Appropriate Use Criteria for Gastrointestinal Transit Scintigraphy

Alan H. Maurer[1], Thomas Abell[2], Paige Bennett[1], Jesus R. Diaz[1], Lucinda A. Harris[3], William Hasler[2], Andrei Iagaru[1], Kenneth L. Koch[2], Richard W. McCallum, Henry P. Parkman, Satish S.C. Rao, and Mark Tulchinsky[4]

[1]Society of Nuclear Medicine and Molecular Imaging, [2]American Gastroenterological Association, [3]American College of Physicians, [4]American College of Nuclear Medicine

EXECUTIVE SUMMARY

The appropriate use of scintigraphy for studying gastrointestinal (GI) motility requires not only an understanding of the normal physiology and pathophysiology of the various disorders that can affect the GI tract, but also an understanding of the numerous methods and associated technical details of the current clinically available modalities for studying GI motility. Developing recommendations on the appropriate use of GI transit scintigraphy requires input from experts in the fields of nuclear medicine, radiology, and gastroenterology. This document has therefore been prepared with input from representatives with this expertise from various professional societies (Appendix A). These experts reviewed the current literature with the methodology described below and established appropriateness ratings for a wide range of clinical scenarios experienced by patients who have symptoms associated with suspected abnormal GI function. The appropriate use criteria (AUC) delineated in this report are intended to assist referring medical practitioners in the diagnosis and management of patients with symptoms thought to arise from altered GI motility in the esophagus, stomach, small bowel, and colon.

INTRODUCTION

Direct measurement of GI motility is classically performed by a gastroenterologist by placing a tube or catheter-based probe within the GI tract to directly measure pressure changes within a lumen, electrical signals, or pH. Recently, less invasive wireless motility capsules have been introduced *(1,2)*. The advantages of scintigraphy for studying GI motility still remain valid despite the long time that has elapsed since the first application of a radiolabeled meal to measure gastric emptying (GE). Scintigraphy is noninvasive, does not disturb normal physiology, and can provide accurate quantification of the bulk transit of an orally administered radiolabeled solid or liquid meal. Compared with radiographic methods, scintigraphy involves low radiation exposure of the patient, is quantifiable, and uses commonly ingested foods rather than barium or nonphysiological radiopaque markers.

Gastroenterologists and primary care physicians are often faced with a wide range of symptoms in a patient, including early satiety, pain, nausea, vomiting, bloating, diarrhea, constipation, or difficulty passing a bowel movement. GI symptoms in patients often overlap and may or may not be associated with meal ingestion. It is difficult to assess whether a patient's symptoms are due to an underlying structural pathology or are functional. The authors of this AUC document recognize that management of these patients is complex and the decision to perform any diagnostic study must take into consideration the entire patient presentation. The recommendations in this document do not preclude the use of other testing. Referring health care providers should always consider the patient history, physical findings, and results of previously acquired tests before using GI scintigraphy studies. This AUC document is presented to assist health care practitioners in the appropriate use of GI scintigraphy in evaluating patients with GI tract symptoms. It is not intended to replace good clinical judgment.

As scintigraphy does not provide detailed anatomic images of the GI tract, it is particularly important to make sure an anatomic cause for the patient's symptoms has been excluded before assuming that the patient has a nonstructural primary motility disorder. This is typically performed by using radiographic imaging or endoscopic methods.

In reviewing the literature on GI transit scintigraphy, it is apparent that although some studies such as GE and esophageal transit have been available for over 50 y, the use of scintigraphy to image and quantify GI motility continues to undergo modernization and advancement. Methods such as esophageal transit scintigraphy (ETS) that were established many years ago have been replaced in many centers by more advanced manometric techniques, although they remain in limited use in select institutions where there is clinical expertise that is often not available in other institutions. GE studies continue to evolve with advances that permit simultaneous measurement of other indices of gastric motility such as accommodation and antral contractions *(3–5)*. Because of such advancements, this AUC report may need to be updated as newer and more specialized techniques are developed.

As with many imaging studies, few multicenter studies have examined clinical outcomes. Our appropriateness ratings are influenced by the clinical experience of the expert panel, which included both imaging specialists and gastroenterologists who perform, order, and use these studies in the diagnosis and management of patients with a wide range of GI symptoms.

These AUC recommendations are intended to apply primarily to adults. Because no well-defined normal values for radiolabeled meals have been established in children (due to concerns about radiation exposure of children involved in research) and because established GI transit protocols require development of normal values, this committee felt that pooled data on normal values in children in the literature were insufficient to confirm the validity of GI transit studies in children. Many sites have, however, developed institutional experience that may be used to validate their local study procedures.

This document may also be useful for nuclear medicine physicians, radiologists, and technologists, as well as for developers of clinical decision support (CDS) tools as guidance in validating requests for imaging patients with GI tract symptoms. Radiology benefit managers and other third-party payers may also use these AUC. It is our intention that the AUC be used to help ensure the appropriate ordering of GI motility scintigraphic testing in patients with GI symptoms who lack appropriate diagnosis and treatment.

METHODOLOGY

Expert Workgroup Selection

The experts of the AUC workgroup were convened by the Society of Nuclear Medicine and Molecular Imaging (SNMMI) to represent a multidisciplinary panel of health care providers to determine the appropriate use of scintigraphy for studying GI motility. In addition to nuclear medicine physicians representing the SNMMI, physicians from the American College of Physicians (ACP), the American Gastroenterological Association (AGA), and the American College of

Nuclear Medicine (ACNM) were included in the workgroup. Twelve physicians were ultimately selected as content experts to participate and contribute to the resulting AUC. A complete list of workgroup participants and external reviewers can be found in Appendix A. Appendix B is a summary of definitions of terms and acronyms, Appendix C provides the disclosures and conflict of interest (COI) statements, and Appendix D describes the solicitation of public commentary.

