Continuing Education: Gastrointestinal Motility
Part 1 – Esophageal Transit and Gastric Emptying

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INTRODUCTION

**Overview**

Motility studies when performed by gastroenterologists typically require placement of a tube or catheter-based probe within the gastrointestinal tract to measure pressures, electrical signals, or pH. More recently wireless capsules have been introduced which are less invasive (1). The advantages of scintigraphy for studying gastrointestinal motility have remained the same since the first description of a radiolabeled meal to measure gastric emptying (GE) (2). In contrast to probe methods, scintigraphy is noninvasive, does not disturb normal physiology, and provides accurate quantification of the bulk transit of radiolabeled solid or liquid meal throughout the entire gastrointestinal tract. Compared with x-ray methods scintigraphy involves low radiation exposure, is quantifiable and uses commonly ingested foods rather than barium or radiopaque markers. This CME review will address gastrointestinal scintigraphy as it applies to motility studies of the esophagus and stomach (Part 1), small bowel and colon (Part 2).

**Clinical Indications**

Gastroenterologists are faced with patient symptoms of pain, nausea, vomiting, bloating, diarrhea, constipation, or difficulty passing feces. There is often symptom overlap and questions about whether the symptoms have a structural or tissue abnormality or are functional (3). Symptoms may be associated with meal ingestion or may be meal-unrelated. A detailed Rome Classification System has been developed in an attempt to better classify functional gastrointestinal disorders where symptoms cannot be explained by an organic cause (4). Table III summarizes the wide range of symptoms that gastroenterologists face and which lead them to order a gastrointestinal motility study in an attempt to explain patient symptoms.

**General Methodology**

A planar gamma camera is typically used for imaging gastrointestinal tract motility studies. Utilizing the entire large field of view of modern cameras to include the mouth to the stomach for esophageal transit studies or the entire abdomen for gastroenterocolonic studies is preferred. To perform dual-isotope, mixed solid and liquid studies a medium energy collimator is used to image the energies of $^{111}$In (172 and 247 keV) and $^{99m}$Tc (140 keV). A low energy collimator is adequate for single isotope $^{99m}$Tc studies.

The two most commonly used radioisotopes for gastrointestinal transit studies are $^{99m}$Tc and $^{111}$In. The final form in which the radioisotope is administered depends on the study to be performed. For upper gastrointestinal transit studies, $^{99m}$Tc is usually administered as oral $^{99m}$Tc sulfur colloid ($^{99m}$Tc-SC). $^{99m}$Tc-SC has a short half life of 6 hours and when properly cooked is physically bound to certain foods. It is nonabsorbable within the gastrointestinal tract resulting in low radiation exposure (5). With a longer half life of 67 hours, $^{111}$In diethylenetriaminepentaacetic acid (DTPA) can be used to image gastrointestinal transit that requires 2-3 days such as colonic transit. $^{111}$In-DTPA is usually given orally suspended in liquid and is also nonabsorbable. $^{67}$Ga complexes have also been used for gastrointestinal transit studies which extend over several days (6).
ESOPHAGEAL TRANSIT

The decision on which diagnostic study is used to evaluate a patient for esophageal dysmotility depends on the patient's symptoms. If dysphagia is present, a barium swallow or endoscopy is usually performed first to exclude an anatomic lesion. If these anatomic studies are not diagnostic, manometry will likely be performed to look for esophageal dysmotility. Manometry is considered the gold standard for the diagnosis of the primary esophageal motility disorders which include: achalasia, scleroderma, diffuse esophageal spasm, hypertensive lower esophageal sphincter, and non specific esophageal motility disorders. Manometry however has limitations as it provides only an indirect measure of peristalsis as the pressure waves recorded do not always correlate with the aboral forces applied to a solid or liquid bolus in the esophagus. In addition, the presence of a manometric tube itself may affect normal physiology and quantification of the volume of retained solids or liquids in the esophagus is not possible.

Early studies of esophageal transit scintigraphy demonstrated a high sensitivity of esophageal transit scintigraphy for detecting a wide range of esophageal disorders (11, 12) but had a lower sensitivity especially for disorders with intact peristalsis but high-amplitude contractions or isolated elevated lower esophageal sphincter pressures (13).

Currently use of esophageal transit scintigraphy is limited in spite of its validation, likely in some part, because no single method for performing esophageal transit scintigraphy has been standardized. In comparison to gastric emptying and bowel transit studies no consensus guideline has been established for esophageal transit scintigraphy. In addition, esophageal manometry as performed by gastroenterologists has matured from a research tool to become more clinically available and standardized which further limits use of esophageal transit scintigraphy (14).

