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Procedure Guideline for Hepatobiliary Scintigraphy

Helena R. Balon, Darlene M. Fink-Bennett, David R. Brill, Lorraine M. Fig, John E. Freitas, Gerbail T. Krishnamurthy, William C. Klingensmith III and Henry D. Royal

William Beaumont Hospital, Royal Oak, Michigan; Geisinger Medical Center, Danville, Pennsylvania; VA Medical Center, Ann Arbor, Michigan; St. Joseph Mercy Hospital, Ann Arbor, Michigan; VA Medical Center, Tucson, Arizona; Porter Hospital, Denver, Colorado; and Mallinckrodt Institute of Radiology, St. Louis, Missouri

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PART I: PURPOSE

The purpose of this procedure guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting and reporting the results of hepatobiliary scintigraphy.

PART II: BACKGROUND INFORMATION AND DEFINITIONS

Hepatobiliary scintigraphy is a diagnostic imaging study that evaluates hepatocellular function and patency of the biliary system by tracing the production and flow of bile from the liver through the biliary system into the small intestine. Sequential images of the liver, biliary tree and gut are obtained. Computer acquisition and analysis as well as pharmacological interventions are frequently used.

PART III: COMMON INDICATIONS

A. Functional assessment of the hepatobiliary system
B. Integrity of the hepatobiliary tree

These broad categories include, for example:

- Evaluation of suspected acute cholecystitis.
- Evaluation of suspected chronic biliary tract disorders.
- Evaluation of common bile duct obstruction.
- Detection of bile leak.
- Evaluation of congenital abnormalities of the biliary tree (e.g., biliary atresia)

PART IV: PROCEDURE

A. Patient Preparation

To permit gallbladder (GB) visualization, the patient must have fasted for a minimum of two and preferably four hours prior to administration of the radiopharmaceutical. If the patient has fasted for 24 hr or longer or is on parenteral nutrition, a false-positive study may occur (*1*). In these cases (especially with total parenteral nutrition (TPN), the patient may be pretreated with sincalide, see IV.F.1. below (*2*).

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For correspondence or reprints contact: Wendy J.M. Smith, Director of Health Care Policy, 1850 Samuel Morse Dr., Reston, VA 20190-5316 or via e-mail at wsmith@snm.org.

Note: All 26 SNM-approved procedure guidelines are available on the Society's home page. We encourage you to download these documents via the Internet at http: \\www.snm.org. If you would like information on the development process of this guideline or to order a compendium of all 26 procedure guidelines for $20.00, please contact Wendy J.M. Smith, Society of Nuclear Medicine at (703) 708-9000, ext. 242 or via e-mail at wsmith@snm.org.

TABLE 1
Radiation Dosimetry for Adults

Radiopharmaceuticals	Administered activity MBq (mCi)	Organ receiving the largest radiation dose*† mGy (rad)	Effective dose*† mSv (rem)
^{99m}Tc-disofenin	50–200 i.v.	0.11	0.024
^{99m}Tc-mebrofenin	(1.5–5.0)	Gallbladder wall (0.41)	(0.089)

*ICRP 53, page 203, normal liver function.
†Per MBq (per mCi).

B. Information Pertinent to Performing the Procedure

The physician should review all available pertinent clinical, laboratory, radiographic and sonographic information about the patient prior to the study. Additional information specifically related to hepatobiliary scintigraphy includes:

1. History of previous surgeries, especially biliary and gastrointestinal.
2. Time of most recent meal.
3. Current medications, including the time of their most recent administration (with particular attention to opioid compounds).
4. Results of bilirubin and liver enzyme levels.
5. Results of ultrasound.

C. Precautions

The test should be performed under the optimal state of fasting to avoid a false-positive result. Interference by opioids can be minimized by delaying the study for 4 hr after the last dose. Additional details are listed in IV.A. ("Patient Preparation") and IV.I. ("Sources of Error").

D. Radiopharmaceutical

Technetium-99m-labeled disofenin (DISIDA, 2,6-diisopropylacetanilido iminodiacetic acid) or mebrofenin (BRIDA, bromo-2,4,6-trimethylacetanildo iminodiacetic acid) is administered intravenously in activities of 50-200 MBq (1.5–5.0 mCi) for adults (Table 1); higher dosages will be needed in hyperbilirubinemia, 100–370 MBq (3–10 mCi) (*3*). Mebrofenin may be selected instead of disofenin in moderate-to-severe hyperbilirubinemia due to its somewhat higher hepatic extraction. For infants and children, the administered activity is 2–7 MBq/kg (0.05–0.2 mCi/kg) with a minimum of 15–20 MBq (0.4–0.5 mCi) (Table 2).

TABLE 2
Radiation Dosimetry for Children (5-yr-old)

Radiopharmaceuticals	Administered activity MBq/kg (mCi/kg)	Organ receiving the largest radiation dose*† mGy (rad)	Effective dose*† mSv (rem)
^{99m}Tc-disofenin	0.7–3.0 i.v.	0.28	0.07
^{99m}Tc-mebrofenin	(0.02–0.08)	Gallbladder wall (1.0)	(0.26)

*ICRP 53, page 203, normal liver function.
†Per MBq (per mCi).

