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Scintigraphy of Gastrointestinal Motility: Best Practices in Assessment of Gastric and Bowel Transit in Adults

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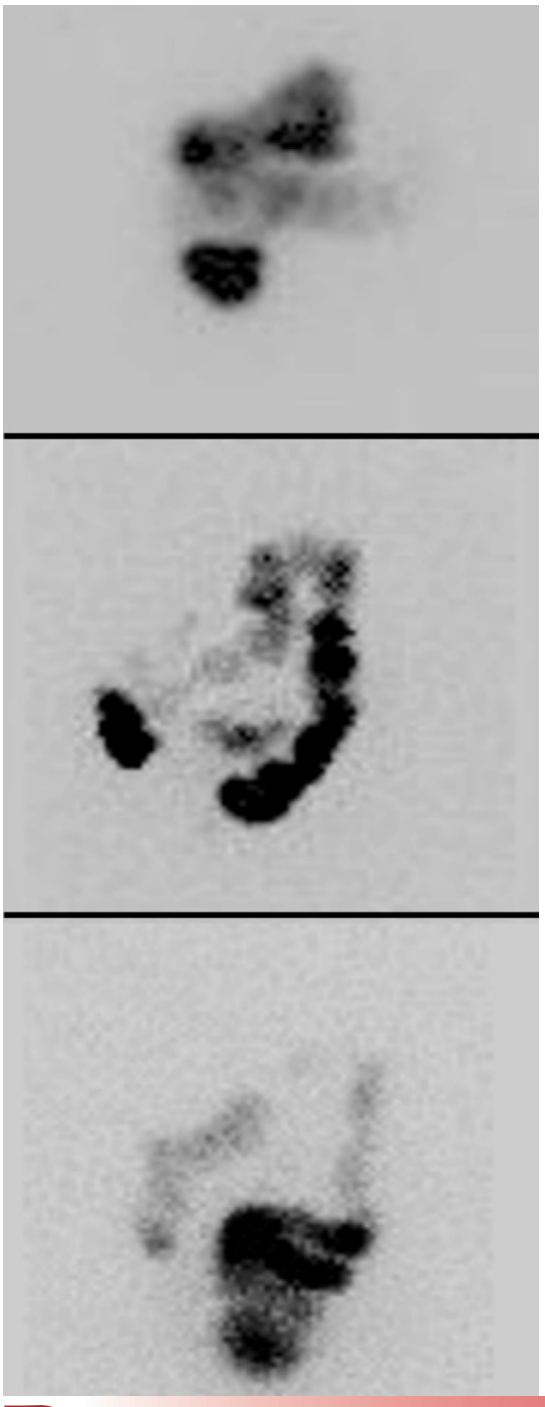
See the invited commentary by Maurer and Parkman in this issue.



Various radiologic examinations and other diagnostic tools exist for evaluating gastrointestinal diseases. When symptoms of gastrointestinal disease persist and no underlying anatomic or structural abnormality is identified, the diagnosis of functional gastrointestinal disorder is frequently applied. Given its physiologic and quantitative nature, scintigraphy often plays a central role in the diagnosis and treatment of patients with suspected functional gastrointestinal disorder. Most frequently, after functional gallbladder disease is excluded, gastric emptying scintigraphy (GES) is considered the next step in evaluating patients with suspected gastric motility disorder who present with upper gastrointestinal symptoms such as dyspepsia or bloating. GES is the standard modality for detecting delayed gastric emptying (gastroparesis) and the less commonly encountered clinical entity, gastric dumping syndrome. Additionally, GES can be used to assess abnormalities of intragastric distribution, suggesting specific disorders such as impaired fundal accommodation or antral dysfunction, as well as to evaluate gastric emptying of liquid. More recently, scintigraphic examinations for evaluating small bowel and large bowel transit have been developed and validated for routine diagnostic use. These can be performed individually or as part of a comprehensive whole-gut transit evaluation. Such scintigraphic examinations are of particular importance because clinical assessment of suspected functional gastrointestinal disorder frequently fails to accurately localize the site of disease, and those patients may have motility disorders involving multiple portions of the gastrointestinal tract. The authors comprehensively review the current practice of gastrointestinal transit scintigraphy, with diseases and best imaging practices illustrated by means of case review.

Introduction

Functional gastrointestinal disorders are extremely common, with a reported prevalence of 40%–69%, and account for 35% of ambulatory care visits in the United States (1–3). The underlying diseases responsible for functional gastrointestinal disorders contribute to a significant proportion of health care utilization, costing an estimated $22 billion annually in the United States, excluding the additional economic burden incurred from lost workdays and productivity (4).

Functional gastrointestinal disorders correspond to a group of disorders related to any combination of the following: a disturbance of gastrointestinal motility, mucosal immune dysfunction, alterations of the normal gut microbiota, visceral organ hypersensitivity, and/or altered processing by the central nervous system (5). Symptoms are frequently vague and include common reports such as dysphagia, nausea and/or vomiting, early satiety, bloating, abdominal or pelvic discomfort or pain, diarrhea, and constipation (6).

Invited Commentary

TestYour Knowledge CME

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Abbreviations: DGE = delayed gastric emptying, DTPA = diethylenetriaminepentaacetic acid, GES = gastric emptying scintigraphy, GIT = gastrointestinal transit, ROI = region of interest, TAC = time-activity curve

TEACHING POINTS

- Since the advent of the 2008 solid GES consensus document, researchers have shown that liquid emptying is often abnormal despite a normal solid GES examination, resulting in identification of 30% more cases of abnormal gastric emptying.
- Medications are reviewed, and any prescriptions that impact gastrointestinal motility are withheld for 2 days before GIT scintigraphy and until after imaging is completed, unless requested otherwise by the ordering provider (such as to assess response to medical therapy).
- A standardized low-fat meal to allow uniform measurement of results was developed (4 oz of liquid egg whites, two slices of white bread, 30 g of strawberry jam, and 120 mL of water, with the egg component labeled with 0.5–1 mCi of ^{99m}Tc-SC).
- Given that small bowel motility is complex, with varying patterns of contraction in the proximal versus distal small bowel with episodes of retrograde movement, a method based on filling of the terminal ileum reservoir (TIR) and colon are used that provide a simple clinically friendly approach.
- It must be noted that an accurate assessment of small bowel transit is dependent on adequate gastric emptying. Fortunately, even moderate delays do not significantly impact the small bowel assessment and, as long as the retention of the labeled liquid is less than 50% at 2 hours, a diagnostic evaluation can be performed.

Gastrointestinal Transit Diagnostic Tools

Various diagnostic tools are available to evaluate functional gastrointestinal disorders. Commonly, endoscopy and colonoscopy are used by gastroenterologists and surgeons to ensure the absence of underlying obstructive or inflammatory pathologic conditions. Barium fluoroscopy is sometimes preferred for this same purpose, with the advantages being it is noninvasive and has a lower cost, but it is limited by the inability to allow simultaneous biopsy of abnormalities. If these examinations are unrevealing, a functional disorder may still be suspected, with the choice of the next diagnostic test based on the part of the gastrointestinal tract suspected as the source of symptoms.

For esophageal concerns, manometry or fluoroscopy may be performed to evaluate the quality and coordination of muscle contractions during swallowing. For suspected biliary disease, US or MR cholangiopancreatography may be performed. For stomach, small bowel, or colon concerns, the choices include scintigraphy, use of a wireless motility capsule that is swallowed by the patient, a gastric emptying breath test to assess gastric emptying, and use of radiopaque markers that are swallowed by the patient and used to measure colonic transit (Table 1).

Scintigraphy

There are several gastrointestinal transit (GIT) scintigraphic examinations currently in use in clinical practice. These include assessments of transit through the esophagus, stomach, small bowel, and colon, all of which can be performed separately or collectively using a whole-gut scintigraphy technique. Fortunately, the examinations share many aspects regarding patient preparation and imaging protocols, facilitating their routine clinical implementation. In the following sections, we discuss these examinations in depth and review best practices, clinical indications, standardized techniques, and interpretation criteria.

Clinical Indications

GES: Solids

By far the most common scintigraphic examination of GIT is GES. It is completely physiologic and can be done in a single day, unlike the wireless motility capsule. The radiation dose is low, with 0.5 mCi (1.85 MBq) of technetium 99m (^{99m}Tc) sulfur colloid (SC) imparting an effective dose equivalent of 0.17–0.31 mSv (17–31 mrem), which is less than half that of an abdominal radiographic examination (16). Other advantages include its noninvasive nature, use of common foods, reproducibility, quantitative data, and ability to look at intragastric meal distribution. The only significant disadvantage is that some patients are intolerant to aspects of the standardized meal (eggs or gluten, most commonly, and alternative meals, while available, have not been universally agreed on or widely studied.

GES is most often performed due to a clinical concern for gastroparesis, also known as delayed gastric emptying (DGE). Patients with suspected gastroparesis present with a range of symptoms that may be suggestive of an upper gastrointestinal source but are otherwise nonspecific. These include nausea, vomiting, abdominal fullness, abdominal distention, and/or early satiety (17–19). Patients with gastroparesis are typically middle aged, with women four times more frequently diagnosed than men (19). Nausea is almost universally present, and the cause is idiopathic in one-third of cases. Identifiable causes include viral injury to either the neural network of the stomach or the interstitial cells of Cajal and long-standing diabetes (20). Gastroparesis occurs late in diabetes, after advanced sequela such as retinopathy, nephropathy, or neuropathy are already present. Less well recognized is that gastroparesis is also frequently encountered in individuals with postural tachycardia syndrome as well as Parkinson disease, often being the presenting symptom in both of these disorders (21,22). Last, it is not uncommonly related to medications or seen following fundoplication or bariatric surgery (23).