The simplest measure of esophageal transit is the esophageal transit time required for a liquid bolus of 15-30 cc of water containing 3.7-11 Mbq (0.1-0.3 mCi) of either 99mTc-DTPA or 99mTc-SC to transit the esophagus following a single swallow. Dynamic images following a swallow are typically recorded at a rapid frame rate of 0.25 – 0.5 seconds per frame for up to 30 seconds to record both regional and total esophageal transit. Either single anterior or posterior views of the chest have been used for esophageal transit scintigraphy.

Quantitative regional and total esophageal transit is usually analyzed by dividing the esophagus into total esophageal, upper, middle, and lower thirds. Time-activity curves are generated for the bolus transit through these regions. Esophageal transit time is reproducible with a normal range of 6 to 15 seconds (13, 15). The resulting regional thirds transit curves appear similar to manometric tracings (FIGURE 1). A composite image which summarizes all the regional transit data into one image may also be utilized (16). The static condensed image has the advantage of summarizing the data in a single image. A careful visual review of the bolus transit in
the esophagus using dynamic(cine) display of the images is however important especially to observe tertiary contractions or subtle gastroesophageal reflux.

In addition to analyzing bolus transit for a single swallow, the percentage of total counts remaining in the esophagus recorded after a single or multiple dry swallows is used to quantify total esophageal emptying. Some measure the percent esophageal activity decrease from peak at 10 seconds (normal > 83%) (17). Others have the patient perform serial dry swallows every 30 seconds for 10 minutes with images acquired for 30 seconds each(11). An esophageal region of interest comprising the entire esophagus is manually defined for this analysis. (FIGURE 2)

The counts in the esophagus(Et) are plotted as a percentage of maximal counts in the total esophageal region of interest(Emax):

\[ \text{% esophageal counts} = \frac{E_{\text{max}} - E_t}{E_{\text{max}}} \]

Normally there is > 82% emptied from the esophagus after 10 minutes of serial dry swallows (Table 2). Using the 10 minute multiple swallow method, the primary esophageal motility disorders demonstrate characteristic esophageal emptying patterns(FIGURE 3). As with review of the single swallow, the multiple swallow dynamic image series should be reviewed both quantitatively and qualitatively using cinematic computer display to detect any episodes of gastroesophageal reflux.

Barium swallow studies have shown that as many as five swallows may be needed to achieve maximal sensitivity for detecting an abnormal swallow. Use of up to six swallows has also been proposed to optimize esophageal transit scintigraphy (18). Esophageal transit scintigraphy using both supine and erect swallows together with single swallow and total esophageal emptying has been compared with manometry and videoesophagography and was found to have similar sensitivity for detecting the primary as well as nonspecific esophageal motility disorders(11). Based on these results, specific criteria for diagnosing the primary esophageal motility disorders have been proposed (Table 2).

A nonspecific esophageal motility disorder is characterized by one or more minor manometric abnormalities. There have been conflicting results on the sensitivity of esophageal transit scintigraphy for non specific esophageal motility disorders with some studies showing low sensitivity (42%-56%) (19). Use of a more viscous or semisolid bolus(jello) have been suggested to increase sensitivity.

While the clinical role of esophageal transit scintigraphy has been limited, it is particularly useful when esophageal manometry is not available or not tolerated by the patient and when esophageal manometry results are equivocal or non diagnostic. The ability of esophageal transit scintigraphy to quantitate total esophageal emptying is useful for assessing response to therapy in achalasia. Esophageal transit scintigraphy and barium videofluoroscopy should be considered complementary for achalasia as optimal sensitivity for detecting esophageal dysmotility is achieved when both are used (20).

**GASTRIC EMPTYING**

Gastric emptying(GE) studies are usually ordered to confirm or exclude whether gastroparesis(delayed GE) is a cause of a patient’s symptoms. Gastroparesis is usually associated with upper gastrointestinal symptoms which include: nausea(92% of patients), vomiting(84%),
abdominal fullness, distention (75%), or early satiety (60%) (21). Etiologies for gastroparesis include diabetes, infections, neuromuscular, autoimmune and connective tissue diseases, cancer, post-surgical, and idiopathic. Diabetic gastroparesis is usually associated with retinopathy, neuropathy, and nephropathy (22).