AUC Development

The process for AUC development was modeled after the RAND/University of California, Los Angeles (UCLA) Appropriateness Method *(6,7)* and included the development of a list of common indications for the use of scintigraphy for studying GI motility, a systematic review of evidence related to these indications, and the development of an appropriateness score for each indication by using a modified Delphi process. This process strove to adhere to the standards of the Institute of Medicine of the National Academies for developing trustworthy clinical guidance *(8)*.

Scope and Development of Clinical Indications

To begin this process, the workgroup discussed various potential clinical indications for the use of scintigraphy for studying GI motility. For all indications, the relevant patients were the populations of interest for esophageal transit, GE, small-bowel transit, and colon transit of all genders, ages, races, and geographic locations.

The workgroup identified 42 clinical indications for the use of scintigraphy for studying GI motility. The indications are intended to be as representative of the relevant patient population as possible for development of AUC. The resulting AUC are based on evidence and expert opinion regarding diagnostic accuracy and effects on clinical outcomes and clinical decision making as applied to each indication. Other factors affecting the AUC recommendations were potential harm— including long-term harm that may be difficult to capture—costs, availability, and patient preferences.

Systematic Review

To inform the workgroup, a systematic review of the relevant evidence was commissioned by an independent group, the Pacific Northwest Evidence-Based Practice Center of Oregon Health and Science University *(9)*. The primary purpose of the systematic review was to synthesize the evidence on the accuracy of ETS for diagnosing esophageal dysmotility, gastroesophageal reflux disease (GERD), and pulmonary aspiration; the proportion of patients undergoing scintigraphy who meet criteria for abnormal (delayed or rapid) gastric, small-bowel, or colon transit; and the effects of GI transit scintigraphy on clinical decision making (i.e., use of therapies, additional testing). The workgroup selected the following key questions to guide the review.

Esophageal transit scintigraphy (ETS)

1. In adults undergoing evaluation of dysphagia, what is the accuracy of ETS versus esophageal manometry for diagnosis of esophageal dysmotility?
2. In adults undergoing evaluation for potential GERD, what is the accuracy of ETS versus 24-h pH monitor, esophageal manometry, barium contrast radiography, and/or endoscopy for diagnosis of GERD?
3. In adults undergoing evaluation for potential pulmonary aspiration, what is the accuracy of ETS versus modified barium swallow (video fluoroscopic swallow study) for diagnosis of pulmonary aspiration?
4. In adults undergoing evaluation of (a) dysphagia, (b) GERD, or (c) pulmonary aspiration, what is the impact of ETS versus no scintigraphy on clinical decision making (use of therapies, additional testing)?
5. In adults who have undergone treatment (pharmacological therapies, gastric stimulator, balloon dilatation) for dysphagia, GERD, or pulmonary aspiration, what is the impact of ETS versus no scintigraphy on clinical decision making (use of therapies, additional testing)?

Gastric emptying scintigraphy (GES)

1. In adults with suspected gastric dysmotility disorder who undergo GES, what proportion are diagnosed with abnormal (delayed or rapid) GE?
2. In adults with suspected gastric dysmotility disorder who undergo GES, what is the effect on clinical decision making?
3. In adults who have undergone treatment (pharmacological therapies, gastric stimulator, balloon dilatation) for delayed GE, what is the impact of GES versus no scintigraphy on clinical decision making (use of therapies, additional testing)?

Small-bowel transit scintigraphy

1. In adults with suspected small-bowel dysmotility who undergo small-bowel transit scintigraphy, what proportion are diagnosed with abnormal small-bowel transit?
2. In adults with suspected small-bowel dysmotility who undergo small-bowel transit scintigraphy, what is the effect on clinical decision making?

Colon transit scintigraphy

1. In adults with symptoms of constipation who undergo colon transit scintigraphy, what proportion are diagnosed with delayed colonic transit?
2. In adults with symptoms of constipation who undergo colon transit scintigraphy, what is the effect on clinical decision making?

The inclusion and exclusion criteria for papers for this review were based on the study parameters established by the workgroup, using the PICOTS (population, intervention, comparisons, outcomes, timing, and setting) approach. The studies included in the review were of patients undergoing esophageal transit in which the diagnostic accuracy for esophageal dysmotility, GERD, or pulmonary aspiration was evaluated against a reference standard as prespecified in the questions, as well as studies (imaging series) of GE, small-bowel transit, or colon transit scintigraphy that reported the proportion of patients with abnormal (delayed or rapid) emptying. The review also included studies that reported effects of GI transit scintigraphy on clinical decision making (use of therapies, subsequent testing). Non-English language articles and studies published only as conference abstracts were excluded.

Searches for relevant studies and systematic reviews were conducted in the following databases: Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Ovid MEDLINE (through January 2018). These searches were supplemented by reviewing the reference lists of relevant publications.

Two investigators independently assessed the quality (risk of bias) of each study as "good," "fair," or "poor" by using predefined criteria that were specific for each study design. The criteria from QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies-2) *(10)* was adapted for studies of diagnostic accuracy. For studies reporting the proportion of patients meeting criteria for abnormal GI transit in imaging series, QUADAS-2 was modified by excluding criteria that addressed use of a reference standard. Discrepancies were resolved through a consensus process. The strength of overall evidence was graded as high, moderate, low, or very low by using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methods on the basis of quality of evidence, consistency, directness, precision, and reporting bias.

Database searches resulted in 2128 potentially relevant articles. After dual review of abstracts and titles, 340 articles were selected for full-text dual review and 72 studies were determined to meet inclusion criteria and were included in this review. Fifteen studies evaluated diagnostic accuracy of ETS against a reference standard of esophageal manometry, pH monitoring, and/or endoscopy (including biopsy

findings); 56 studies reported the proportion of patients who met criteria for abnormal GI transit scintigraphy (GES, small-bowel scintigraphy, or colon scintigraphy); and 4 studies reported effects of GI transit scintigraphy studies on clinical decision making.