E. Image Acquisition

A large field of view gamma camera equipped with a low-energy, all-purpose, or high-resolution collimator is usually used. For a smaller field of view gamma camera, a diverging collimator may be needed. Whenever possible, continuous computer acquisition should be performed (1 frame/min for 30–60 min). Imaging should commence at injection and continue serially for 60 min (1–2 frames/min) or until activity is seen in both the gallbladder (which confirms patency of the cystic duct) and the small bowel (which confirms patency of the common bile duct). Additional views (e.g., right lateral, left or right anterior oblique) may be obtained as needed to clarify anatomy.

The digital data can be reformatted to 5–15 min images for filming. Cinematic display of the data may reveal additional information not readily apparent on the film.

When acute cholecystitis is suspected and the gallbladder is not seen within 40–60 min, 3–4 hr delayed images should be obtained, or morphine augmentation (see below) may be used in lieu of delayed imaging.

Delayed imaging at 18–24 hr may be necessary in some patients (e.g., severely ill patient, suspected common bile duct obstruction, suspected biliary atresia).

If the patient is being studied for a biliary leak, delayed imaging (3–4 hr or later) and patient positioning maneuvers (e.g., decubitus views) may be helpful.

F. Interventions

A variety of pharmacologic or physiologic interventions may enhance the diagnostic value of the examination. Appropriate precautions should be taken to promptly detect and treat any adverse reactions caused by these maneuvers.

1. Sincalide Pretreatment: Sincalide, a synthetic C-terminal octapeptide of cholecystokinin, in doses of 0.01–0.02 μg/kg, may be given intravenously 30–60 min prior to the hepatobiliary tracer injection to minimize the potential for a false-positive study. This may occur in patients who have fasted longer than 24 hr, are on parenteral hyperalimentation (especially TPN) or have a severe intercurrent illness. Sincalide should be administered slowly (over a minimum of 3 min) to prevent biliary spasm and a false-positive study. A slower infusion rate may also be used (see IV.F.3.).
2. Morphine Sulfate: When acute cholecystitis is suspected and the GB is not seen by 40–60 min, morphine sulfate, 0.04 mg/kg, may be administered intravenously over 2–3 min (*4–8*). If the cystic duct is patent, flow of bile into the GB will be facilitated by morphine-induced temporary spasm of the sphincter of Oddi. The intrahepatic biliary tree and common bile duct (CBD) must contain radioactive bile, and tracer activity should be present in the small bowel at the time of morphine injection. A second injection of radiopharmaceutical (booster dose) may be necessary prior to morphine, if the remaining liver/biliary tree activity appears insufficient to permit GB visualization (*3*). Shielding the bowel activity with lead may also be helpful.
Imaging is usually continued for another 30 min following morphine administration but may be extended if desired. Contraindications to the use of morphine include respiratory depression in nonventilated patients (absolute), morphine allergy (absolute) and acute pancreatitis (relative).
3. Sincalide Stimulation: Gallbladder emptying may be evaluated by determining the gallbladder ejection fraction (GBEF) response to sincalide (*3,9–13*). The study involves a 3 min intravenous injection or a 15–45 min infusion of 0.01–0.02 μg/kg sincalide after the gallbladder is maximally filled with radiopharmaceutical (usually 60 min after the injection) and there is minimal activity in the liver. Computer (1–2 frames/min) acquisition then continues for 20–30 min. When performing and interpreting this procedure, the physician must adhere to a specific technique (i.e., dosage and duration of infusion) and normal values validated for that technique preferably at the local institution.
4. Fatty Meal Stimulation: Gallbladder ejection fraction measurement using a fatty meal or other fatty stimuli instead of sincalide has also been described.
5. Phenobarbital: In jaundiced infants in whom biliary atresia is suspected, pretreatment with phenobarbital, 5 mg/kg/day, is usually given orally in two divided doses daily for a minimum of 3–5 days prior to the hepatobiliary imaging study to enhance the biliary excretion of the radiotracer and increase the specificity of the test. Mebrofenin may be preferred over disofenin in suspected biliary atresia (*14*). A study using mebrofenin without phenobarbital induction was recently reported (*15*).

G. Processing

Gallbladder Ejection Fraction: Using the immediate pre-sincalide and the post-sincalide data, regions of interest (ROIs) are drawn around the GB (taking into account patient motion) and adjacent liver (background) using any standard nuclear medicine software package. The liver background ROI is selected taking care to exclude ductal activity. GBEF is calculated from the GB time-activity curve as:

$$\text{GBEF}(\%) = \frac{(\text{net GB cts}_{max}) - (\text{net GB cts}_{min})}{\text{net GB cts}_{max}} \times 100$$

H. Interpretation/Reporting

1. Normal: A normal hepatobiliary scintigram is characterized by immediate demonstration of hepatic parenchyma, followed by activity in the intra- and extrahepatic biliary ductal system, gallbladder and upper small bowel. All these structures should be seen within one hour. GB visualization implies a patent cystic duct and excludes acute cholecystitis with a high degree of certainty. Normal excretion of a small percentage of the tracer by the kidneys may

mimic gallbladder or small bowel on occasion, but may be clarified by a lateral image.