More recently, attention has turned to the less common but also clinically important diagnosis of rapid gastric emptying, also known as dumping syndrome. While gastroparesis is a well-known complication of chronic diabetes, it is now recognized that rapid gastric emptying is also a complication, particularly in the early stages of the disease (24). Rapid gastric emptying can manifest with symptoms of functional dyspepsia and may be due to impaired stomach accommodation of a meal, with food reaching the duodenum too quickly (25). Recently, an entity known as cyclic vomiting syndrome has gained recognition. Cyclic vomiting syndrome is an incompletely understood disorder characterized by recurrent episodes of severe vomiting separated

Table 1: Nonscintigraphic Techniques Commonly Used for Assessment of GIT

Test	Indications	Technique	Limitations
Gastric emptying breath test	Suspected gastroparesis	All medications effecting gastrointestinal motility are withheld, and the patient fasts for 8 hours Standardized meal is consumed including spirulina (an edible blue-green algae) or octanoic acid (a fatty acid) labeled with carbon 13 (^{13}C) (7–10) Meal enters the stomach, where it is transformed to chyme before exiting into the duodenum Radiolabeled substrate is digested and absorbed in the duodenum and then metabolized by the liver and exhaled through lungs as ^{13}C dioxide ($^{13}CO_2$) Seven breath samples are obtained over 4 hours, and ^{13}C percentage is measured	Dysfunction in duodenal, liver, or pulmonary function may limit accuracy
Wireless motility capsule (SmartPill; [Medtronic])	Suspected gastroparesis Chronic constipation	Battery-powered capsule measures 2.7 cm long; 120-hour lifespan Ingested in conjunction with standardized 260-kcal nutrient bar (SmartBar [Medtronic]) and 50 mL of water (11) Patients wear a belt monitor throughout the test to record data transmitted from the capsule until passed, usually for 3–5 days Temperature, pH, and pressure measurements allow its localization during transit (7). When measuring gastric emptying, sudden increase in pH identifies the transition from the acidic stomach to the relatively basic environment of the duodenum. A small distinct drop in pH signals the capsule has reached the colon. The end of large bowel transit shows an appropriate drop in temperature as the capsule exits the rectum.	Not physiologic Difficult to swallow for some patients
Radiopaque markers (eg, SitzMarkers [Konsyl Pharmaceutical])	Chronic constipation	Radiopaque markers, typically ring or cylindrical shaped, are plastic and contain barium Ingested via dissolving capsules typically containing 20–24 markers Depending on the protocol, the capsule is ingested on day 1, and abdominal radiographs are obtained at 24-hour intervals for up to 5 days; or, conversely, capsules can be administered serially on days 1, 2, and 3, and a radiograph is obtained on day 4 (72 hours after initial ingestion), as well as on day 7 and day 10, if needed Based on the number of markers remaining in the large bowel and their location, diagnostic information regarding colorectal function can be obtained (7) Using the single-capsule technique, most healthy adults pass the majority of radiopaque markers by day 5 (<20% of rings remaining is normal) (14,15)	Lack of standardization of protocols Radiation exposure 5–10 days in length (7,12,13)

Note.—GIT = gastrointestinal transit.

by asymptomatic intervals (26). While a small number of these individuals do demonstrate slow or even normal gastric emptying, two-thirds have rapid gastric emptying at examination (27). The same surgical procedures that lead to DGE (weight loss and antireflux procedures) can also increase the risk for developing gastric dumping.

Since disorders of gastric transit result in the caloric content of food and liquids reaching the bowel too slowly or too quickly, they can impact the established balance between diet and medications, manifesting as a loss of glycemic control. Therefore, a related indication for GES is assistance with management of diabetes in patients who develop poor glycemic control but may not have symptoms.

Similarly, severe gastroesophageal reflux disease may trigger a referral for GES, since severe delay in gastric emptying can increase gastric acid levels and affect lower esophageal sphincter function (28). Performing GES in patients with reflux significant enough to warrant fundoplication allows identification of potential concomitant gastroparesis and the need for pyloroplasty as part of the surgery (29).

GES is also beneficial when evaluating patients with chronic constipation who are being considered for colectomy. Colorectal specialists are aware that a significant number of these patients will have coexistent disorders of gastric emptying or small bowel transit in addition to their delayed colonic transit. In those cases, whole-gut transit scintigraphy should be performed to identify patients who may not benefit from surgery to correct their symptoms (30). Finally, GES can also be performed to evaluate response to pharmacologic treatment, for example, after initiation of prokinetic therapy (31).

GES: Liquid

A major factor impacting gastric emptying is the composition of the meal: solid, semisolid, liquid, or a mix thereof. Liquid emptying is independent of antral function since it does not need to undergo trituration. It is instead felt to be predominately under the influence of the proximal to distal pressure gradient from fundal contraction. Historically, it was believed that because of the perceived simpler nature

Table 2: Common Clinical Indications for Esophageal, Gastric, Small Bowel, and Colonic Transit Scintigraphy

Indication	Esophageal	Gastric	SB	Colonic
Achalasia	×			
Esophageal stricture	×			
Suspected gastroparesis		×		
Symptoms of dumping syndrome		×		
Diabetes mellitus with new loss of glycemic control		×		
Severe refractory GERD		×		
Preoperative gastric fundoplication		×		
Chronic idiopathic intestinal pseudo-obstruction			×	×
Malabsorption syndrome			×	×
Celiac disease			×	×
Scleroderma	×		×	×
Chronic diarrhea			×	×
Functional dyspepsia		×	×	×
Chronic constipation		×	×	×
Assess response to therapy	×	×	×	×

Sources.—References 35, 36.
Note.—GERD = gastroesophageal reflux disease, SB = small bowel, × = yes.

of liquid emptying from the stomach, it would invariably be abnormal only in the setting of an abnormal solid GES. Hence, it was generally reserved only for very young pediatric patients and others who could not tolerate the solid meal. Since the advent of the 2008 solid GES consensus document, researchers have shown that liquid emptying is often abnormal despite a normal solid GES examination, resulting in identification of 30% more cases of abnormal gastric emptying (32). Therefore, some advocate its use routinely while others see it as most helpful in further assessing patients with normal solid GES results.

Small Bowel and Colonic Transit Scintigraphy

Differentiating upper and lower gastrointestinal tract dysfunction can on occasion be exceedingly difficult. In a study of 104 patients with either dyspepsia or constipation, Bonapace et al (33) found one-third of patients with dyspepsia to have abnormal colonic transit and another 10% to have slow small bowel transit. Over a quarter of patients with clinical symptoms of constipation had a gastric or small bowel motility disorder (33). This changed the diagnosis in almost half of the patients and impacted management in two-thirds.

Very similar results have been reproduced in a study of 103 patients with nonspecific symptoms of a GIT disorder (34). The authors found the same impact on management and reported that over one-fifth of patients had more than one region of abnormal motility, with the stomach as the dominant region in two-thirds of those instances. Hence, it is reasonable to consider a whole-gut transit examination in patients with symptoms suggestive of either DGE or rapid gastric emptying in addition to the classic indications for a lower GIT examination (Table 2).

Patient Preparation

Proper patient preparation for any GIT scintigraphy examination begins when scheduling the appointment. Patients are queried regarding food allergies (particularly eggs and gluten), as well as any other dietary restrictions. Medications are reviewed, and any prescriptions that impact gastrointestinal motility are withheld for 2 days before GIT scintigraphy and until after imaging is completed, unless requested otherwise by the ordering provider (such as to assess response to medical therapy) (Table 3). If colonic transit is being investigated, laxatives are also withheld for 2 days prior and throughout the entire 4 days of imaging (40).

Although the original research by Tougas et al (41) did not show any variations in stomach gastric emptying due to sex or menstrual phase, others have shown a difference in stomach motility attributed to hormonal variations. Hence, for GES, it is recommended by the original consensus group to try and perform the test during the first 10 days of the menstrual cycle (37). Additionally, the same group recommended cessation of smoking from the morning of the GES examination through the completion of the examination because some research has shown that smoking delays gastric emptying. However, there is no complete agreement on this topic, and the later major societal guidelines (Society of Nuclear Medicine and Molecular Imaging [SNMMI]) and practice parameters (American College of Radiology) do not address smoking (36,42). Similarly, while the guidelines do not discuss cannabinoids, its prevalence as a social drug and impact on gastric emptying raise the question of screening for its use among patients (43).

Given its duration, GIT scintigraphy is typically scheduled to begin in the morning, with the patient instructed to fast overnight. If an afternoon time is scheduled, they should

Table 3: Medications That Alter Gastric Emptying, Either Intentionally or as a Side Effect

Class Drug	Examples
Increase gastrointestinal motility	
Dopamine receptor antagonist	Metaclopramide (Reglan [ANI Pharmaceuticals]), domperidone (Motilium [Janssen])
Serotonin agonist	Tegaserod (Zelnorm [Alfasigma USA]), cisapride (Propulsid [Janssen])
Acetyl cholinesterase inhibitors	Neostigmine, pyridostigmine
Macrolide antibiotics	Erythromycin, azithromycin, clarithromycin
Laxatives*	Bulk forming, psyllium, dietary fiber, methylcellulose, osmotics, lactulose, sorbitol, polyethylene glycol, milk of magnesia, lubricants, mineral oil
Decrease gastrointestinal motility	
Opioids	Meperidine (Demerol [Pfizer]), codeine, morphine, oxycodone (OxyContin [Purdue], Percocet [Endo Pharmaceuticals])
Antispasmodic	Glycopyrrolate (Robinul [Rising])
Anticholinergic	Dicyclomine (Bentyl [Teva])
Muscarinic antagonist	Hyoscyamine (Levsin [Alaven Pharmaceutical])
Combination (anticholinergic and antispasmodic)	Donnatal (combination belladonna alkaloids and phenobarbital)
Glucogon-like peptide 1 (GLP-1) agonists	Dulaglutide (Trulicity [Eli Lilly]), semaglutide (Ozempic [Novo Nordisk])
Cannabis, cannabinoids	Marijuana, tetrahydrocannavinal (THC), cannabidiol (CBD)

Note.—These should be discontinued for 48 hours prior to the examination and until imaging is complete on the day of examination (if not contraindicated). If the patient is undergoing colonic transit scintigraphy, then the medications should also be withheld until all 4 days of imaging are completed. Patients requiring medication for severe nausea or vomiting that may interfere with the examination may take a serotonin antagonist such as ondansetron (Zofran [Sandoz]), which has little effect on gastric emptying (37). GLP-1 agonists and cannabis and cannabinoids are not discussed in existing guidelines but have also been shown to slow gastrointestinal motility (38). Likewise, cannabis and its byproducts have a similar impact (39).
* Only pertinent for colonic transit studies.

be instructed not to eat or drink for the preceding 6 hours (extended to 8 hours if the small bowel or colonic transit is being assessed) (40). A small amount of water is permissible as needed to take other prescribed medications.

On the morning of GIT scintigraphy, patients with diabetes should bring their blood glucose monitoring device, as well as their insulin. Blood glucose levels should be measured and the value reported with the results of the study. The original 2008 consensus document stated that glucose levels should be below 275 mg/dL before performing the examination for the results to be accurate because hyperglycemia slows gastric emptying (44). This value has been revised down to 200 mg/dL in subsequent guidelines and parameters (36,42). If it is too high, the patient should administer their insulin to achieve an appropriate level. If the level is normal at the time of initial testing, an option is to have a patient take half of their normal morning insulin dose. This amount was chosen to avoid hypoglycemia during the duration of the 4 hours of imaging given there is no other caloric intake besides the test meal, although there is no widely agreed-on approach (45).

It should be noted that some experts advocate for measuring blood glucose levels in all patients, similar to that performed before administration of fluorine 18–labeled fluorodeoxyglucose (^{18}F-FDG). Hyperglycemia can delay gastric emptying in patients without diabetes, and recent research has shown that over 10% of individuals presenting for GES have undiagnosed diabetes and another one-third meet the criteria for prediabetes (46,47).