Rating and Scoring Process

In developing these AUC for GI motility, the workgroup members used the following definition of appropriateness to guide their considerations and group discussions: "The concept of appropriateness, as applied to health care, balances risk and benefit of a treatment, test, or procedure in the context of available resources for an individual patient with specific characteristics" *(11)*.

At the beginning of the process, workgroup members convened via webinar to develop the initial clinical indications. On evaluating the evidence summary of the systematic literature review, the workgroup further refined its draft clinical indications to ensure their accuracy and facilitate consistent interpretation when scoring each indication for appropriateness. Using the evidence summary, workgroup members were first asked individually to assess the appropriateness and provide a score for each of the identified indications. Workgroup members then convened in a group setting for several successive webinars to discuss each indication and associated scores from the first round of individual scoring. After deliberate discussion, a consensus score was determined and then assigned to the associated appropriate use indication. For this scoring round, the expert panel was encouraged to include their clinical expertise in addition to the available evidence in determining the final scores. All members contributed to the final discussion, and no one was forced into consensus. After the rating process was completed, the final appropriate use ratings were summarized in a format similar to that outlined by the RAND/UCLA Appropriateness Method.

The workgroup scored each indication as "appropriate," "may be appropriate," or "rarely appropriate" on a scale from 1 to 9. Scores 7–9 indicate that the use of the procedure is appropriate for the specific clinical indication and is generally considered acceptable. Scores 4–6 indicate that the use of the procedure may be appropriate for the specific indication. This implies that more research is needed to classify the indication definitively. Scores 1–3 indicate that the use of the procedure is rarely appropriate for the specific indication and generally is not considered acceptable.

As stated by other societies that develop AUC, the division of these scores into 3 general levels of appropriateness is partially arbitrary, and the numeric designations should be viewed as a continuum. In addition, if there was a difference in clinical opinion for an indication such that workgroup members could not agree on a common score, that indication was given a "may be appropriate" rating to indicate a lack of agreement on appropriateness on the basis of available literature and the members' collective clinical opinion, indicating the need for additional research.

ESOPHAGEAL TRANSIT SCINTIGRAPHY (ETS)

Introduction/Background

There are several tests of esophageal motor function. The decision about which diagnostic study to use 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. Manometry is considered the gold standard for diagnosis of primary esophageal motility disorders, including achalasia, scleroderma, diffuse esophageal spasm (DES), impaired lower esophageal sphincter (LES) relaxation, hypertensive LES, and nonspecific esophageal motility disorders. Manometry, however, has limitations: 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; 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 scintigraphy studies of esophageal transit demonstrated a high sensitivity for detecting a wide range of esophageal motility disorders but a low sensitivity for disorders with intact peristalsis but high-amplitude contractions or isolated elevated pressures in the LES *(12,13)*. The use of manometry potentially supplemented by ETS for equivocal manometry results will, in large part, be determined by local expertise and availability.

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of nuclear medicine and final AUC scores in esophageal transit are presented in Table 1.

Scenario 1: Dysphagia (e.g., symptoms of achalasia, scleroderma, DES, hypertensive LES, nonspecific motility disorder, esophageal outflow obstruction) (Score 7 – Appropriate). The use of ETS for evaluation of dysphagia is typically limited to when results of barium swallow, endoscopy, and manometry are nondiagnostic or equivocal. It has been shown that as many as 50% of patients with dysphagia and normal manometry and barium studies demonstrate esophageal dysmotility on scintigraphy *(14)*. From the systematic review of the literature, the sensitivity of ETS ranged from 44% to 95% and the specificity ranged from 47% to 96% *(14–20)*. Obtaining an ETS for the evaluation

TABLE 1

Clinical Scenarios for Esophageal Transit (Often Performed with GER Studies)

Scenario no.	Description	Appropriateness	Score
1	Dysphagia (e.g., symptoms of achalasia, scleroderma, DES, hypertensive LES, nonspecific motility disorder, esophageal outflow obstruction)	Appropriate	7
2	Quantification of response to therapy (treatment for achalasia)	Appropriate	7
3	Aspiration	May be appropriate	4
4	Rumination	May be appropriate	4
5	Gastroesophageal reflux (e.g., symptoms of liquid or solid regurgitation, heartburn)	May be appropriate	5
6	Pre- and post-fundoplication	May be appropriate	5

of dysphagia was considered appropriate by unanimous agreement of the panel.

Scenario 2: Quantification of response to therapy (treatment for achalasia) (Score 7 – Appropriate). Response to treatment of esophageal disorders, such as achalasia, is often assessed by improvement in symptoms. Improvement in esophageal transit and emptying may also be helpful. Although few studies were found that use ETS to quantitate the response to therapy for esophageal motility disorders such as achalasia, the expert panel considered by unanimous agreement that ETS is appropriate when there is a need to objectively quantitate the response to some therapies *(14,21)*.

Scenario 3: Aspiration (Score 4 – May be Appropriate). A limited number of studies have evaluated the accuracy of ETS compared with that of a modified barium swallow as the reference standard to detect aspiration *(22)*. From the systematic review of the literature, the sensitivity of ETS ranged from 65% to 88% and the specificity from 62% to 95% *(15)*. One study of patients with known pulmonary aspiration who underwent ETS found that 89% had reduced liquid diet restrictions following scintigraphy *(23)*. There was unanimous agreement of the panel that ETS may be appropriate in the evaluation of patients with suspected pulmonary aspiration.

Scenario 4: Rumination (Score 4 – May be Appropriate). Rumination is an eating disorder in which a person brings up food that has already been swallowed and partially digested. No studies were found from the systematic review for assessing ETS for the evaluation of rumination. However, on the basis of their clinical experience, the panel considered this indication as may be appropriate by unanimous agreement.