Patients often do not have well defined gastrointestinal symptoms and present with complaints of dyspepsia (symptoms thought to originate in the upper gastrointestinal tract). Dyspepsia can be defined as any pain or discomfort in the upper abdomen. In 50% of patients with dyspepsia no cause is found and the dyspepsia is classified as either idiopathic, essential, functional or nonulcer dyspepsia (23). The Rome III classification of dyspepsia associated with gastroduodenal symptoms (Table 1) can further be classified as: postprandial fullness, early satiation, epigastric pain, and epigastric burning (24). The goal of diagnosing delayed GE is to identify patients who will benefit from either a prokinetic drug or other treatment to alleviate symptoms. A GE study is indicated for patients with suspected gastroparesis and/or dyspepsia only after an anatomic cause for symptoms has been excluded. A GE study may also be indicated, in the absence of gastric symptoms for patients with: severe gastroesophageal reflux disease not responding to acid suppressants to see if delayed GE contributes to reflux, as a part of a work up to identify a diffuse gastrointestinal motility disorder, or for evaluating a diabetic with poor glycemic control.

GE scintigraphy performed with a radiolabeled meal has remained the gold standard for measuring GE based on the fact that once the meal is radiolabeled, the counts measured by the gamma camera are directly proportional to the volume of the meal in the stomach independent of any geometric assumptions. As currently performed in most centers, analysis of GE scintigraphy is limited to measurement of either a delay or acceleration in the emptying of a solid radiolabeled meal. Numerous studies however have shown a weak correlation between patients’ symptoms and the results of measuring only total GE. Several studies including one large meta-analysis of 17 studies of 868 patients found only up to a 40% incidence of delayed GE in symptomatic patients (25, 26).

Because of the weak correlation of measurement of GE to symptoms, more recent studies have sought to determine a relationship between symptoms and factors other than just total GE that can be evaluated during GE scintigraphy. (FIGURE 4) Postprandial pain, belching, and weight loss have been associated with visceral hypersensitivity to gastric distension (27). Impaired fundal accommodation has been associated with early satiety (28) and fullness has been associated with late fundal retention (29). The rate of gastric emptying is affected by feedback mechanisms which coordinate antral contractions with pyloric relaxation. Nutrient receptors (glucose and osmolar) in the duodenum further control the rate of nutrient flow into the proximal small bowel (30).

It is important therefore to understanding the multiple factors that affect GE when interpreting GE studies, particularly the separate roles of the fundus and antrum. Visual inspection of the early distribution of the solid meal in the stomach has become increasingly recognized as important. While liquids show rapid distribution throughout the stomach, solids normally will initially localize predominantly in the fundus until slow sustained fundal contractions move the solids to the antrum. This early preferential localization of solids in the fundus (accommodation response) is visually apparent in the initial images of a solid meal GE study (FIGURE 5). A persistent transverse band separating the fundus and antrum may be observed.
As solids move from the posteriorly located fundus down into the more anteriorly located antrum this will cause an increase in measured counts as the solids move closer to the gamma camera when positioned in front of the patient. Depth related attenuation correction is performed using the geometric mean (anterior counts x posterior counts) \(^{1/2}\). This correction results in only a 3 - 4% error in counts for the depths typically encountered (31). Geometric mean data collection using anterior and posterior views does not require a dual-headed camera system. As gastric counts will not change significantly in one minute, a single-head camera can be used by simply having the patient turn first front and then back to the camera for each 1 minute gastric image. If the patient is unable to stand for anterior and posterior views, a single left anterior oblique view can be used for attenuation correction (32).

After the solids have moved into the antrum peristaltic contractions work by a process called trituration to mix and break down the large solids into small particles in the presence of gastric digestive fluids. The solids must be reduced into particles of 1-2 mm before they will pass through the pylorus. The contractile activity of the antrum is controlled by a pacemaker located high on the greater curvature at the boundary between the fundus and the antrum. The time required to complete trituration so that solid particles are small enough to empty from the stomach has been referred to as the lag phase. Once triturated, the small solid particles are suspended in the liquid within the stomach they then empty monoexponentially at the same rate as the liquids (33).

Emptying of liquids is controlled by a sustained pressure gradient generated by the fundus. Liquids require no trituration and empty monoexponentially (FIGURE 5) and more rapidly than solids with no lag phase. A previously held belief was that liquid GE added little to the evaluation of patients with dyspepsia (34, 35). It was felt that since the liquids require no trituration, liquid GE was normal until only an advanced stage of gastroparesis and that liquids were therefore less sensitive than solids for detecting early gastroparesis (36). One early study found delayed liquid but normal solid emptying in 24% of diabetic patients (37).

Recently there has been increased interest in the role of liquid GE studies to supplement solid-meal GE. An association of delayed GE of solids and liquids with symptoms of postprandial fullness, nausea, and vomiting has been reported. Multivariate analysis has shown that postprandial fullness and early satiety are associated with delayed liquid GE (38). Liquid GE studies have also been used clinically because rapid emptying of nutrient-containing liquids may be associated with early satiety, nausea, and/or vomiting in the “dumping syndrome” (35).

