5):1066–1068.
- Brown ED, Chen MY, Wolfman NT, Ott DJ, Watson NE Jr. Complications of renal transplantation: evaluation with US and radionuclide imaging. *RadioGraphics* 2000;20(3):607–622.
- Sharfuddin A. Imaging evaluation of kidney transplant recipients. *Semin Nephrol* 2011;31(3):259–271.

24. Dreikorn K. Problems of the distal ureter in renal transplantation. *Urol Int* 1992;49(2):76–89.
25. Niederkohr RD, McDougall IR. Incidental gallbladder visualization on nonhepatobiliary nuclear medicine studies: case series and review of the literature. *Clin Nucl Med* 2007;32(12):915–919.
26. Kanchanabat B, Siddins M, Coates T, et al. Segmental infarction with graft dysfunction: an emerging syndrome in renal transplantation? *Nephrol Dial Transplant* 2002;17(1):123–128.
27. Hilton TC, Thompson RC, Williams HJ, Saylor R, Fulmer H, Stowers SA. Technetium-99m sestamibi myocardial perfusion imaging in the emergency room evaluation of chest pain. *J Am Coll Cardiol* 1994;23(5):1016–1022.
28. Kontos MC, Jesse RL, Schmidt KL, Ornato JP, Tatum JL. Value of acute rest sestamibi perfusion imaging for evaluation of patients admitted to the emergency department with chest pain. *J Am Coll Cardiol* 1997;30(4):976–982.
29. ACR-SNM-SPR practice guideline for the performance of pulmonary scintigraphy in adults and children. <http://www.acr.org/Quality-Safety/Standards-Guidelines/Practice-Guidelines-by-Modality/Nuclear-Medicine>. Accessed July 26, 2012.
30. Hunt JM, Bull TM. Clinical review of pulmonary embolism: diagnosis, prognosis, and treatment. *Med Clin North Am* 2011;95(6):1203–1222.
31. Freitas JE, Sarosi MG, Nagle CC, Yeomans ME, Freitas AE, Juni JE. Modified PLOPED criteria used in clinical practice. *J Nucl Med* 1995;36(9):1573–1578.
32. Biello DR, Mattar AG, McKnight RC, Siegel BA. Ventilation-perfusion studies in suspected pulmonary embolism. *AJR Am J Roentgenol* 1979;133(6):1033–1037.
33. Biello DR. Radiological (scintigraphic) evaluation of patients with suspected pulmonary thromboembolism. *JAMA* 1987;257(23):3257–3259.
34. Dillehay GL. Ventilation-perfusion scintigraphy. In: Henkin RE. *Nuclear medicine*. 2nd ed. Maryland Heights, Mo: Mosby Elsevier, 2006; 1369–1422.
35. Gandara E, Wells PS. Diagnosis: use of clinical probability algorithms. *Clin Chest Med* 2010;31(4):629–639.
36. Royal DR. Pulmonary imaging for nonthromboembolic disease. In: Henkin RE. *Nuclear medicine*. 2nd ed. Maryland Heights, Mo: Mosby Elsevier, 2006; 1423–1438.
37. Weckesser M, Schober O. Brain death revisited: utility confirmed for nuclear medicine. *Eur J Nucl Med* 1999;26(11):1387–1391.
38. Scripko PD, Greer DM. An update on brain death criteria: a simple algorithm with complex questions. *Neurologist* 2011;17(5):237–240.
39. Conrad GR, Sinha P. Scintigraphy as a confirmatory test of brain death. *Semin Nucl Med* 2003;33(4):312–323.
40. Wijdicks EF, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology. Evidence-based guideline update: determining brain death in adults—report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2010;74(23):1911–1918.
41. Medlock MD, Hanigan WC, Cruse RP. Dissociation of cerebral blood flow, glucose metabolism, and electrical activity in pediatric brain death. Case report. *J Neurosurg* 1993;79(5):752–755.
42. Marrache F, Mégarbane B, Pirnay S, Rhaoui A, Thuong M. Difficulties in assessing brain death in a case of benzodiazepine poisoning with persistent cerebral blood flow. *Hum Exp Toxicol* 2004;23(10):503–505.
43. Graham P, Howman-Giles R, Johnston I, Besser M. Evaluation of CSF shunt patency by means of technetium-99m DTPA. *J Neurosurg* 1982;57(2):262–266.
44. MacDonald A, Burrell S. Infrequently performed studies in nuclear medicine: part 2. *J Nucl Med Technol* 2009;37(1):1–13.

## Nuclear Medicine in the Acute Clinical Setting: Indications, Imaging Findings, and Potential Pitfalls

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### Page 378

Premature discontinuation of cholescintigraphy in a patient with a biliary perforation or a bile leak may lead to a false-negative interpretation.

### Page 382

Activity in the urinary tract, especially the ureters and bladder, also may simulate radiotracer extravasation into the GI tract. Lateral or “tail-on-detector” views can be helpful to distinguish these normal structures from rectal bleeding.

### Page 386

For the imaging evaluation of renal transplants, scintigraphy alone does not allow reliable differentiation between arterial and venous compromise, and renal Doppler US may be useful for this purpose.

### Page 390

When the ventilation portion of a pulmonary ventilation-perfusion study is performed with an aerosol, the count rate of the  $^{99m}\text{Tc}$ -MAA activity (measured as counts per minute) in the perfusion portion of the study must be at least four times the count rate of the activity in the ventilation portion of the study. Verification of the count rates allows the detection of an inadequate number of injected  $^{99m}\text{Tc}$ -MAA particles, which may be indicative of extravasation of the injected radiopharmaceutical.

### Page 392

The initial injected bolus must be clearly visualized in transit through the common carotid arteries during the angiographic portion of the study to achieve a technically adequate study.