Scenario 5: Gastroesophageal reflux (GER) (e.g., symptoms of liquid or solid regurgitation, heartburn) (Score 5 – May be Appropriate). Currently, esophageal pH probe monitoring is the gold standard used to confirm the presence of GER by using either a nasally based catheter or a pH capsule attached to the esophagus. The systematic review of the literature revealed that the sensitivity of ETS ranged from 43% to 90% and the specificity ranged from 64% to 100% *(19,22,24,25)*. The expert panel considered by unanimous agreement that ETS may be appropriate in the assessment of patients with GER.

Scenario 6: Pre- and post-fundoplication (Score 5 – May be Appropriate). One study in the systematic review evaluated findings following fundoplication *(26)*. The panel considered by unanimous agreement that the use of ETS may be appropriate in assessing patients following fundoplication.

Summary of Recommendations

Esophageal manometry, barium swallow radiography, and pH monitoring are typically used for first-line evaluation of patients with suspected esophageal dysmotility and GER. Use of ETS is limited by the availability of local expertise with experience in the methodology, but when available, such expertise is most commonly used when there are equivocal or nondiagnostic findings from first-line studies.

GE OF SOLIDS (SOLID NUTRIENT OR EQUIVALENT)

Introduction/Background

GE studies are usually ordered to confirm or exclude whether gastroparesis (delayed GE) is a cause of the patient's symptoms. Gastroparesis is usually associated with upper GI symptoms, which include nausea (92% of patients), vomiting (84%), abdominal fullness or distention (75%), and early satiety (60%) *(27)*. Etiologies for gastroparesis include diabetes; postgastric surgical conditions; infections (especially postviral); neuromuscular, autoimmune, and connective tissue diseases; and idiopathic disease.

Patients often do not have well-defined GI symptoms and present with concerns about dyspepsia (symptoms of any pain or discomfort thought to originate in the upper GI tract). The goal of diagnosing delayed GE is to identify patients who will benefit from a prokinetic drug or other treatment to alleviate symptoms. A GE study is indicated for patients with suspected gastroparesis or dyspepsia after an anatomic cause for symptoms has been excluded. A GE study may also be indicated in the absence of dyspeptic symptoms, such as those with severe GERD not responding to acid suppressants (to see whether delayed GE contributes to reflux), those requiring a workup to identify a diffuse GI motility disorder, and those who are diabetic and have poor glycemic control. GE studies can also be used to assess patients for dumping syndrome, in which GE is rapid. Classically, this occurs after surgery, but is now being described in patients with autonomic dysfunction, cyclic vomiting syndrome (CVS), and functional dyspepsia (FD).

GES is currently the gold standard method for measuring GE and is the standard to which other diagnostic tests have been compared. It should be performed by using the currently accepted, standardized low-fat solid meal that is endorsed by the American Neurogastroenterology and Motility Society and SNMMI *(28–30)*. Advantages of this test include good tolerability of the meal by the majority of patients, validated multicenter normal values, and a reproducible methodology. Patients who cannot tolerate the current egg-based solid meal can be tested with the nutritional supplement Ensure PLUS *(31,32)*. The advantages of this substitute meal are that it uses the same imaging protocol and that it has normal GE values that are similar to those of the solid egg-based meal. A rice-based solid meal substitute that is gluten free and vegan has documented normal values but may not be widely available *(33)*. Although many variations of solid and liquid GE meals are used by some diagnostic facilities, they are not recommended until they have had sufficient validation in the literature.

Recently, a non-nutrient water-only GE test was compared with the standard solid meal and showed a delay in water GE in 32% of patients with normal solid GE *(34,35)*. The potential advantages of a water-only meal are meal tolerability, a shorter acquisition time, and added sensitivity. Currently there are only single-center data to support the use of a non-nutrient water meal.

To fully integrate the results of a GES test into patient management, it is important to document GI symptoms, prior surgical procedures, and all drugs in use *(36)*. An abbreviated list of interfering medications includes the following: anticholinergics; calcium channel blockers; clonidine; proton pump inhibitors; tricyclic antidepressants; lithium; exenatide; liraglutide; pramlintide; dopamine agonists; progesterone-containing agents; nicotine by smoking and/or use of containing agents; medications containing opioids, octreotide, or other somatostatin analogs; and tetrahydrocannabinol by smoking and/or use of its ingestible derivatives. Interfering medications should be stopped for 3 d or 6–10 half-lives of the drug. Concealed use of an illicit drug can be an overlooked reason for GI symptoms and GE dysfunction. In patients with diabetes, blood glucose must be checked and documented immediately before the test to avoid slowing of GE due to hyperglycemia *(37–40)*.

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of nuclear medicine and final AUC scores in GE of solids are presented in Table 2.

Scenario 1: Symptoms of gastroparesis (e.g., diabetic or idiopathic) (Score 9 – Appropriate). Studies that have examined GES findings in relation to GI concerns show that symptoms that correlate best with delayed GE at 4 h are early satiety, nausea, vomiting, postprandial fullness, and loss of appetite The 4-h value is the most sensitive and specific indicator of gastric dysfunction *(41)*. A pivotal investigation showed that 37% of patients with normal GE results at 2 h were delayed at 4 h *(42,43)*. All time points must be considered, as a delay in GE at 2 h may show normalization at 4 h *(42,43)*. Delayed GE documented on GES fulfills 1 of the 3 criteria for establishing the diagnosis of gastroparesis in combination with the other 2: symptoms of

gastroparesis and absence of gastric outlet obstruction or ulceration *(36)*. This indication was considered appropriate by unanimous agreement of the panel.

Scenario *2: Functional dyspepsia ((e.g., symptoms of upper abdominal pain/discomfort, early satiety, nausea, vomiting, bloating, postprandial fullness) (Score 9 – Appropriate).* Although the pathophysiology of FD is multifactorial, recent studies suggest that it includes a gastric motility disorder. The main pathophysiology in FD appears to include delayed GE, impaired fundal accommodation, and/or visceral hypersensitivity *(44–46)*. Delayed GE has been considered a mechanism of dyspeptic symptoms, especially in the FD category of postprandial distress syndrome (early satiety and abdominal fullness after meals) rather than in the epigastric pain syndrome subgroup (abdominal pain/discomfort symptoms present at night while fasting, as well as postprandial symptoms). However, correlations between severity of FD and delayed GE have been weak, with approximately 40% of patients with a working diagnosis of FD also showing delayed GE *(47)*.