Using combined, dual-isotope solid and liquid-phase meals (\(^{99m}\)Tc- labeled egg and In-111-DTPA in water) liquids may demonstrate abnormal liquid GE when solid GE is normal. One study of 476 patients found only a 5% incidence of delayed liquid GE when solid GE was normal (39). Another study however found 26% of patients (57 nondiabetic) had normal solid GE but delayed liquid GE (40). Abnormal GE of solids was mildly correlated with nausea, vomiting, loss of appetite, early satiety, and feeling excessively full after meals. Liquid GE was more associated with early satiety and loss of appetite.

Ziessman et al reported on a combined retrospective and prospective study of patients who were studied with a non-nutrient, water GE study performed independently from a solid meal (41). The liquid meal consisted of 500 mL of tap water mixed with \(^{99m}\)Tc –SC. The solid and liquid GE studies were performed on 2 separate days retrospectively and then sequentially (liquid meal for 30 minutes followed by solid meal for 4 hours in a prospective study. In the retrospective study, 17 of 21 patients had normal solid GE. Of these, 13 (76%) had delayed liquid GE. In the prospective
study, 10 (33%) patients with normal solid GE had delayed liquid GE. In a second larger study of 101 patients who underwent both solid and liquid meal GE on the same day with the same protocol, delayed GE was found in 36% of liquid and 16% of solid studies. Of patients with normal solid emptying, 32% had delayed liquid emptying. Based on these results, these authors suggest that a non-nutrient, liquid GE study may detect fundal gastric dysmotility and help to improve the detection rate of gastric dysmotility in patients with FD (42).

These recent studies further suggest a role for liquid GE studies but the physiologic effects of a non-nutrient, water meal have not been well studied in patients with FD. When a water load is given after a nutrient meal it has been shown to inhibit antral motility and increase cholecystokinin (CCK) release in healthy subjects. It is theorized that an increase of CCK is a response to inflow of fatty chyme into the duodenum with resultant feedback slowing entry of the meal into the duodenum. This duodenogastric interaction has been termed the “duodenal break” (43). Further studies of the physiology and clinical significance of use of a non-nutrient, water–liquid meal is needed.

As noted previously, until recently there were no accepted standards for performing GE scintigraphy. This raised concerns about the continued acceptance of GE scintigraphy without consistent methodology (8). As a result, in 2007 a consensus recommendation was published jointly by the Gastrointestinal Council of the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society (22). The consensus group recommended a solid-meal GE test “using readily available technology and normative data, which can provide clinicians with standardized results.” This consensus recommendation was also adopted by the Society of Nuclear Medicine and Molecular Imaging(SNMMI) (44) and in a joint American College of Radiology (ACR)/Society for Pediatric Radiology (SPR) and Society of Nuclear Medicine(SNM) practice guideline(ACR-SNM-SPR Practice Guideline for the Performance of GastrointestinalScintigraphy (http://www.acr.org/SecondaryMainMenuCategories/quality_safe/takes/guidelines/nuc_med/gi_scintigraphy.aspx )).

Normal values were established not only for the meal but also for the method used for image acquisition and processing. GE was also standardized for body position, smoking, phase of the menstrual cycle and the time of day the test is performed (45-47). Medications such as prokinetic agents, antisecretory drugs, gastric acid suppression, and narcotics affect GE. Patients are instructed to fast overnight and to stop any medications that might affect GE. Prokinetic drugs that can accelerate GE, such as metoclopramide (Reglan®, Baxter Pharmaceutical), tegaserod (Zelnorm®, Novartis), erythromycin, and domperidone (Motilium®, Janssen Pharmaceutica), are stopped at least 2 days before the test. Drugs that can delay GE such as opiates, including meperidine(Demorol®,Sanofi-Aventis), codeine, morphine, oxycodone (OxyContin®,Purdue Pharma) and anticholinergic antispasmodic agents, such as dicyclomine(Bentyl®, Aptalis Pharma US), beladonna and phenobarbital(Donnatal®, Rebel Distributors Corp), hyoscyamine (Levsin®, Alaven Pharmaceutical), and glycopyrrolate (Robinul®, Baxter Healthcare) are also stopped for 2 days before the test. Patients may take other medications with a small quantity of water the morning of the test. Smoking is prohibited starting the morning of the test and for the 4 hours of imaging.