Scintigraphic Techniques

GES: Solid

In the 1990s, Tougas et al (41) were looking to assess the effects of gastric pacing on stomach emptying in patients with intractable gastroparesis. They developed a standardized low-fat meal to allow uniform measurement of results (4 oz of liquid egg whites, two slices of white bread, 30 g of strawberry jam, and 120 mL of water, with the egg component labeled with 0.5–1 mCi of ^{99m}Tc-SC) (43). Liquid egg whites were chosen in part because the SC binds to the protein albumin found in the egg whites but does not bind to egg yolks. Using only the egg whites helps ensure that the radiotracer does not separate from the cooked egg in the acidic milieu of the stomach where it could potentially be absorbed by or bound to the stomach wall, leading to spurious results (41). In 2008, a working group of the American Motility Society and the SNMMI built on this protocol and published their consensus guidelines on a standardized methodology for GES that addressed not only the meal but also patient preparation, imaging technique, processing, and interpretation (37).

The liquid egg is mixed thoroughly with the 0.5–1.0 mCi of ^{99m}Tc-SC. It can be cooked either using a skillet (nonstick frying pan) or microwaved to the consistency of a firm omelet, with either technique showing good labeling (48). If the radiotracer is added after cooking, the labeling efficiency decreases markedly due to poor binding of the SC and albumin (45).

The meal is consumed as an egg sandwich along with the water. Patients should consume the meal within 10 minutes. Prolonged or incomplete ingestion should be documented in the report. Similarly, incomplete meal ingestion or emesis should also be documented, as the rate of gastric emptying may be overestimated in these instances (49). Recent research suggests that GES examinations with partial meals with consumption of at least 50% still yielded diagnostic results using the stand normative criteria (50).

Imaging is performed with the patient upright, obtaining anterior and posterior acquisitions for 1 minute each. The anterior and posterior images may be obtained simultaneously with a dual-head ɣ-camera or sequentially if using a single-head camera. Otherwise, the left anterior oblique position is the best alternative to parallel the path of the stomach (51). Initial imaging at time zero is performed immediately after meal consumption and then again at 1 hour, 2 hours, and 4 hours. While not reflected in the current guidelines and parameters, a 30-minute acquisition is also recommended given its utility in the assessment of rapid gastric emptying (49).

Acquiring the 4-hour image for solid GES extends the time the patient must be present for the examination and is an additional, albeit small, burden on the clinic workflow. However, two studies have demonstrated the diagnostic impact of extending the imaging time from 2 to 4 hours, allowing identification of up to 30% more patients with DGE who had shown normal results at the 2-hour time point (52–54).

For time point 0, a region of interest (ROI) is drawn on both the anterior and posterior images to include all radiotracer in the field of view, regardless of whether it is in the stomach or has reached the small bowel. Failure to include this extragastric portion of activity will spuriously underestimate gastric emptying at subsequent time points. For 1-, 2-, and 4-hour images, ROIs are drawn around the entire stomach, including the fundus through the antrum. It is important on these images to ensure no activity from the adjacent small bowel is included within the ROI to prevent spuriously underestimating gastric emptying.

Because the examination is performed over 4 hours and ^{99m}Tc has a 6-hour half-life, radioactive decay correction must be performed to correct the number of counts at each time point. Failure to do so will overestimate the rate of stomach transit. Once the counts are corrected, attenuation correction is then applied by use of the geometric mean. This step is important because of the relative posterior (fundus) to anterior (antrum) movement of ingested material as it traverses the stomach. Failure to apply attenuation correction can also cause underestimation of the rate of gastric emptying by 10%–30%, depending on the habitus of the patient (45).

The results of the decay-corrected geometric means are used to determine the percent retention in the stomach at each time point by dividing the total counts at the time point by the initial total counts. The percent retention can then be graphed over time (Fig 1). Measuring the time it takes half of the radiolabeled meal to leave the stomach (half-emptying time) is not recommended because it can be less accurate, particularly in cases of delayed emptying when extrapolation of the data are necessary to determine the half-emptying time.

GES: Liquid

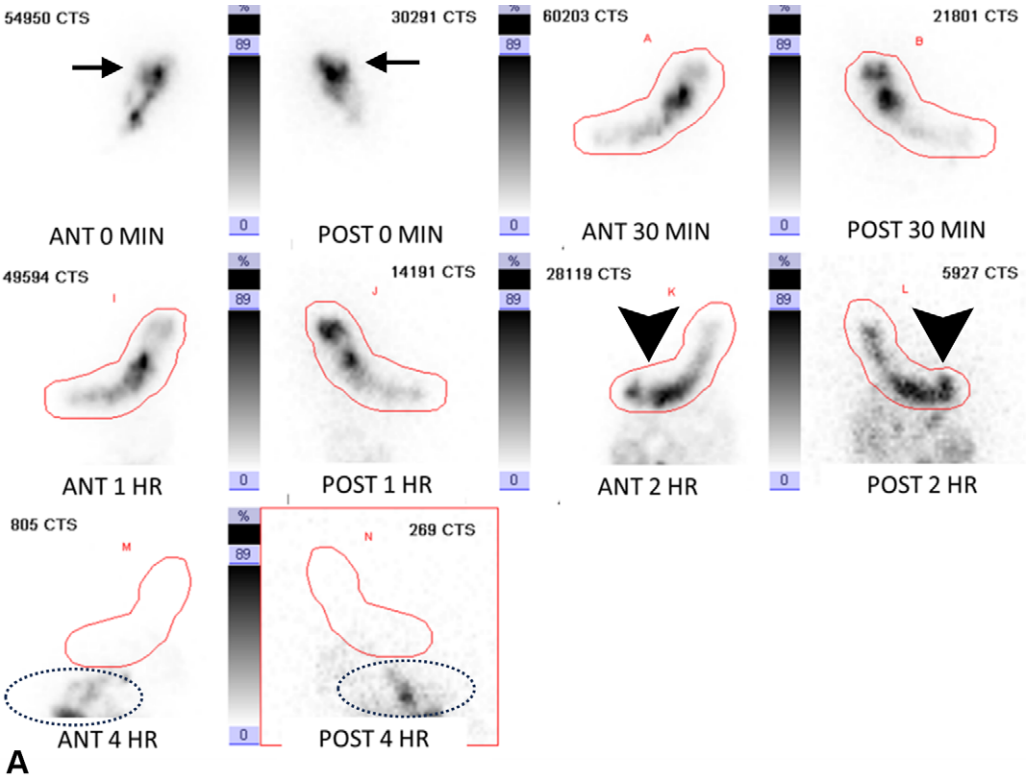
Fortunately, a liquid GES examination is relatively easy to perform and can either be accomplished on the same day as a solid GES (as well as small bowel and colonic transit examinations discussed later) or on separate days. When done on a different day, the water is labeled with 0.5–1 mCi of ^{99m}Tc-SC or diethylenetriaminepentaacetic acid (DTPA). If done on the same day, the liquid GES is performed using 300 mL of water labeled with 0.2 mCi of indium-111 (^{111}In) DTPA (effective dose equivalent to 163–182 mrem [1.63–1.82 mSv]) (16). This provides alternative photopeaks of 171 keV and 247 keV for imaging, thus ensuring any residual activity will not impact the accuracy of the subsequent solid GES or other GIT examinations (55). Left anterior oblique images are acquired in a continuous fashion using 1-minute frames, with imaging beginning with ingestion and continuing for 30 minutes. A half time of emptying is then calculated, with normal being less than 25 minutes (Fig 2).

A combined solid and liquid examination with a dual isotope has been described for gastric emptying. The standardized meal is used with ^{111}In-DTPA labeling the water and the ^{99m}Tc-SC labeling the solid component of the meal. The different photopeaks of the radiotracers then allow separate measurement of the two components. It should be noted that the transit of liquid in the stomach is impacted by several factors, including the presence of solids that increase the time it takes for the water to transit the stomach. Hence, the liquid results from a combined study do not correlate with the results obtained from a liquid-only examination. In a study of 18 healthy controls, authors found that the upper limits of normal half-emptying time for liquid when consumed with the consensus meal was 74 minutes (34).

Small Bowel Transit Scintigraphy

Scintigraphic evaluation of the small and large bowel has been performed since the 1970s. However, it was only in 2013 that a practice guideline became available. Subsequently, in 2016 the Current Procedural Terminology (CPT) code 86266 was instituted for gastric emptying with the addition of the small bowel and/or colon, providing practitioners a means to perform the examination with standardized technique and interpretation (40).

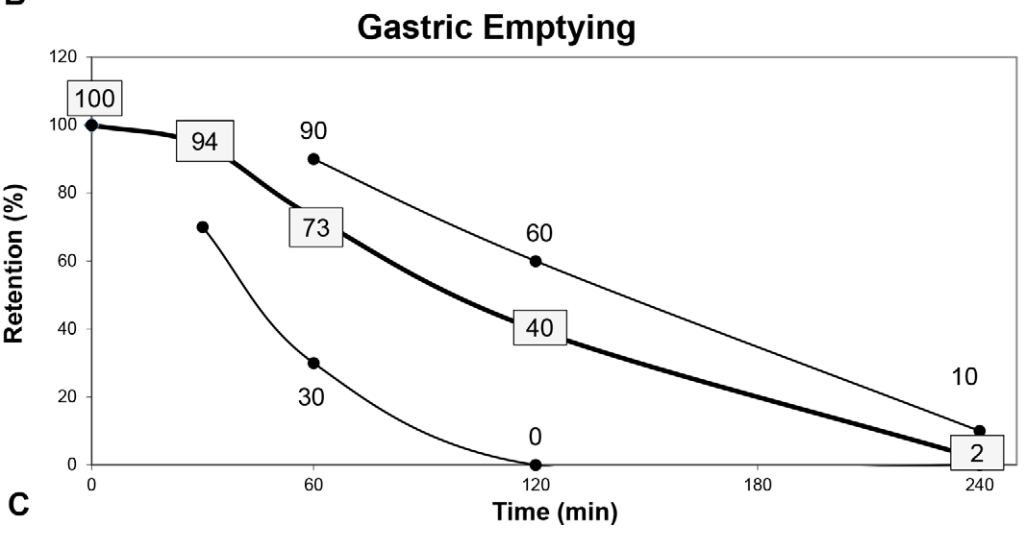
Current guidelines offer different protocols that may be used for assessment of the small bowel, measurement of colon transit, or a whole-gut examination evaluating the stomach and bowel transit (40). In many ways, these protocols are similar to and are an extension of the consensus approach to solid GES with the addition of water labeled with ^{111}In-DTPA and later imaging time points to evaluate small and/or large bowel transit (Table 4). If gastric emptying is to be part of the examination, then the consensus solid meal is used but with the addition of 0.1–1.0 mCi of ^{111}In-DTPA in 300 mL of water as used in liquid-only GES. Although this is a larger volume of water compared with the 120 mL of water in the standard solid consensus meal, probably there is no or only little effect on the solid gastric emptying results since the volume of liquid does not appear to significantly impact the transit of solids (56). If measurement of gastric emptying is not necessary, then only the water is labeled but ^{111}In-DTPA



A

Time to be Imaged	Time Imaged	Time Elapsed	Anterior Counts	Posterior Counts	% Retained (Patient)	Normal Low	Normal High
0 min	0852 AM	0	54950	30291	100	100	100
30 min	0922 AM	30	60230	21801	94	70	
60 min	0952 AM	60	49594	14191	73	30	90
120 min	1052 AM	120	28119	5927	40	0	60
240 min	1252 PM	240	805	269	2	0	10

B



C

Figure 1. Normal solid GES examination. Paired anterior *(ANT)* and posterior *(POST)* images **(A)** of the stomach at 0 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours show ROIs (red outlines) that each appropriately include the entire stomach. The meal appropriately localizes to the fundus at early time points due to normal fundal accommodation (arrow) (time *[T]* = 0). It then progresses distally to the antrum (arrowhead, T = 2 hours) and into the small bowel (dashed ovals, T = 4 hours). The counts *(CTS)* are used to create a geometric mean [square root of (anterior counts × posterior counts)] and can be provided in a table **(B)** and/or graph **(C)** format with upper and lower limits of normal included.

is still used given its longer half-life (67.2 hours), which is necessary for the later time points. If necessary, gallium-67 (^{67}Ga) citrate with its half-life of 78.3 hours can be used as an alternative agent (35).