The documentation of delayed GE is a starting point for treatment strategies in this clinically heterogeneous group, which includes patients in whom accelerated GE can be an unexpected finding. Analysis of proximal stomach (fundal) emptying as part of standard GES, as well as dynamic antral scintigraphy to assess antral contractions, may unmask a subset of patients with FD with normal GE results but impaired fundal accommodation or antral motility *(48)*. This indication was considered appropriate by unanimous agreement of the panel.

Scenario 3: Postsurgical-induced symptoms of dyspepsia, questionable rapid GE (e.g., symptoms of postsurgical gastroparesis, postvagotomy gastroparesis) (Score 9 – Appropriate). Some patients who have an accidental vagotomy during standard fundoplication surgery for GER develop symptoms of postvagotomy gastroparesis or, alternatively, "dumping." The symptoms may be clinically indistinguishable. The subtle differentiating characteristics are more postprandial abdominal pain, less vomiting, and more urge to defecate or experience postprandial early diarrhea in dumping syndrome *(49)*. Late dumping symptoms (hypoglycemia, weakness, and fainting) may also help to differentiate between the 2 complications. Postvagotomy gastroparesis can result in severely delayed GE because pyloric relaxation is impaired and there is often bezoar formation that can block GE *(50)*. This indication was considered appropriate by unanimous agreement of the panel.

Scenario 4: Poorly controlled diabetes without dyspeptic symptoms (Score 5 – May be Appropriate). Gastroparesis diabeticorum is a term that describes patients with diabetes who have no symptoms of gastroparesis but are noted to have retained food in the stomach. This observation has been extrapolated to mean that when poorly controlled diabetes cannot be explained by nonadherence to the treatment regimen, gastroparesis may be the reason for excessive swings in blood glucose. The lack of GI symptoms may be related to concomitant neuropathy that causes impaired gastric sensations. GES is able to objectively resolve this working diagnosis of gastroparesis without GI symptoms and was considered as may be appropriate by the consensus panel.

Scenario 5: Poorly controlled GER without dyspeptic symptoms (Score 6 – May be Appropriate). Delayed GE has been reported in the 28%-56% of patients who have GERD and its presence can explain poor control of symptoms, particularly nocturnal symptoms *(51)*. Correlation of delayed GE with poor nocturnal control of GERD may guide management toward combining prokinetic agents with proton

TABLE 2

Clinical Scenarios for Gastric Emptying of Solids (Including Postinfectious Symptoms)

Scenario no.	Description	Appropriateness	Score
1	Symptoms of gastroparesis (e.g., symptoms of diabetic or idiopathic)	Appropriate	9
2	FD (e.g., symptoms of upper abdominal pain/discomfort, early satiety, nausea, vomiting, bloating, postprandial fullness)	Appropriate	9
3	Postsurgical-induced symptoms of dyspepsia, questionable rapid GE (e.g., symptoms of postsurgical gastroparesis, postvagotomy gastroparesis)	Appropriate	9
4	Poorly controlled diabetes without dyspeptic symptoms	May be appropriate	5
5	Poorly controlled GER without dyspeptic symptoms	May be appropriate	6
6	Suspected generalized GI motility disorder (intestinal pseudo-obstruction)	May be appropriate	6
7	CVS	May be appropriate	6
8	Anorexia nervosa	May be appropriate	5
9	Suspected impaired gastric accommodation (e.g., symptoms of early satiety, postprandial fullness, and/or abdominal pain)	Appropriate	7
10	Pre- and/or postbariatric surgery	May be appropriate	5
11	Postsurgical evaluation (for neurostimulator, pyloroplasty, pyloromyotomy, partial gastric resection)	May be appropriate	6
12	Postsurgical treatment	May be appropriate	6
13	Postsurgical neurostimulator placement	May be appropriate	6
14	Postsurgical pyloroplasty	May be appropriate	6
15	Following surgical or endoscopic pyloromyotomy	May be appropriate	6
16	Postsurgical partial gastric resection	May be appropriate	6

pump inhibitor therapy. In addition, objective delay in GE gives credence to adjusting evening meal timing and content, elevation of the head of the bed, and/or sleeping on the left side to improve symptoms of GERD. This indication was considered as may be appropriate by the consensus panel.

Scenario 6: Suspected generalized GI motility disorder (intestinal pseudo-obstruction) (Score 6 – May be Appropriate). A suspected generalized motility disorder, so-called intestinal pseudo-obstruction, can be from neuropathic and myopathic causes. This can be seen in connective tissue disorders, typically systemic sclerosis, in which the esophagus, small intestine, and colon are commonly affected *(52)*. Dyspeptic symptoms such as nausea, vomiting, and epigastric fullness are often observed in patients with scleroderma. A range of 47%–66% of patients with scleroderma have delayed GE of solids *(53)*. It is hypothesized that collagen replacement of the gastric smooth muscle may lead to subsequent stomach hypomotility. Evidence of delayed GE supports initiation of promotility therapy. This indication for obtaining a GE study in patients with suspected generalized GI motility disorder, including intestinal pseudo-obstruction, was considered as may be appropriate by the consensus panel.

Scenario 7: Cyclic vomiting syndrome (CVS) (Score 6 – May be Appropriate). GE studies on CVS can be crucial for separating this entity from gastroparesis and, hence, change the course of treatment as well as the long-term prognosis. In the largest published study of GE in nearly 100 CVS patients, GE results were rapid in 30% and normal in 70% *(54)*, whereas GE is delayed in patients with gastroparesis.