The importance of glucose control in diabetic patients is emphasized. Diabetic patients should have their fasting glucose checked before starting the test. If glucose is ≥275 mg/dL, a small
A dose of short-acting insulin may be administered before meal ingestion and the patient is then monitored until the glucose is below 275 mg/dL. Diabetic patients should be instructed to bring their insulin with them, and if glucose is under 275 mg/dL, they are told to take approximately half of their standard daily dose of insulin with ingestion of the test meal because no eating will take place during the next 4 hours.

The consensus group recommended use of a low-fat meal based on normative data from a large multicenter study (48). The meal is composed of 4 ounces (120 grams) liquid egg white (Eggbeaters®; ConAgra Foods, or a generic liquid, egg-white equivalent) mixed with 18.5-37 mBq (0.5-1.0 mCi) ⁹⁹ᵐTc-sulfur colloid, 2 slices of white bread (120 kcal), strawberry jam (30 grams, 74 kcal), and water (120 mL). The total calories of the meal is 255 kcal (72% carbohydrate, 24% protein, 2% fat, and 2% fiber). ⁹⁹ᵐTc-sulfur colloid binds to the egg white during cooking. A recent study has shown that the liquid egg-white can be cooked either using a skillet or in a microwave, provided it is cooked to a firm consistency (49).

The patient is instructed to consume the meal within 10 minutes. Immediately after eating the meal, the patient is imaged preferably standing, or if necessary, in a supine position. Supine positioning can significantly slow gastric emptying of solids (50). GE scintigraphy images are recommended at 0, 60, 120, 180, and 240 minutes after meal ingestion. A 30 minute image may be helpful if rapid GE or impaired fundal accommodation is suspected. Computer regions of interest corresponding to the stomach are typically manually defined to analyze the total gastric counts. Decay and depth (attenuation) corrected total gastric counts are calculated for each time point. The percentage of activity remaining in the stomach normalized to 100% for maximal gastric counts is reported.

Using the consensus recommended solid meal, GE is delayed if gastric retention is > 60% at 2 hours and > 10% at 4 hours. As the symptoms of rapid GE can mimic those of delayed GE, the consensus also provides values for rapid GE as < 70% retained at 30 minutes or < 30% retained at 1 hour.

Other ancillary methods have been used to analyze GE data (see below). These include the time to 50% emptying of the meal (T ½). It is recommended that GE scintigraphy should be performed for up to 4 hours as studies have shown the percent gastric retention has greater sensitivity for detecting abnormal GE (51) and is most reproducible (52). If there is abnormal retention at 2 hours, the study may be terminated as GE is already delayed. One group of investigators has published criteria for early termination at 2 hours. While this could reduce the total time of imaging for some patients, there was a small loss of sensitivity (53).

Because of the individual roles of the fundus and antrum, some patients may be abnormal at 2 hours and normal at 4 hours. Others may be normal at 2 hours and abnormal at 4 hours. This is not unexpected because the early phase (0-2 h) of a solid GE study reflects more fundal function and the later phase (2-4 h) reflects antral triturating and propulsion of the meal into the duodenum. Therapies in the future may reflect targeting differently the fundus and antrum.

The consensus GE group also provided recommendations on ancillary issues of importance in reporting GE studies. All reports should include an estimate by the performing technologist of the total amount of the meal ingested. Since the normal values for GE are based on ingestion of the entire standard meal, if only a small portion of the meal is ingested, the study cannot be considered diagnostic. If the patient has not ingested the full meal the report should include a statement that
the results may overestimate the rate of emptying. The GE report should also describe if any incidental abnormal findings are observed, including esophageal retention or reflux of the meal, hiatal hernia, fundal wrap, or lack of fundal accommodation.

The consensus group recognized the complexity of GE and limitations of their current recommendations. They acknowledged that numerous items will require further clarification including: optimization of image times, need for normative data on other substitute meals, the role of glycemic control in diabetic patients, the value of monitoring symptoms during the study, a scale to assess the severity of delayed GE, the need for normal post-surgical gastric reference data, the clinical role of analyzing fundal and antral gastric function, and other potential methods of quantitation (curve fitting, lag phase, total abdominal counts).

Delayed GE may be suspected in infants who have vomiting, abdominal pain, or early satiety. The above consensus recommendations were developed only for adults. Unfortunately no adequate standards have been developed for measuring GE in children. In infants GES is usually performed with evaluation of gastroesophageal reflux. This may be performed with the child’s milk or formula to which $^{99m}$Tc-SC is added. Adequate normal values for GE for children for various meals have not been established. A range of gastric retention between 40-70% at one hour has been reported (54).