2. Acute Cholecystitis: The hallmark of acute cholecystitis (acalculous as well as calculous) is persistent gallbladder nonvisualization after morphine administration or on the 3–4 hr delayed image.

   A pericholecystic hepatic band of increased activity (the rim sign) (*18–20*) is often associated with severe phlegmonous/gangrenous acute cholecystitis, a surgical emergency.

3. Chronic Cholecystitis and clinical settings associated with physiologic failure of the gallbladder to fill with radiotracer (e.g., prolonged fasting for >24–48 hr, severely ill or postoperative hospitalized patients) may result in GB nonvisualization within the first hour but may be separated from acute cholecystitis using low dose intravenous morphine (see above) or delayed imaging. In chronic cholecystitis, the GB will usually be seen within 30 min of morphine administration or on 3–4 hr delayed images, while true cystic duct obstruction (acute cholecystitis) will result in persistent GB nonvisualization. Visualization of the gallbladder after visualizing the bowel has a significant correlation with chronic cholecystitis. Further evaluation with ejection fraction determination may be useful. Severely ill patients and those on TPN will have a high incidence of gallbladder nonvisualization even after morphine, despite a patent cystic duct.
4. Reduced gallbladder ejection fraction in response to sincalide may be indicative of chronic cholecystitis or gallbladder dyskinesia or the cystic duct syndrome (*12*).
5. Common Bile Duct Obstruction: Delayed biliary-to-bowel transit beyond 60 min raises the suspicion for partial common bile duct (CBD) obstruction, although this may be seen as a normal variant in up to 20% of individuals. It also occurs in chronic cholecystitis, opioid administration, etc. Addition of a fatty stimulus (e.g., Lipomul) may help to evaluate a transient delay of tracer passage into the bowel, particularly in patients pretreated with sincalide. Conversely, activity in the small bowel seen within 60 min does not entirely exclude partial CBD obstruction. High-grade CBD obstruction should be suspected when neither the intrahepatic biliary tree, GB or the small bowel are seen within 18–24 hr post-tracer injection. Severe hepatocellular dysfunction may appear similar.
6. Biliary Leak: A bile leak is present when tracer is found in a location other than the liver, gallbladder, bile ducts, bowel or urine. This may be seen more easily using a cinematic display or decubitus positioning (see above).
7. Biliary Atresia: Biliary atresia can be excluded scintigraphically by demonstrating transit of radiotracer into the bowel. Failure of tracer to enter the gut can be caused by hepatocellular disease or immature intrahepatic transport mechanisms and is not necessarily related to biliary atresia or CBD obstruction. Urinary excretion of the tracer (especially in diaper) may be confused with bowel activity and is a potential source of erroneous interpretation.
8. Duodenogastric Bile Reflux: During hepatobiliary scintigraphy, tracer may reflux from the duodenum into the stomach. This bile reflux may be abnormal since it is highly correlated with bile gastritis, a cause of epigastric discomfort (*21–24*).
9. Post-cholecystectomy Sphincter of Oddi Dysfunction: Following pre-treatment with Sincalide, a combination of visual and quantitative indices (the "scintigraphic score") may be used when this entity is suspected (*25*).

I. Quality Control

None

J. Sources of Error

The causes of a false-positive study (gallbladder nonvisualization in the absence of acute cholecystitis) include:

1. Insufficient fasting (<2–4 hr) (*26*).
2. Prolonged fasting (>24–48 hr), especially TPN (despite sincalide pre-treatment and morphine augmentation).
3. Severe hepatocellular disease.
4. High grade common bile duct obstruction.
5. Severe intercurrent illness (despite sincalide pre-treatment and morphine augmentation) (*27*).
6. Pancreatitis (rare) (*28,29*).
7. Rapid biliary-to-bowel transit (insufficient tracer activity remaining in the liver for delayed imaging).
8. Severe chronic cholecystitis.
9. Previous cholecystectomy.

The causes of a false-negative study (gallbladder visualization in the presence of acute cholecystitis) are rare, but include:

1. Bowel loop simulating gallbladder (drinking water may help to clarify anatomy).
2. Acute acalculous cholecystitis (*31*).
3. The presence of the "dilated cystic duct" sign simulating GB (*32*).
4. Bile leak due to GB perforation (*33*).
5. Congenital anomalies simulating gallbladder.

PART V: DISCLAIMER

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different than the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

PART VI: ISSUES REQUIRING FURTHER CLARIFICATION

None

PART VII: CONCISE BIBLIOGRAPHY

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PART VIII: LAST HOUSE OF DELEGATES APPROVAL DATE

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PART IX: NEXT ANTICIPATED APPROVAL DATE

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