The key to studying GE in CVS is the timing of the study: It should be performed during the remission phase of CVS. A major confusion in previous literature was the performance of GE in the hospital where CVS patients typically receive narcotics for their abdominal pain. This results in delayed GE and the misdiagnosis of gastroparesis. In addition, marijuana use is common in a subset of CVS patients (termed "cannabis hyperemesis syndrome") and here GE may also be slow as a result of recent marijuana use *(55)*. The finding of normal or rapid GE is regarded as specific for CVS and separates this entity from gastroparesis. This is crucial, especially when CVS occurs in the setting of diabetes mellitus. This indication was considered as may be appropriate by the consensus panel.

Scenario 8: Anorexia nervosa (Score 5 – May be Appropriate). Anorexia nervosa in childhood or early adulthood can result in altered GE function, where despite subsequent improvement in eating habits, there is no recovery of the gastric atrophy. Another possible explanation for delayed GE could be that it is secondary to endocrine dysfunction (i.e., hypoadrenalism), which is observed in patients with eating disorders. Anorexia and bulimia have been associated with dyspeptic symptoms and delayed GE. In a study of 16 female patients with anorexia nervosa, GE of the solid food phase was significantly delayed in 80% of patients *(56)*. With improvement of the eating disorder and recovery of normal body weight, GE can improve. This indication was considered as may be appropriate by the consensus panel.

Scenario 9: Suspected impaired gastric accommodation (e.g., symptoms of early satiety, postprandial fullness, and/or abdominal pain) (Score 7 – Appropriate). Studies have shown an association between symptoms of nausea, early satiety, abnormal distention, and GER with proximal gastric retention, whereas vomiting may be more associated with distal gastric retention *(57)*. Two methods for performing GES measurement of gastric accommodation have been reported. One uses standard planar (2-dimensional) GES and examines intragastric meal distribution immediately after meal ingestion. The second uses a 3-dimensional single-photon emission computed tomography (SPECT) acquisition and estimates gastric volume by imaging the gastric mucosa. The SPECT method is therefore not influenced by GE, is independent of intragastric content, and can assess both fasting and postprandial gastric volume during the first 10 min after meal ingestion.

Measurements of gastric volume by SPECT differ significantly from the estimates of gastric accommodation based on intragastric meal distribution measured immediately after food ingestion by the 2-dimensional method *(58)*. Current literature shows that both methods independently correlate with symptoms. There is significant evidence that the SPECT method measures gastric volume changes comparably to the intragastric barostatically controlled balloon *(59)* and has excellent performance characteristics *(60)*. In addition, improvement in FD symptoms with low-dose antidepressants has recently been associated with increased SPECT-measured gastric accommodation *(61)*. Current evidence is more limited to support that measurement of gastric accommodation based on 2-dimensional scintigraphy improves diagnosis and provides for specific treatment of impaired accommodation *(4,5,58)*. This indication was considered as appropriate by the consensus panel.

Scenario 10: Pre- and/or postbariatric surgery (Score 5 – May be Appropriate). Gastric bypass surgery may result not only in weight loss, but also in reverse type 2 diabetes. Objective measurement of a delay in GE can be taken to support the recommendation for gastric bypass surgery rather than for laparoscopic sleeve gastrectomy. In patients who develop vomiting after gastric bypass, a GE study can identify significant delay in GE from the pouch, an indication of stenosis at the gastric-jejunal anastomosis. If gastric pouch emptying shows expected rapid GE, the ongoing vomiting is either from overeating or rumination syndrome. Therefore, GES before bariatric surgery may guide selection of the surgical technique, and in patients with symptoms of postsurgical vomiting, it may disclose an actionable surgical complication. The evidence for using GES before or after bariatric surgery, however, is currently limited *(62)*. When used, it should be combined with an endoscopic and/or radiographic assessment. This indication was considered as may be appropriate by the consensus panel.

Scenario 11: Postsurgical evaluation (for neurostimulator, pyloroplasty, pyloromyotomy, partial gastric resection) (Score 6 – May be Appropriate). Oral contrast radiographic studies are routinely performed to document uncomplicated gastric surgeries. Assessment of symptoms that may still be present in a patient with gastroparesis who has undergone surgical treatment can be crucial. Gastric electrical neurostimulation does not predictably change GE *(63)*, whereas pyloroplasty will accelerate it *(64)*. If GE is not sufficiently accelerated, incomplete pyloromyotomy or the presence of a gastric bezoar should be suspected. In the future, endoscopic pyloromyotomy may become another indication for GES, as one recent study has already shown acceleration of GE by endoscopic pyloroplasty *(65)*. This indication was considered as may be appropriate by the consensus panel.

Scenario 12: Postsurgical treatment (Score 6 – May be Appropriate). A recent study suggests that the GE rate from a gastric pouch has an inverse correlation with weight loss after Roux-en-Y gastric bypass (ReYGB) surgery *(66)*. Therefore, rapid dumping was correlated with failed ReYGB in achieving target weight loss. Several studies show that patients with failed ReYGB benefit from salvage banding, in which an adjustable band is applied either over the gastric pouch (to control excessive dilation) or over the gastrojejunostomy to control dilation of the opening *(67)*. GES results may help guide where to place the salvage band; however, currently no evidence exists to support this strategy. This indication was considered as may be appropriate by the consensus panel.

Scenario 13: Postsurgical neurostimulator placement (Score 6 – May be Appropriate). GES may provide supportive evidence for surgical success. If GE results are abnormal after surgery aimed to treat gastroparesis, additional therapy to promote GE may be helpful. Use of a neurostimulator is one such option. It has worked synergistically with pyloroplasty *(64)*.

Hence, addition of a neurostimulator would be reasonable if GES remains abnormal in a patient with gastroparesis who remains symptomatic after pyloroplasty. Other complications from GI surgery that result in slow GE may benefit from neurostimulator placement. Case

reports anecdotally support such intervention in these patients. This indication was considered as may be appropriate by the consensus panel.