Images are acquired in both the anterior and posterior projections. The 140 keV photopeak is included if solid GES is included. If not, only the 171 keV and 247 keV photopeaks are captured. Up through 6 hours, 60-second acquisitions are obtained and then 4 minutes if a 24-hour image is obtained. Counts are decay corrected and then the geometric mean is calculated as described previously.

Given that small bowel motility is complex, with varying patterns of contraction in the proximal versus distal small bowel with episodes of retrograde movement, a method

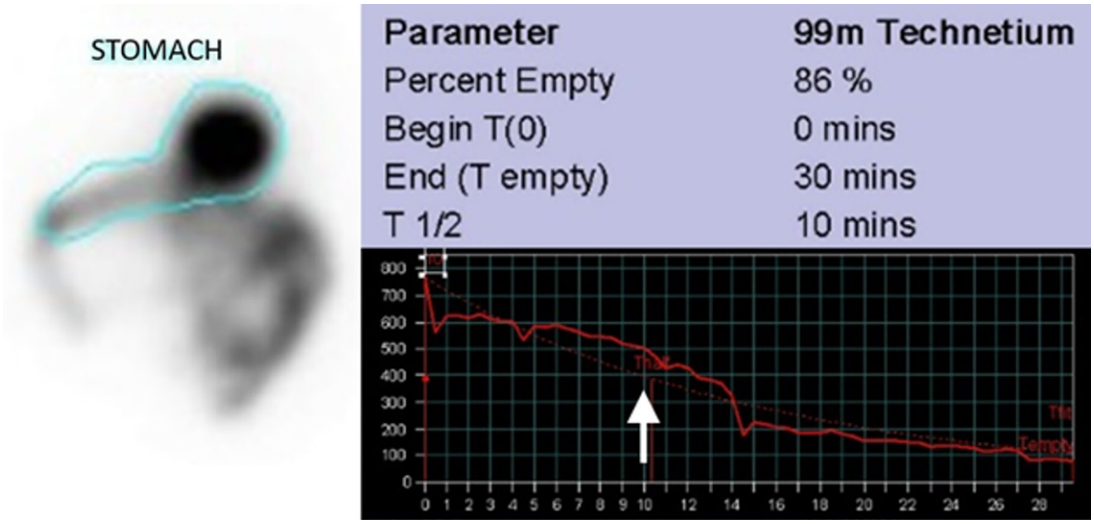


Figure 2. Normal liquid GES examination. Representative 1-minute left anterior oblique image (left) shows the stomach from a 30-minute acquisition with the ROI (outline). The time-activity curve (TAC) (bottom right) shows normal rapid transit of the water with a half-emptying time *(T1/2)* of 10 minutes (arrow). Normal is less than 25 minutes. Of note, the small dips in the data at 0–1, 4–5, and 14–15 minutes are typically due to patient motion and, if necessary, can be eliminated by manually adjusting the stomach ROI for those individual frames. *T* = time.

Table 4: Imaging Time Points to Acquire during Small Bowel, Colonic, or Whole-Gut Transit Scintigraphy

Imaging Time Point (Meal Consumed in 10 min)	Solid Gastric Emptying	Small Bowel Transit	Colonic Transit	Acquisition Time (min)
0 min	×	×		1
30 min	×			1
1 h	×	×		1
2 h	×	×		1
3 h		×		1
4 h	×	×		1
5 h		×		1
6 h		×		1
24 h		Optional	×	4
48 h			×	4
72 h			×	4

Note.—Zero, 1-, 2-, and 4-hour time points provide data for both gastric and small bowel transit, while the 24-hour image aids the assessment of small and large bowel transit. All images are acquired using a 128 × 128–pixel matrix. If imaging with ^{99m}Tc, a low-energy high-resolution (LEHR) or general-purpose collimator is best, set for a photopeak of 120 keV with a 20% window (36). If imaging with ^{111}In or both radiotracers, a medium-energy collimator is recommended with 172-keV and 247-keV photopeaks with 15% windows for the ^{111}In, and the window for ^{99m}Tc is also reduced to 15%. If there is significant spillover from the ^{99m}Tc activity into the lower-energy 172-keV ^{111}In photopeak, a single 247-keV peak for ^{111}In can be used (35). × = when to acquire.

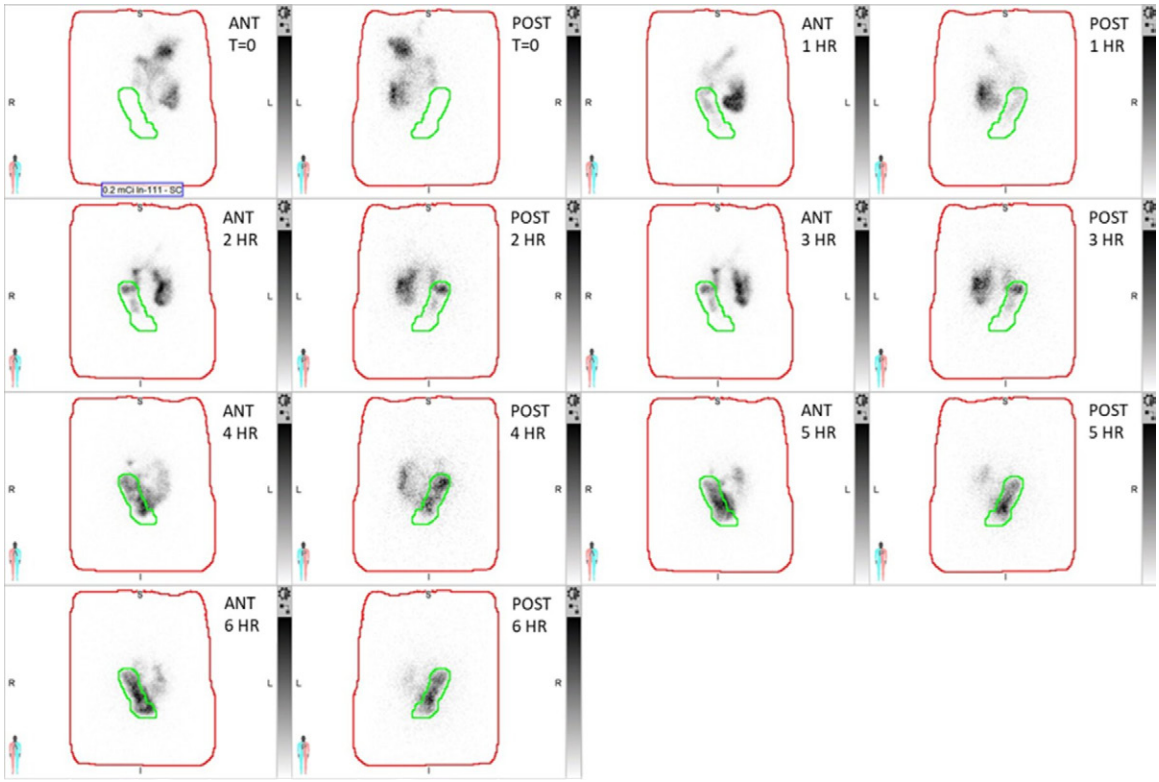
based on filling of the terminal ileum reservoir (TIR) and colon are used that provide a simple clinically friendly approach (57). This was chosen because most patients reliably demonstrate a pooling of activity in the right lower quadrant before visualization of radiotracer progressing to the colon (58). Localizing this region is relatively easy in transit scintigraphy and allows a manual ROI to be drawn in this region with facility (33). The total abdominal counts at the 2-, 3-, 4-, and 5-hour time points are measured and an average is calculated. Then at 6 hours, ROIs are drawn to include the radiotracer activity in the TIR, as well as any activity that has passed into the colon (measurement at the 24-hour time point may be necessary to help define the anatomy of the colon and TIR) (Fig 3). The percent small bowel transit is then calculated as follows using the decay-corrected geometric mean values: percent of small bowel transit = (total counts TIR + colon) / average total abdominal counts.

Since the guidelines were published, researchers have described a simplified technique for determining the total abdominal counts by measurement of only a single time point while using the remaining time points for qualitative assessment and localization of the TIR (59). Additionally, in equivocal cases at 6 hours, having the patient drink a commercially available liquid nutrient meal and reimaging 20 minutes later can frequently help localize the TIR and ascending colon, obviating the need for a 24-hour follow-up image (56).

Colonic Transit Scintigraphy

Imaging for colonic transit begins at 24 hours after meal administration and is repeated at 48 and 72 hours. The 72-hour image

Figure 3. Scintigraphic images show normal small bowel transit. The total abdominal counts are measured (red ROI), and the average is calculated from the 2-, 3-, 4-, and 5-hour time points. The activity in the TIR and the cecum and ascending colon (green ROI) at 6 hours is used to measure the small bowel transit. The value in this patient was 56%, above the normal cutoff of 40%–50%. *ANT* = anterior, *POST* = posterior.