Ancillary tests of gastric function

As noted previously, delayed GE is found in a significant, but only limited (30-70%), number of symptomatic patients with diabetes or functional dyspepsia (55). It is increasingly recognized that a more detailed study of GE beyond just total stomach emptying is needed to fully evaluate gastric function. Analysis of GE in the future will likely include attention to separate fundal and antral motor function, fundic relaxation (accommodation response), visceral hypersensitivity, asynchronous antroduodenal coordination, and gastric dysrhythmias (56-58). Other measures of gastric function that have been studied as a part of GE scintigraphy but currently are not routinely performed are included below.

Lag Phase Analysis

Numerous studies have confirmed the presence of an early lag (trituration) phase for solids followed by a phase during which the stomach empties solids at a characteristic rate (59-61). To completely characterize these phases of GE, it is best to fit the data to a mathematic function known as a modified power exponential (33) given by the equation:

$$y(t) = 1 - [1 - \exp(-kt)]^B$$

where $y(t)$ is the percentage of gastric activity remaining at time $t$; $k$ is the slope of the exponential portion of the curve; and $B$ is the y intercept. The lag phase ($\ln (B/k)$) corresponds to the time of peak activity in the antrum which physically corresponds to maximal filling of the antrum just before the adequately triturated, small suspended solid particles begin to empty at the same uniform rate ($k$) as liquids. Imaging at only 0, 1, 2, and 4 hours does not permit adequate curve fitting analysis. Lag phase analysis requires earlier and more frequent time points. There are little
data however to support routine clinical analysis of the lag phase. In a recent study Bonta et al found that the lag phase was not predictive of delayed GE (53).

**Fundal Accomodation and Intragastric Distribution Studies**

Fundal relaxation (accommodation) is an established physiologic response which allows the stomach to increased intragastric volume without increasing intragastric pressure (62). Early satiety is the predominant symptom associated with a poor accommodation response. Studies show a correlation between dyspeptic symptoms and hypersensitivity to fundal distension and impaired fundal accommodation (63, 64).

The gastric barostat test measures the volume to which a gastric balloon can inflate at a given pressure and measures fundal compliance. Patients with visceral hypersensitivity experience symptoms at low levels of distention. While barostat testing is the best direct measurement of fundal accommodation it has been criticized as invasive (65). A less invasive water load test has also been used to study the correlation between impaired accommodation and dyspeptic symptoms. Both water loading and nutrient liquid meals can be used to assess accommodation and produce symptoms in approximately 50% of patients with FD (66).

SPECT gastric accommodation studies make use of the fact that the gastric mucosa accumulates 99mTc pertechnetate after intravenous administration. 3D SPECT volumetric imaging of the outer wall of the stomach can then be performed. SPECT has been validated as a non-invasive method to measure gastric volumes (67, 68). It is also possible to simultaneously assess the relationship of liquid or solid meal emptying and gastric accommodation. Such studies have shown maximal gastric volume change (mean = 185%) occurs immediately after meal ingestion and persists in spite of relatively rapid emptying of the meal (69). Direct comparison of gastric postprandial/fasting volume ratios between a balloon barostat and SPECT have shown SPECT to be an accurate measurement of the accommodation response in healthy and postfundoplication patients (70).

The added clinical utility of SPECT measurements of accommodation response was demonstrated in a review of a large number of patients with dyspepsia. Of 214 patients, gastric accommodation was impaired in 47% of patients with dyspepsia and 25% of patients with normal GE had impaired accomodation (71). A recent study comparing a water drink load test with SPECT gastric volumes found that fasting gastric volumes were significantly higher in patients with FD compared with controls. The patients with FD ingested significantly less water and had an impaired filling of the distal stomach after the water load test. However, symptoms of bloating, pain, and fullness were determined more by the proximal rather than distal stomach volume (72).

Abnormal intragastric distribution patterns have also been associated with symptoms of dyspepsia. In a study using SPECT, early proximal GE was lower and the $T_{1/2}$ of the proximal stomach was longer when SPECT gastric accommodation was impaired (73). In another study of accommodation response the stomach was simply divided into proximal and distal segments. Early satiety was associated with early distal redistribution of the meal and fullness was associated with later proximal retention (29).
Since abnormal fundal accommodation can be observed in routine planar GE images the recent consensus recommendation on gastric emptying recommends evaluating the images for the presence of an abnormal accommodation response (22). The normal fundal accommodation response is best observed in the first set of images after solid meal ingestion (t = 0 minute time point). Typically the majority of the solid meal will be localized in the upper half of the stomach. If normal fundal accommodation is lacking this may be an additional important finding to explain patient symptoms especially when GE is normal. (Figure 6)

There have been conflicting reports that impaired fundal accommodation results in more rapid GE. Impaired gastric accommodation from surgical fundoplication, gastric banding, and balloon placement promotes displacement of solids into the distal stomach and may result in rapid GE. In one study of patients with FD and low gastric accommodation, 13% of patients were found to have rapid GE and 28% had normal GE (71). In contrast, Camilleri et al found that proximal stomach emptying was reduced in patients with low postprandial accommodation but that overall GE in these patients was normal (73). They theorized that compensatory mechanisms accelerate overall GE despite delayed proximal GE.