Scenario 14: Postsurgical pyloroplasty (Score 6 – May be Appropriate). Since GES objectively documents the effectiveness of surgery, it may also guide further management when GE remains abnormal in a patient with persistent symptoms. Such patients are known to benefit from combination therapy with the addition of a neurostimulator *(64)*. This indication was considered as may be appropriate by the consensus panel.

Scenario 15: Following surgical or endoscopic pyloromyotomy (Score 6 – May be Appropriate). Surgical pyloromyotomy is performed in infants with hypertrophic pyloric stenosis. When these patients were studied as adults, the GE results of a nutritious liquid meal were found to be overall normal *(68)*. However, pyloric motility results in the same patients were abnormal, as would be exp ected. This observation is consistent with the concept that the stomach has the capacity to compensate for changes in pyloric motility to minimize effects on GE. This mechanism may fail in some patients and manifest as GI symptoms. There are no published studies on using a GE study in such a patient population. Nevertheless, performance of a GE study was considered reasonable and may be appropriate in relating abdominal concerns to the development of GE dysfunction in these patients. Another patient population treated with surgical pyloroplasty or pyloromyotomy can be treated with electrical stimulation for the treatment of severe gastroparesis. These patients can experience significant improvement in their symptoms and show improved GE *(64)*. GES serves as objective evidence for successful treatment by this combined surgical procedure. Recently, endoscopic pyloromyotomy was also found to effectively treat severe gastroparesis, with marked improvement in symptoms and GE *(65)*. This indication was considered as may be appropriate by the consensus panel.

Scenario 16: Postsurgical partial gastric resection (Score 6 – May be Appropriate). Partial gastric resections, either Billroth I (antrectomy) or Billroth II (gastro-jejunal anastomosis), have unpredictable effects on GE. When these procedures are performed in the context of peptic ulcer disease, GE is generally expected to be accelerated after surgery. However, as many as 50% of these patients may later display abdominal symptoms of gastroparesis after Billroth I surgery. Demonstration of delayed GE is diagnostic of gastroparesis when the stomach is shown to be patent by endoscopy. These patients may benefit from completion gastrectomy *(69)*. An antral resection without a pyloroplasty may not change GE and may delay it in a significant proportion of these patients. This procedure is typically done in patients with gastric cancer resection. It is a standard of care in these patients to follow up with endoscopy for early detection of cancer recurrence. However, there is often significant residual food after standard preparation of patients after Billroth I, which interferes with diagnostic endoscopy. Delayed GE in these patients predicted interference of significant food remnants with endoscopy and correlates well with development of postsurgical abdominal symptoms of gastroparesis *(70,71)*. This indication was considered as may be appropriate by the consensus panel.

Summary of Recommendations

GES remains the standard for measuring both solid and liquid GE. Recent advances in GES now permit additional measurements of gastric motility, including intragastric meal distribution, gastric accommodation response, and antral contraction frequency and amplitude. Although current treatments for gastroparesis are limited, it is anticipated that these newer measures of gastric dysmotility may lead to improved treatment.

GE OF LIQUIDS (NUTRIENT AND NON-NUTRIENT/WATER MEALS)

Introduction/Background

Determination of GE rates of a non-nutrient water meal is not well established. Use of a water meal dates back to the early use of a saline load test for gastric outlet obstruction. There is limited evidence for the existence of a subset of patients with gastroparesis with normal solid GE but abnormal GE of water *(34,35)*. Use of a water meal has not

TABLE 3

Clinical Scenarios for Gastric Emptying of Liquids (Non-Nutrient/Water Meal)

Scenario no.	Description	Appropriateness	Score
1	Symptoms of gastroparesis (e.g., symptoms of diabetic vs. idiopathic) if solid emptying is normal	Appropriate	7
2	FD (e.g., symptoms of upper abdominal pain/discomfort, early satiety, nausea, vomiting, bloating, postprandial fullness)	Appropriate	7
3	Poorly controlled diabetes without dyspeptic symptoms	May be appropriate	4
4	Poorly controlled GER without dyspeptic symptoms	Rarely appropriate	3
5	Suspected generalized GI motility disorder (intestinal pseudo-obstruction)	Rarely appropriate	3
6	CVS	Rarely appropriate	3
7	Anorexia nervosa	May be appropriate	4
8	Gastrostomy evaluation	May be appropriate	5
9	Unable to tolerate solid meal	Appropriate	8
10	After a normal solid meal when symptoms suggest gastric motility disorder	Appropriate	8
11	Small-bowel transit study (when combined with liquid GE)	Appropriate	7

been validated in multicenter studies. Because water by definition has no caloric value, it is clinically of greater pertinence to address the GE of a nutrient liquid meal. A nutrient liquid meal is indicated for patients referred for GES who have egg and/or gluten allergies or other reasons for intolerance of the standard solid meal. The GE characteristics of a validated liquid nutrient meal is similar to those of the standard solid meal but with a slightly faster emptying rate *(31,32,72)*.

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of nuclear medicine and final AUC scores in GE of liquids (non-nutrient/water meal, including postinfectious symptoms) are presented in Table 3.

Scenario 1: Symptoms of gastroparesis (e.g., symptoms of diabetic vs. idiopathic) if solid emptying is normal (Score 7 – Appropriate). A retrospective study of combined tap water and standard solid meal GES evaluated 21 patients with GI symptoms. Investigators found that in 17 patients with normal solid GE, the water GE was abnormal. The same group then initiated another prospective study of 101 patients, the key difference being that water and solid GES were done consecutively to eliminate simultaneous liquid and solid meal ingestion as in the first investigation. Delayed GE was found in 36% of plain water GES results and 16% of solid GES results. Similar to the first study, water GE was delayed in 32% of all patients with normal solid emptying *(34,35,73)*. Although advantages of plain water include availability and short acquisition time (30 min), there is currently insufficient evidence to support its routine clinical use. In patients who cannot tolerate the standard solid meal, this indication was considered as appropriate by the consensus panel.