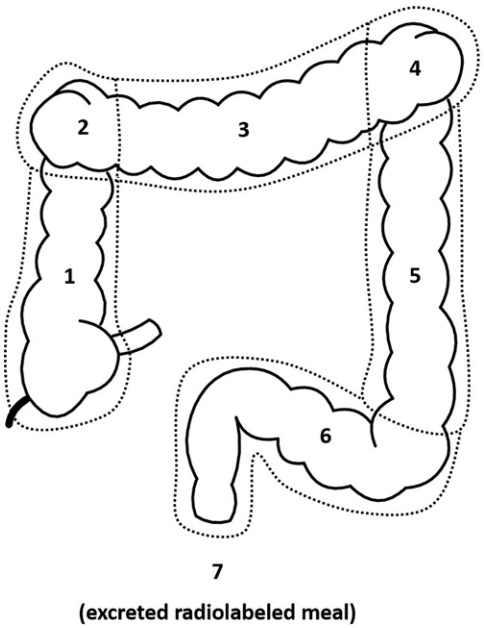


Figure 4. Diagram shows the division of the colon for calculation of the geometric center. The colonic activity is divided into seven segments, with the weighted values increasing distally: *1* = cecum and ascending colon; *2* = hepatic flexure; *3* = transverse colon; *4* = splenic flexure; *5* = descending colon; *6* = sigmoid colon and rectum; *7* = the amount excreted, which is calculated by subtracting the amount retained throughout the colon from the initial total abdominal counts. (Adapted and reprinted, with permission, from reference 35.)

is particularly helpful to diagnose functional rectosigmoid outlet obstruction and to best localize other forms of functional colonic obstruction. As mentioned with small bowel imaging, 4-minute acquisitions in the anterior and posterior projections are obtained and the geometric means are calculated.

Societal guidelines (36, 40) recommend that the evaluation of colonic transit be performed by calculating the geometric center of the counts at each of the time points. The geometric mean is a weighted average of where the activity is in the large bowel. The colonic activity is divided into seven segments: cecum and ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, rectosigmoid, and the amount excreted, with the excreted value being based on the total initial counts minus the retained counts. Each segment of the colon is given a sequentially increasing integer as a weighting factor (cecum and ascending colon = 1, excreted amount = 7) (Figs 4, 5). The geometric center is then calculated as the decay-corrected geometric mean of each segment multiplied by its designated weighted factor. A low geometric center is seen with activity predominately in the proximal colon, while a high geometric center indicates that the activity is located more in the distal colon.

An alternative approach has been developed by Antoniou et al (34). Using the 6-hour counts as the total, the percent of colonic emptying is calculated at 24, 48, and 72 hours. These values have been shown to correlate well with results using

Figure 5. Division of the colon at 24, 48, and 72 hours for calculation of the geometric center in a patient with generalized colonic delay. (Reprinted under a CC BY 4.0 license from reference 60.)

Table 5: Normal Limits of Gastric Retention Using the Consensus Meal

Time Point	Lower Limit (% Retention)	Upper Limit (% Retention)
30 min	70	...
1 h	30	90*
2 h	...	60
4 h	...	10

Note.—A value below the lower limit at 30 minutes or 1 hour defines rapid gastric emptying, while a value exceeding 60% at 2 hours or 10% at 4 hours is consistent with DGE.
* While a retention of greater than 90% was found to be abnormal at 1 hour, this is not used in more recent literature as a criterion for defining DGE (35,62).

the geometric center method (34). However, this method does not provide the numerical anatomic localization of the site of predominant colon activity provided by the geometric center method.

Imaging Interpretation

Gastric Emptying

Normal values for gastric emptying of solids for the standardized protocol and the consensus meal were established by Tougas et al (41) using a study of 123 normal subjects across 11 different medical facilities. A subsequent reanalysis of the data also provided values for rapid gastric emptying (Table 5) (61).

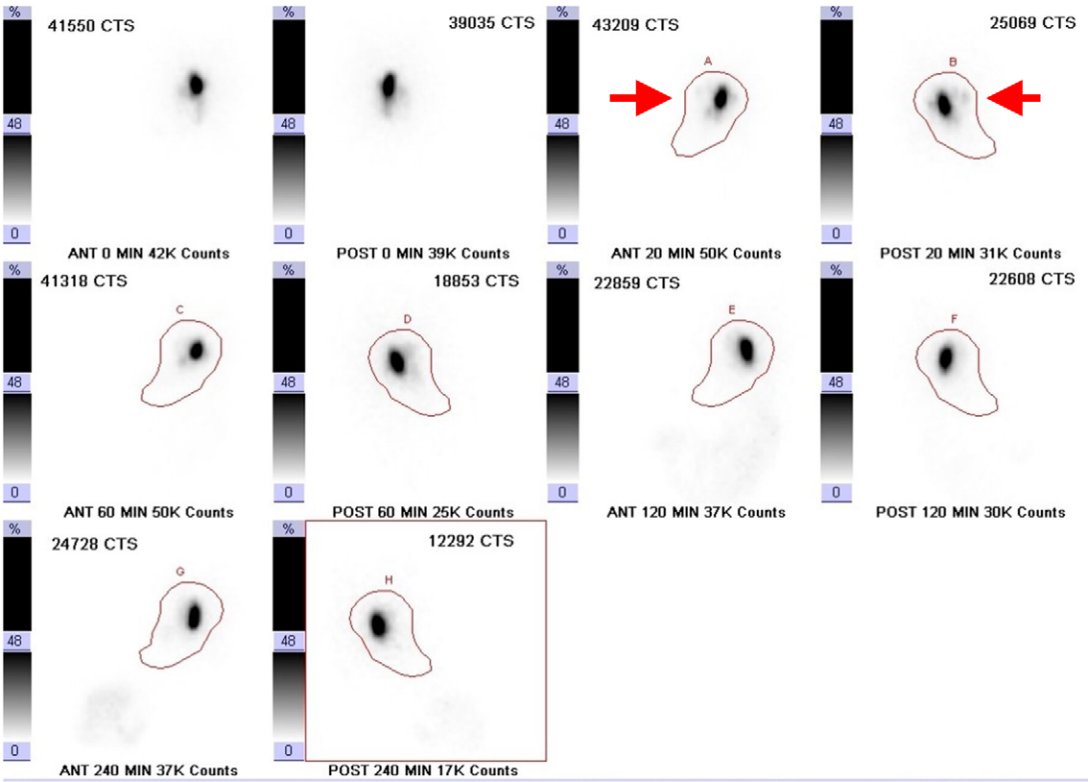
A normal solid gastric emptying examination with normal transit shows the meal activity to localize predominately to the fundus at time point 0, and it serves as an indirect means of assessing fundal accommodation (for a discussion of scintigraphic techniques for directly assessing fundal accommodation, the reader is referred to Bennink et al [63] and Orthey et al [64]). The meal subsequently progresses from the fundus to the gastric body, the antrum, and into the small bowel. Retentions fall within the standardized upper and lower limits of normal at each time point.

With DGE, the percent retention is greater than 60% at 2 hours and/or 10% at 4 hours with a failure of normal gastric transit. As touched on briefly in reporting, it can be helpful, if possible, to describe the pattern of DGE. This can be due to fundal dysfunction, when the fundus fails to contract and thus the meal does not transition in normal fashion to the body and antrum, manifesting as prolonged retention of the meal in the proximal stomach (Fig 6).

Alternatively, DGE may manifest with only abnormal increased retention at 2 or 4 hours and be due to antral dysfunction. The antrum performs trituration, where solids and semisolids are ground down into 1–2-mm particles by muscular contractions and then are passed through the pylorus by peristalsis. In this situation, the radiolabeled meal will be seen to transit normally during the first half of the examination when fundal function predominates and then fail to transition from the antrum into the small bowel (Fig 7).

In some instances, the examination will demonstrate DGE but no clear regional abnormality. These may be due to a diffuse abnormality of gastric emptying or combined fundal and antral dysfunction. Less commonly, the visual assessment of the examination might suggest fundal or antral dysfunction despite activity curves being within the limits of normal (Fig 8).

Rapid gastric emptying is diagnosed by abnormalities involving the 1-hour time point or 30-minute time point, if acquired. This results in the meal too rapidly reaching the duodenum, resulting in symptoms in addition to alterations in blood glucose levels. Like with cases of DGE, it is important to assess the intragastric meal distribution to determine if a regional abnormality can be identified. If a regional abnormality is present with rapid gastric emptying, it is a failure of fundal accommodation where the meal fails to localize in the fundus on time point–0 images and possibly on 30-minute images due to inappropriate relaxation with the ingestion of a meal (Fig 9). Given the relation between fundal dysfunction and issues of fundal accommodation, it is worth noting that a direct means of scintigraphically assessing fundal accommodation has been validated (65).



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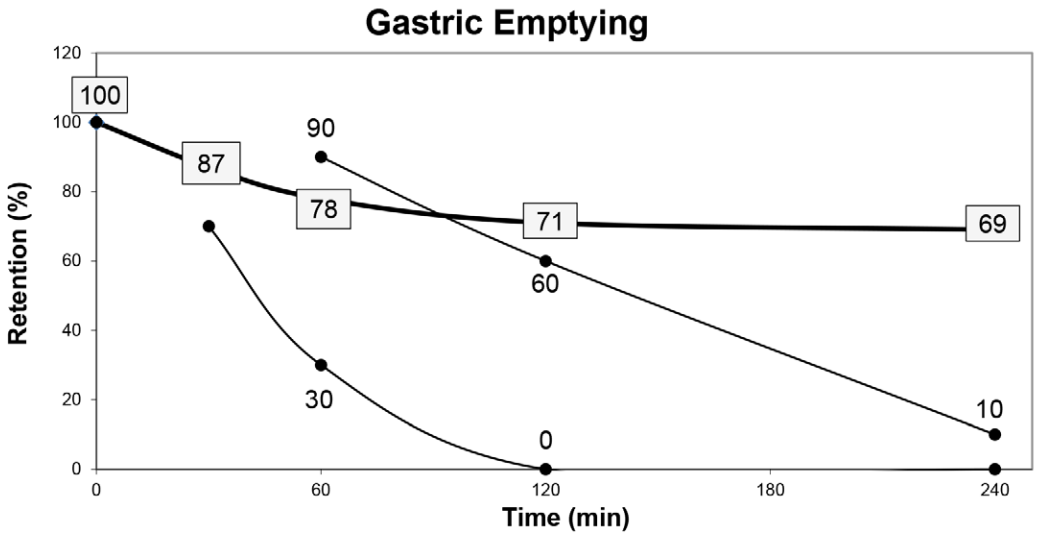

B

Time to be Imaged	Time Imaged	Time Elapsed	Anterior Counts	Posterior Counts	% Retained (Patient)	Normal Low	Normal High
0 min	0855 AM	0	41550	39035	100	100	100
30 min	0927 AM	30	43209	25069	87	70	
60 min	0955 AM	60	41318	18853	78	30	90
120 min	1055 AM	120	22859	22608	71	0	60
240 min	1255 PM	240	24728	12292	69	0	10

C

Figure 6. DGE due to fundal dysfunction. **(A)** Paired anterior *(ANT)* and posterior *(POST)* scintigraphic images of the stomach at 0 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours. The meal appropriately localizes in the fundus (arrows) initially due to fundal accommodation but then fails to transition distally because the fundus does not appropriately contract. *CTS* = counts. **(B, C)** TAC **(B)** and table **(C)** show abnormally increased gastric retention at both 2 and 4 hours.