**Bicompartmental (Fundal-Antral) Gastric Emptying**

Since scintigraphy easily permits analysis of the intragastric distribution of the test meal between the fundus and antrum it is ideal for measuring both regional and total GE. Studies have shown an association between symptoms of nausea, early satiety, abdominal distention and acid reflux with proximal gastric retention whereas vomiting is associated more with delayed distal GE. Inspection of fundal and antral gastric emptying in the images and quantification of regional emptying can be helpful for explaining dyspeptic symptoms especially when total GE values are normal (29, 74).

**Antral Contraction Scintigraphy**

Methods for measuring the frequency and amplitude of antral contractions have been developed. Normal antral contractions occur at a rate of three per minute. The ability to measure both the frequency and the strength of antral contractions has increased our understanding of normal and abnormal GE. In diabetic gastroparesis, GE is delayed not only due to retention of food in the fundus but also to decreased strength of antral contractions which occur at a higher frequency (75). A majority of patients with gastroparesis are women with up to an 82% predominance in one large study (76). Differences in normal male and female GE have been shown to be due to the amplitude of antral contractions and not the frequency. Using scintigraphy to measure the amplitude of antral contractions, women have been shown to have lower amplitude contractions not associated with the phase of the menstrual cycle (77).

**PET Neuroactivation**

While not associated with conventional GE imaging, a future role for PET brain imaging to assess the brain-gut axis and its relationship to gastric function may gain importance in understanding patients with dyspepsia. PET of the brain has demonstrated specific neuroactivation pathways linked to fundal distention and symptoms of dyspepsia (78).
Conclusion

While not as well standardized as GE scintigraphy, esophageal transit scintigraphy when performed in a comprehensive manner including both quantitative and qualitative analysis of single and multiple swallow studies is clinically useful when expertise in esophageal manometry is not available or not tolerated and when esophageal manometry or barium videofluoroscopy results are equivocal or non diagnostic. GE scintigraphy has undergone much needed standardization. Both solid and liquid gastric emptying studies play an important role in assessing patients with upper gastrointestinal symptoms. Because measurement of simple total gastric emptying is often not sufficient to explain patient symptoms there is a need to expand the analysis of GE scintigraphy to include the separate roles of the fundus and antrum as well as to include the complex interactions the stomach has with other organ systems.
REFERENCES


Figure 1. Normal esophageal transit (Single Swallow).
Sequential dynamic images (left, 0-25 sec) demonstrate normal bolus transit through the esophagus. A composite image (center) is produced by summing all the images from the initial 30 seconds. Regions of interest (dotted lines) that define the upper, middle, and lower thirds of the esophagus are shown. Time-activity curves (right) show the counts recorded in each region as the bolus progresses down the esophagus. The esophageal transit time (11 sec) is measured from the leading to trailing edges of the upper and lower esophageal third time activity curves. Reprinted from (79).
Figure 2. Normal global esophageal emptying (Multiple Swallows). Sequential images at 15 sec per image are shown(left). A region of interest(rectangular box) is drawn over the entire esophagus. From this region a time activity curve(right) is generated showing the percent of activity retained in the esophagus at each time. The amount of activity retained after multiple swallows can be used to help characterize the primary esophageal motor disorders(Figure 3,Table 1) or to follow therapeutic interventions as in achalasia. Reprinted from (79).
Figure 3. Esophageal emptying for the primary esophageal motility disorders. The mean data for normal subjects are shown compared to diffuse esophageal spasm (DES), achalasia, and scleroderma. The emptying curve for patients with esophagitis from gastroesophageal reflux is similar to DES. Reprinted from (79).
Figure 4. Multiple factors associated with gastric emptying are considered important to explain dyspeptic patient symptoms. Total gastric emptying, impaired fundal accommodation and visceral hypersensitivity are the three major factors currently under study. Antral-duodenal coordination and duodenal-gastric feedback mechanisms are also considered important but are not as well characterized. Modified from (80).
Figure 5. Normal dual-isotope, solid-liquid gastric emptying study. (Anterior views only).
These images demonstrate early rapid distribution of liquids throughout the stomach (T = 0 min).
The liquid emptying curve is monoexponential. In contrast solids show preferential early fundal localization (accommodation) (double arrows). Over time the solids progress down into the antrum (triple arrows). The solid emptying curve is sigmoidal in shape due to the early lag phase for solids. Over time one can observe small bowel transit of solids and liquids with a buildup of activity in the terminal ileal reservoir (oval region of interest). Reprinted from (79).
Figure 6. Impaired fundal accommodation. (Anterior views only)
In the first, post meal ingestion image (T = 0 minutes) there is lack of normal fundal accommodation with the majority of the meal seen in the distal stomach rather than the fundus (arrow). Overall gastric emptying was normal with 42% retained at 2 hours (120 min) and 8% at 4 hours (240 min).
Table 1 Rome III Functional Gastrointestinal Disorders