Delayed liquid gastric emptying is present if the half-emptying time is greater than 25 minutes. Some experts suggest this examination may help identify a subset of fundal dysfunction not always seen at solid GES, given that the liquid meal does not undergo trituration in the antrum and thus is only dependent on the fundal proximal-to-distal pressure gradient (Fig 10).

Small Bowel Transit

In healthy individuals, 40%–50% or more activity will reach the TIR and beyond by the 6-hour image, depending on the reference (34,40). Alternatively, the small bowel transit is normal if 10% or more can be seen in the colon (Fig 11). In the setting of delayed small bowel transit, the 6-hour image will

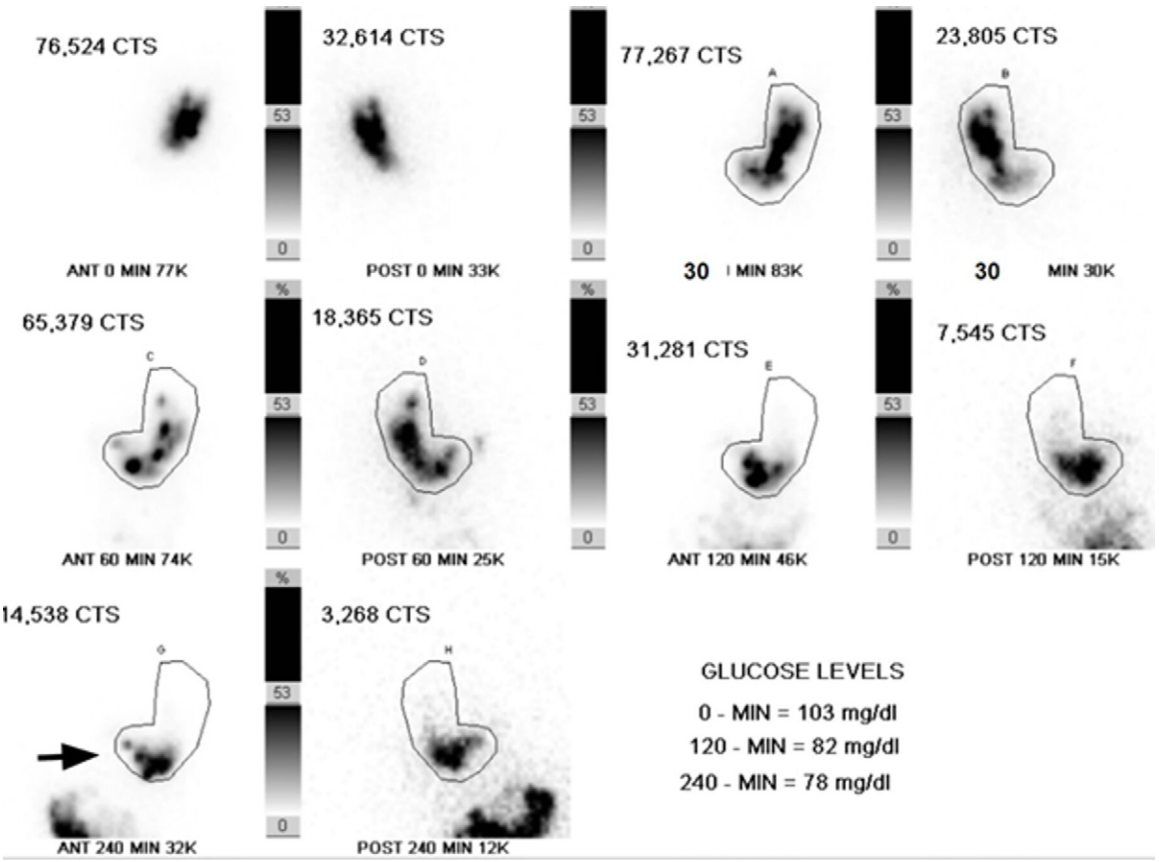

Figure 7. DGE due to antral dysfunction. **(A)** Paired anterior *(ANT)* and posterior *(POST)* images of the stomach at time zero, 30 minutes, 1 hour, 2 hours, and 4 hours. The meal appropriately localizes in the fundus and then transitions distally. Once it reaches the antrum (arrow), it is delayed with too little reaching the small bowel. **(B)** TAC shows abnormally increased gastric retention of 22% at 4 hours. *CTS* = counts.

usually demonstrate activity throughout the small bowel in the central abdomen without significant radiotracer in the terminal ileum or colon. Quantitatively, this will be less than 50% of the total activity in the TIR and cecum (Fig 12). Occasionally, rapid small bowel transit is present. This is quantified as greater than or equal to 10% of activity in the cecum or beyond at the 1-hour time point (40).

It must be noted that an accurate assessment of small bowel transit is dependent on adequate gastric emptying. Fortunately, even moderate delays do not significantly impact the small bowel assessment and, as long as the retention of the labeled liquid is less than 50% at 2 hours, a diagnostic evaluation can be performed (40).

Colonic Transit

Geometric center normal values are 2.0–7.0 at 24 hours, 4.6–7.0 at 48 hours, and 6.2–7.0 at 72 hours (37). Using the colon percentage emptying, normal values are 4% or greater (24 hours), 41% or greater (48 hours), and 67% or greater (72 hours) (Fig 13) (34). Certain patterns of abnormal colonic retention can be used to further characterize the subtype of delayed transit, including:

1. Colonic inertia: 4.1 or less at both 48 and 72 hours with failure of the radiotracer to significantly progress beyond the splenic flexure (Fig 14);

2. Generalized colonic delay: 4.1 or less at 48 hours; and 4.1 or more but 6.2 or less at 72 hours with a diffuse pattern of retained activity;

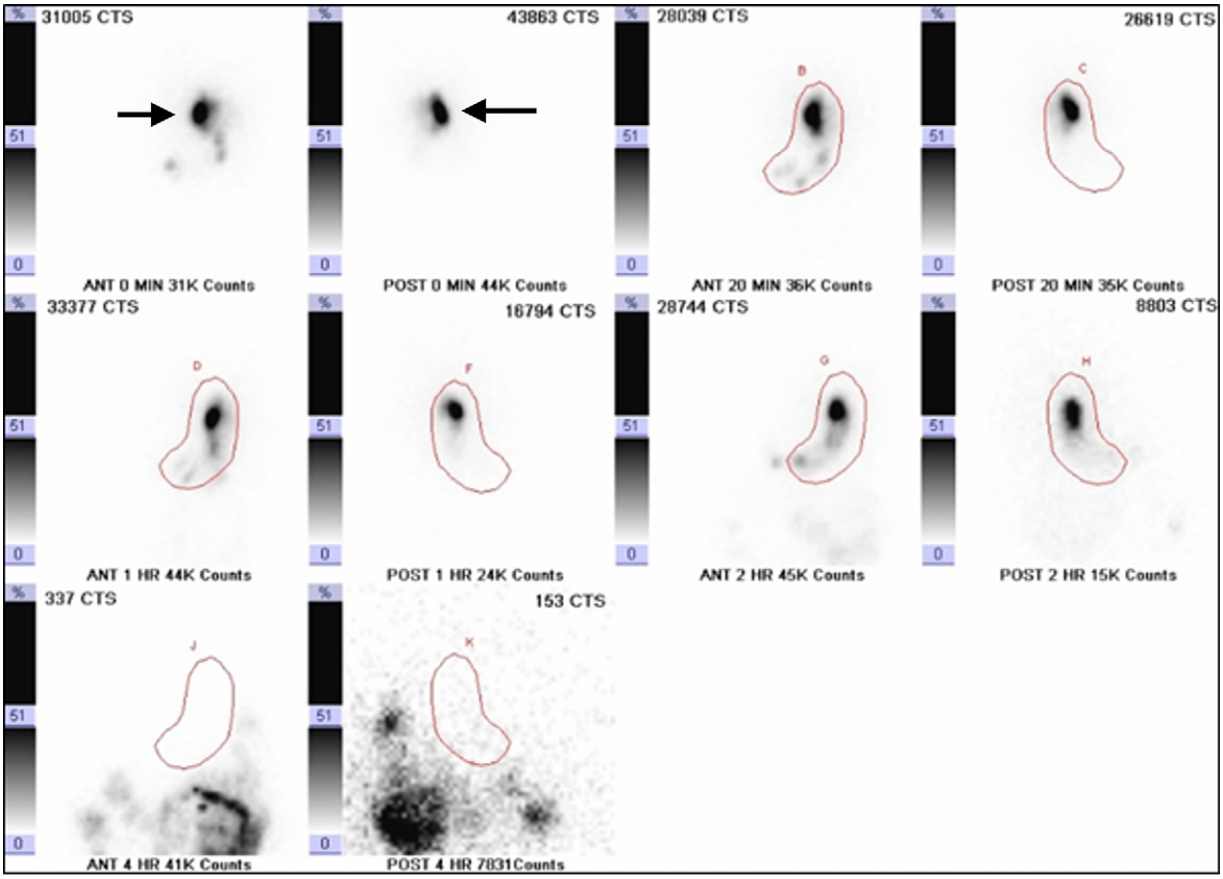

Figure 8. Normal gastric emptying but with an appearance highly suggestive of fundal dysfunction. **(A)** Paired anterior *(ANT)* and posterior *(POST)* images of the stomach at time zero, 30 minutes, 1 hour, 2 hours, and 4 hours. The meal appropriately localizes in the fundus (arrows) initially due to fundal accommodation but then fails to transition distally because the fundus does not appropriately contract. **(B)** Despite the appearance on images, the TAC shows normal gastric retention at both 2 and 4 hours. *CTS* = counts.

3. Functional outlet obstruction: 4.1 or more at 48 hours; and 6.2 or less at 72 hours with the activity being retained in the rectum and sigmoid colon (Fig 15); and

4. Chronic diarrhea: 6.1 or more at 24 hours (35).

Esophageal Transit Scintigraphy: Brief Note

While performed infrequently, esophageal transit scintigraphy can be helpful in patients with scleroderma, achalasia, and esophageal strictures, particularly in individuals who do not tolerate endoscopy or manometry or when results of such examinations are inconclusive (66). Like other GIT scintigraphic examinations, it provides helpful physiologic and quantitative information. Esophageal transit scintigraphy is performed with 15–30 mL of water labeled with ^{99m}Tc-SC or ^{99m}Tc-DTPA. Two metrics can be obtained: transit time and transit percentage. The transit time is the number of seconds it takes from the initial swallow for 90% of the activity to clear the esophagus, with less than 15 seconds considered normal. Percentage transit is the number of counts at peak minus the number of counts 10 seconds after the peak divided by the peak counts, with 83% the lower limit of normal. For more information regarding esophageal transit scintigraphy, the reader is directed to the article by Maurer (49).

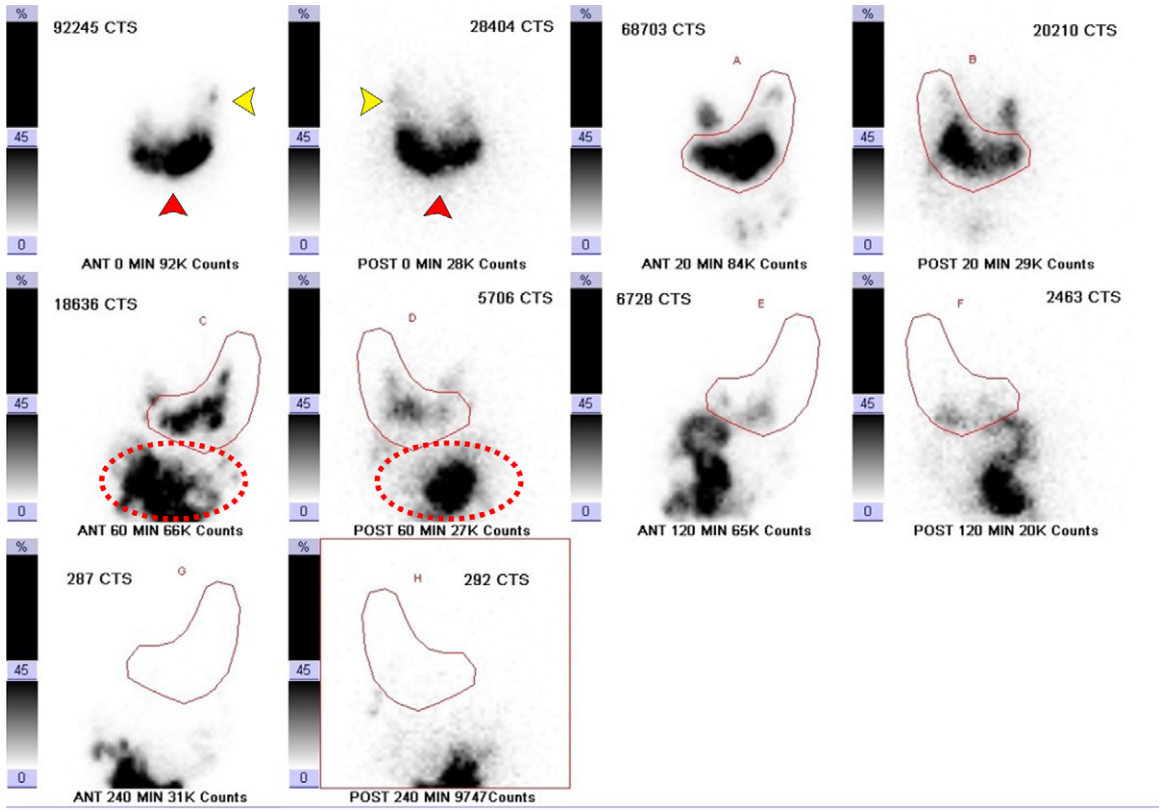

Figure 9. Rapid gastric emptying due to impaired fundal accommodation. **(A)** Paired anterior *(ANT)* and posterior *(POST)* images of the stomach at time 0 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours. The meal bypasses the fundus (yellow arrowheads) and is near completely present in the body and antrum (red arrowheads) at 0 minutes. It then rapidly begins to empty with a large amount of the meal present in the small bowel by 1 hour (dashed ovals). **(B)** TAC shows normal retention at 30 minutes (77%) but below normal at 1 hour (23%). *CTS* = counts.

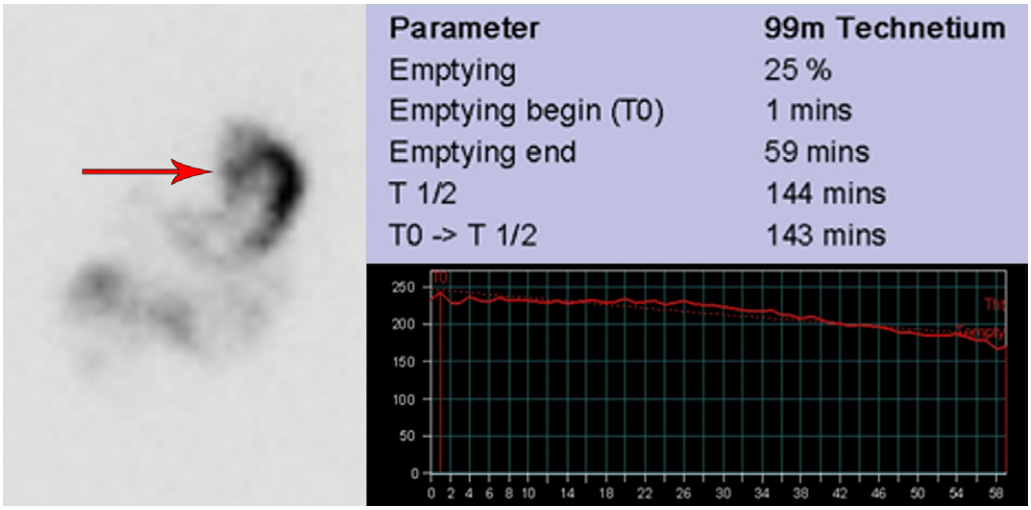

Figure 10. DGE due to fundal dysfunction. Liquid gastric emptying using 0.5 mCi of ^{99m}Tc-SC. The majority of the labeled water remained abnormally pooled in the fundus (arrow) due to its failure to contract and provide a proximal to distal pressure gradient. Extrapolated half-emptying time *(T1/2)* was markedly elevated at 59 minutes (normal, <25 minutes). *T* = time.

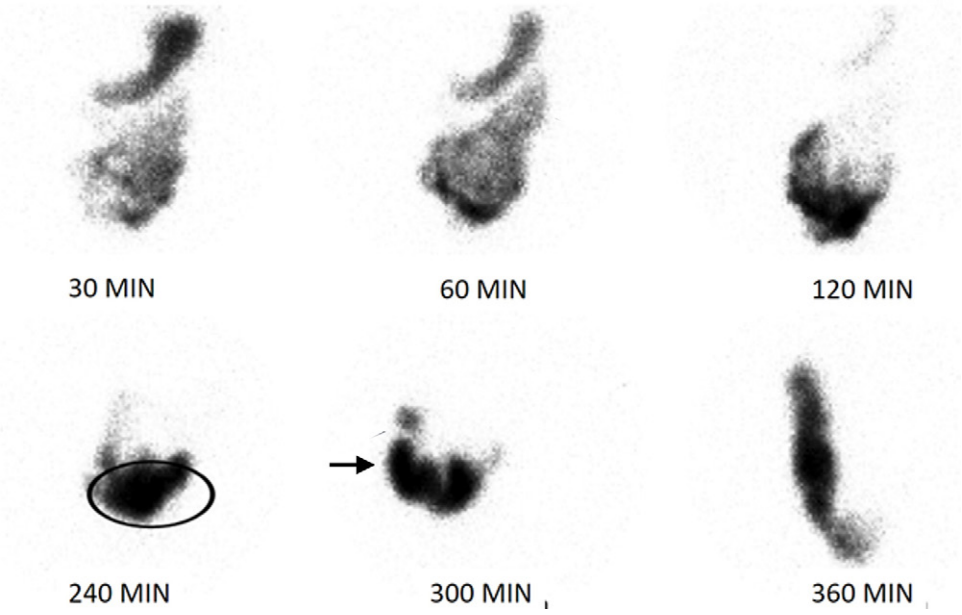

Figure 11. Anterior views of normal small bowel transit after a liquid ^{111}In-DTPA meal. Early in the examination there is diffuse small bowel activity that subsequently accumulates in the TIR (oval). More than 60% of total activity is already in the TIR by 4 hours, followed by further progression into the cecum and ascending colon (arrow) at 5 hours. (Reprinted, with permission, from reference 35.)

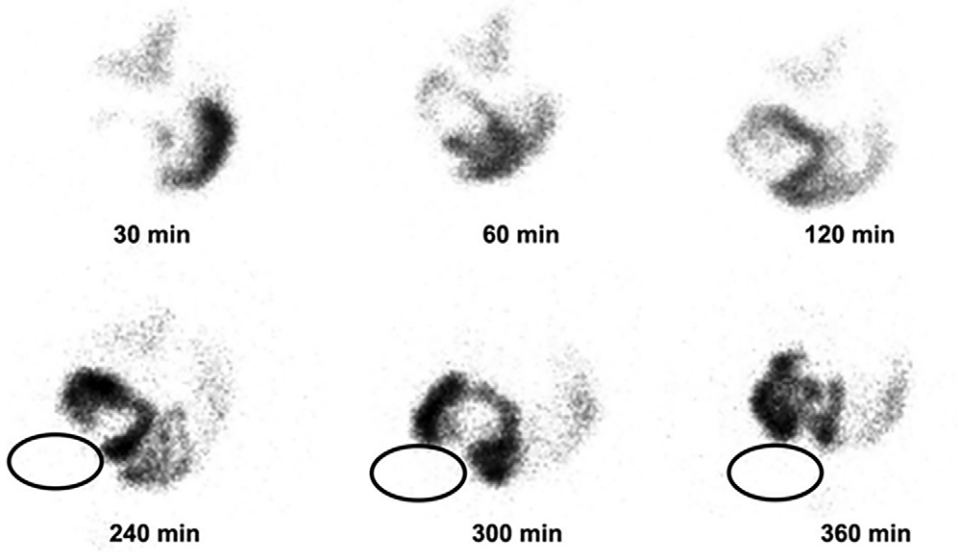

Figure 12. Anterior views of delayed small bowel transit after a liquid ^{111}In-DTPA meal. Small bowel transit is delayed, with persistent diffuse activity within multiple proximal loops of small bowel and no activity in the TIR (ovals) by 6 hours and absence of activity in the cecum or ascending colon. (Adapted and reprinted, with permission, from reference 35.)

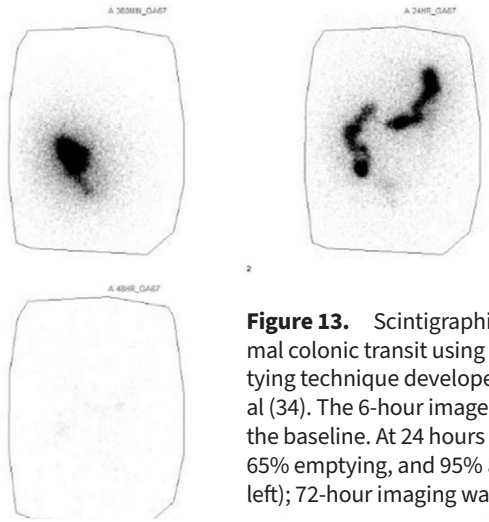

Figure 13. Scintigraphic images show normal colonic transit using the percent emptying technique developed by Antoniou et al (34). The 6-hour image (top left) is used as the baseline. At 24 hours (top right), there is 65% emptying, and 95% at 48 hours (bottom left); 72-hour imaging was not necessary.