<table>
<thead>
<tr>
<th>Adult Categories</th>
<th>Pediatric Categories</th>
<th>Child/Adolescent Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>A – Esophageal Subsets:</td>
<td>G1 – Infant regurgitation</td>
<td>H1 – Vomiting and aerophagia Subsets:</td>
</tr>
<tr>
<td>A1 – Heartburn</td>
<td></td>
<td>H1a – Ruminant</td>
</tr>
<tr>
<td>A2 – Chest pain</td>
<td></td>
<td>H1b – Cyclic vomiting</td>
</tr>
<tr>
<td>A3 – Dysphagia</td>
<td></td>
<td>H1c – Aerophagia</td>
</tr>
<tr>
<td>A4 – Globus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B – Gastroduodenal</td>
<td>G2 – Infant reumination</td>
<td>H2 – Abdominal Pain Subsets:</td>
</tr>
<tr>
<td>Subsets:</td>
<td></td>
<td>H2a – Dyspepsia</td>
</tr>
<tr>
<td>B1 – Dyspepsia</td>
<td></td>
<td>H2b – Irritable bowel</td>
</tr>
<tr>
<td>B2 – Belching</td>
<td></td>
<td>H2c – Abdominal migraine</td>
</tr>
<tr>
<td>B3 – Nausea/Vomiting</td>
<td></td>
<td>H2d – Childhood abdominal pain</td>
</tr>
<tr>
<td>B4 – Rumination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C – Bowel Subsets:</td>
<td>G3 – Cyclic vomiting</td>
<td>H3 – Constipation and incontinence Subsets:</td>
</tr>
<tr>
<td>C1 – Irritable Bowel</td>
<td></td>
<td>H3a – Functional constipation</td>
</tr>
<tr>
<td>C2 – Bloating</td>
<td></td>
<td>H3b – Nonretentive fecal incontinence</td>
</tr>
<tr>
<td>C3 – Constipation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C4 – Diarrhea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5 – Unspecified</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D – Functional Abdominal Pain</td>
<td>G4 – Infant colic</td>
<td></td>
</tr>
<tr>
<td>E – Biliary</td>
<td>G5 – Functional diarrhea</td>
<td></td>
</tr>
<tr>
<td>F – Anorectal</td>
<td>G6 – Infant dyschezia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>G7 – Functional constipation</td>
</tr>
<tr>
<td>Condition</td>
<td>Visual Bolus Transit Analysis From Dynamic Display</td>
<td>Esophageal Transit Time (sec)</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal aboral bolus transit through upper, middle, and lower 1/3rd esophagus with normal relaxation of the LES</td>
<td>&lt; 14 sec</td>
</tr>
<tr>
<td>Non Specific Esophageal Motility Disorder</td>
<td>Any localized abnormal retrograde-antegrade bolus movement (mild transient retrograde movement in distal esophagus before relaxation of LES which clears rapidly is normal)</td>
<td>&gt; 14 sec</td>
</tr>
<tr>
<td>Isolated LES Dysfunction</td>
<td>Normal bolus transit upper, middle esophagus with delayed transit localized at gastroesophageal junction</td>
<td>&gt; 14 sec</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>Marked delay in bolus transit, typically localized to distal esophagus</td>
<td>&gt; 30 sec</td>
</tr>
<tr>
<td>Diffuse Esophageal Spasm</td>
<td>Repetitive retrograde/antegrade contractions throughout the esophagus</td>
<td>&gt; 14 sec</td>
</tr>
<tr>
<td>Achalasia</td>
<td>Marked delay in bolus transit throughout esophagus (may progress normally in upper esophagus from oropharyngeal propulsion)</td>
<td>&gt; 30 sec</td>
</tr>
</tbody>
</table>