Pitfalls and Sources of Error

Several potential factors can impact the accuracy of GIT scintigraphy and must be assessed for when interpreting each examination. Most commonly, these are related to failing to follow the standardized technique (using a nonstandard meal, failing to acquire anterior and posterior images, not applying decay correction, or not calculating the geometric mean). Patient-related factors include vomiting or gastroesophageal reflux, failing to eat a majority of the meal, or having recently eaten and/or taken interfering medications (Fig 16). Additionally, with solid GES, activity in the small bowel may occasionally overlap the gastric ROI, artifactually increasing the calculated percent retention (Fig 17). Finally, these studies and normal values were derived from individuals with no gastrointestinal surgical history. It is not infrequent for individuals who have previously undergone

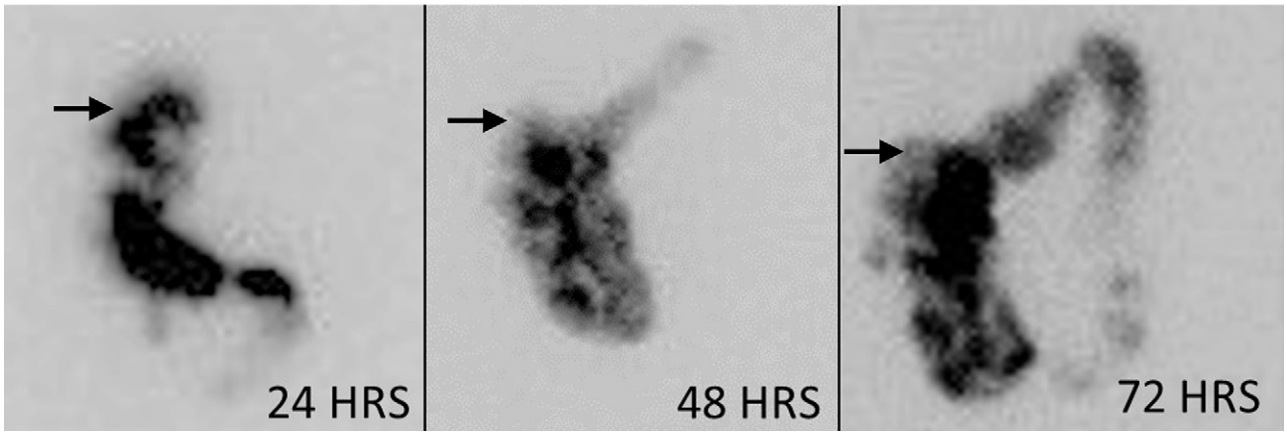

Figure 14. Colonic scintigraphic images show typical findings of colonic inertia. There is predominant right-sided colonic retention with most activity remaining proximal to splenic flexure (arrows). The geometric center is less than 4 at both 48 and 72 hours.

Figure 15. Colonic scintigraphic images show findings of functional outlet obstruction. The geometric center is 4.1 or more at 48 hours but 6.2 or less at 72 hours, with the activity retained predominantly in the rectum and sigmoid colon.

a weight-loss–related surgery to be referred for GIT transit scintigraphy, and the validity of applying these normal values has not been well established.

Importance of Standardization

Despite the availability of practice parameters, societal guidelines, and consensus documents all providing clear and similar guidance regarding how these scintigraphic examinations should be properly performed, there is a surprising lack of standardization in clinical practice. Several studies have examined compliance around the most common examination, solid GES, and have showed similar poor adherence to all aspects of the recommended techniques (67,68). As mentioned previously, this failure to use the validated techniques is an avoidable source of error and precludes comparison across facilities, as well as reduces the validity of these studies by referring clinicians.

Conclusion

Accurate clinical assessment of patients presenting with symptoms of a GIT motility disorder is extremely difficult, despite it being a commonly encountered disease. Fortunately, GIT scintigraphy provides a noninvasive means for evaluating transit of solids and liquids in a physiologic method that provides both qualitative and quantitative results. While various nuclear medicine procedures have long been available for diagnostic use, it is only in recent years that standardized approaches have been codified and endorsed by the major stakeholders. These include assessment of solid and liquid gastric emptying, small bowel transit, and colonic motility, with examinations able to be performed separately or in combination, depending on the clinical need. Widespread adoption of these standardized protocols, with strict adherence to the use of standardized meals, time points, and interpretation criteria, will further strengthen the utility of GIT scintigraphy for patients and providers alike.

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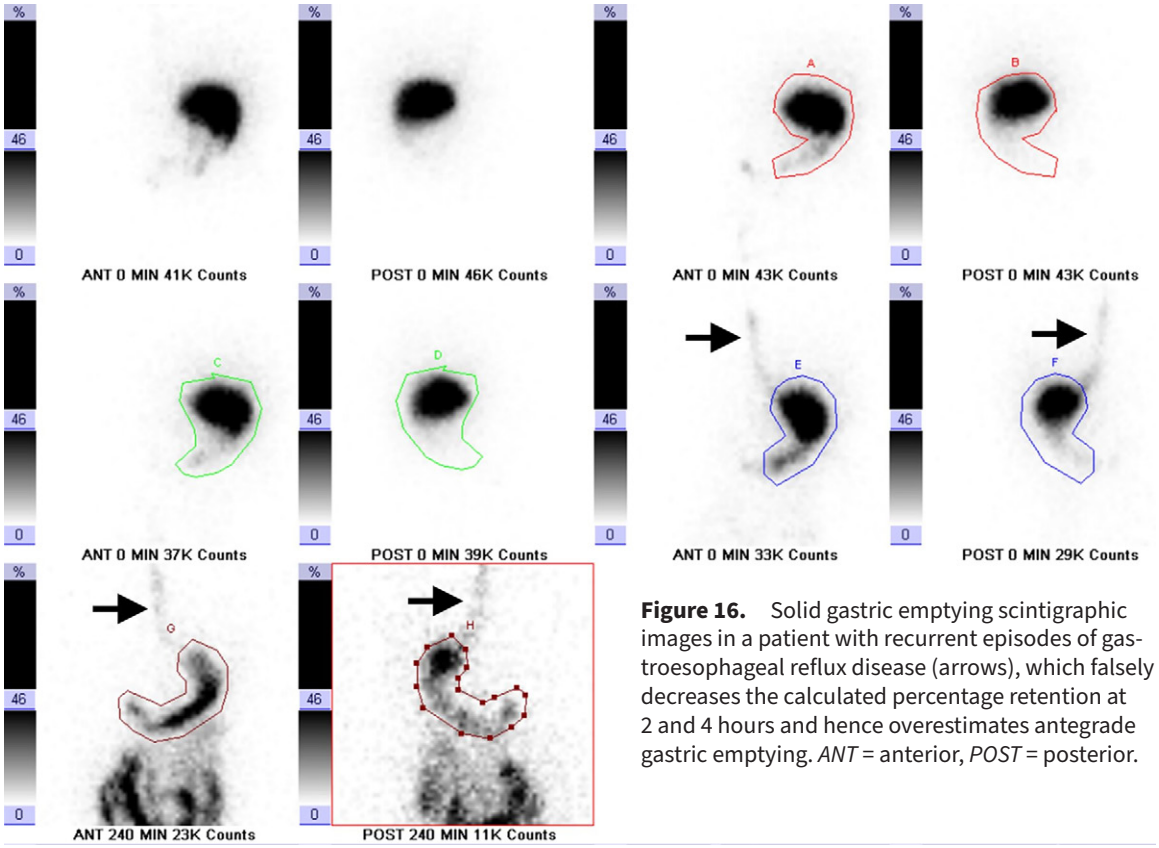

Figure 16. Solid gastric emptying scintigraphic images in a patient with recurrent episodes of gastroesophageal reflux disease (arrows), which falsely decreases the calculated percentage retention at 2 and 4 hours and hence overestimates antegrade gastric emptying. *ANT* = anterior, *POST* = posterior.

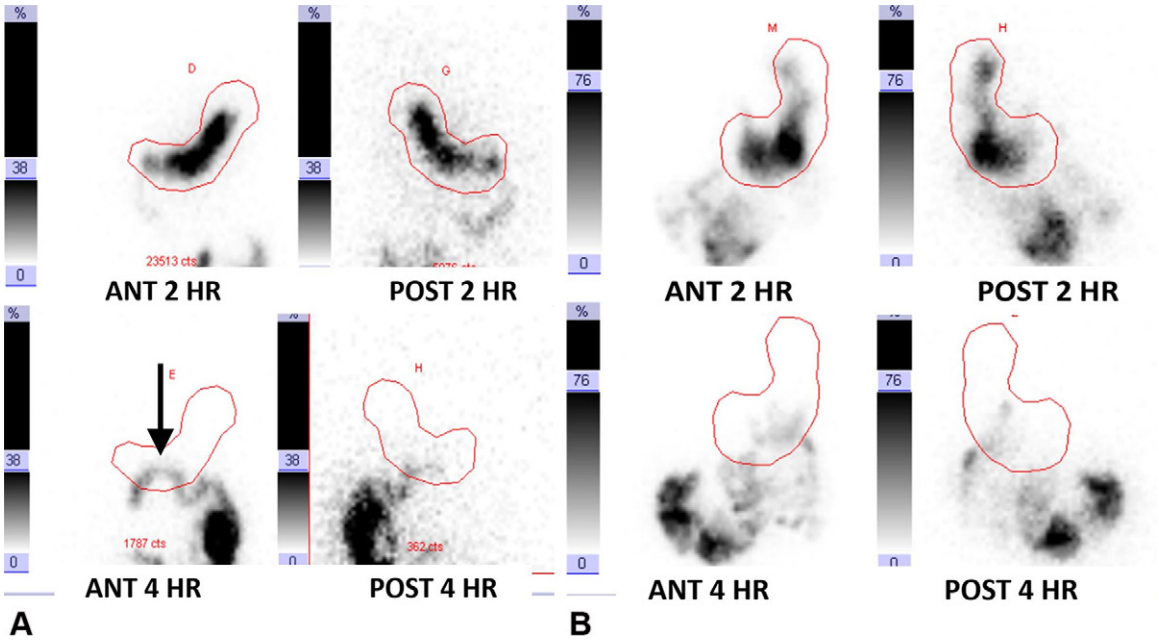

Figure 17. Solid gastric emptying scintigraphic images with portions of the radiolabeled meal (arrow) in the large **(A)** and small **(B)** bowel overlapping the gastric ROI, artifactually increasing the calculated percentage retention at 4 hours. The serpiginous nature of the activity is a clue to this potential source of error. If the measured retention at 4 hours is greater than 10%, then the interpreter must make a qualitative assessment of gastric emptying. *ANT* = anterior, *POST* = posterior.

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