Scenario 2: Functional dyspepsia (FD) (e.g., symptoms of upper abdominal pain/discomfort, early satiety, nausea, vomiting, bloating, postprandial fullness) (Score 7 – Appropriate). Non-nutrient plain water GES may be useful, especially when other validated nutritional meals cannot be tolerated. See Scenario 1.

Scenario 3: Poorly controlled diabetes without dyspeptic symptoms (Score 4 – May be Appropriate). Plain water GES may be useful if other validated meals with nutritional value cannot be tolerated. A noncaloric meal may be useful to avoid the known physiological effects of hyperglycemia, which can slow GE. This indication was considered as may be appropriate by the consensus panel.

Scenario 4: Poorly controlled GER without dyspeptic symptoms (Score 3 – Rarely Appropriate). There is no literature evidence for the validity of plain water GES in this indication. Non-nutrient plain water GES may be useful, especially if other validated nutritional meals cannot be tolerated. This indication was considered as rarely appropriate by the consensus panel.

Scenario 5: Suspected generalized GI motility disorder (intestinal pseudo-obstruction) (Score 3 – Rarely Appropriate). There is no literature evidence for the validity of plain water GES in this indication. Non-nutrient plain water GES may be useful, especially if other validated nutritional meals cannot be tolerated. This indication was considered as rarely appropriate by the consensus panel.

Scenario 6: Cyclic vomiting syndrome (CVS) (Score 3 – Rarely Appropriate). There is no literature evidence for the validity of plain water GES in this indication. Non-nutrient plain water GES may be useful, especially if other validated nutritional meals cannot be tolerated. This indication was considered as rarely appropriate by the consensus panel.

Scenario 7: Anorexia nervosa (Score 4 – May be Appropriate). There is no literature evidence for the validity of plain water GES in this indication. Non-nutrient plain water GES may be useful in this patient population, especially if other validated nutritional meals cannot be tolerated. This indication was considered as may be appropriate by the consensus panel.

Scenario 8: Gastrostomy evaluation (Score 5 – May be Appropriate). There is no literature evidence for the validity of plain water GES in this indication. Non-nutrient plain water GES may be useful, especially if other validated nutritional meals cannot be tolerated. This indication was considered as may be appropriate by the consensus panel.

Scenario 9: Unable to tolerate solid meal (Score 8 – Appropriate). There is no literature evidence for the validity of plain water GES in this indication. Non-nutrient plain water GES may be useful, especially if other validated nutritional meals cannot be tolerated. On the basis of their clinical experience, the consensus panel considered this indication as may be appropriate.

Scenario 10: After a normal solid meal when symptoms suggest gastric motility disorder (Score 8 – Appropriate). Non-nutrient plain water GES may be useful, especially if other validated nutritional meals cannot be tolerated. Recently, a non-nutrient water-only GE test was compared with the standard solid meal and showed a delay in water GE in 32% of patients with normal solid GE *(35)*. A water-only meal has potential advantages, including meal tolerability, a shorter acquisition time, and added sensitivity. Currently, there are limited clinical data to support the use of a non-nutrient water meal, but the consensus panel felt the existing data show that its use is appropriate for this clinical scenario.

Scenario 11: Small-bowel transit study (when combined with liquid GE) (Score 7 – Appropriate). For some patients with vague symptoms consistent with a functional GI disorder, it can be challenging to diagnose whether the abnormality involves the stomach, small bowel, or colon. In such instances, transit of a water meal may disclose a small-bowel transit abnormality. Although combining liquid (water) and solids by using a dual isotope technique to measure both solid and liquid GE and then following the liquid transit through the small bowel has been previously confined to the research setting, it has recently become a clinically validated study to assess small-bowel motility *(73–76)*. This indication was considered as appropriate by the consensus panel.

Summary of Recommendations

GES of solids remains the gold standard for measuring GE. There are limited data on the clinical value of liquid GE alone. Liquid GE is, however, typically combined with solids when additional small-bowel or colonic transit studies are needed. A substitute liquid meal can be of clinical value for patients who cannot tolerate the standard radiolabeled egg meal.

SMALL-BOWEL TRANSIT

Introduction/Background

The function of the small bowel is to transport food as it empties from the stomach and to mix it with bile and with pancreatic and intestinal secretions to facilitate absorption over the bowel mucosal surface. Measurement of small-bowel transit is complex because entry of a meal into the small intestine depends on GE and because small-bowel chyme spreads over a large distance as it progresses toward the colon. There is no simple small-bowel peristaltic pattern. Antegrade and retrograde movements of intestinal chyme occur in the jejunum and ileum, with some areas progressing rapidly and others slowly. Jejunal peristaltic activity is typically more rapid and intense, with slowing of peristalsis seen in the ileum *(77)*.

The simplest approach to scintigraphic measurement of small-bowel transit is to measure orocecal transit time by imaging the leading edge of radiotracer transit through the bowel. Accurately defining the leading edge (the first visualized arrival of activity in the cecum), however, requires frequent (every 10–15 min) and prolonged imaging because of the stasis in the terminal ileum.

An alternative scintigraphic method of measuring small-bowel transit does not attempt to characterize the complex temporal or spatial peristaltic small-bowel patterns or leading-edge transit, but simply measures the overall bulk movement of radiotracer as it progresses distally into the terminal ileum. Typically, the radiolabeled meal collects

in a terminal ileal reservoir. This region is also referred to as the ileocolonic junction. The recent SNMMI/European Association of Nuclear Medicine guideline on small-bowel transit recommends use of the percentage of administered liquid meal that has accumulated in the terminal ileum at 6 h after meal ingestion as a simple index of small-bowel transit *(78)*. Small-bowel transit is considered normal if more than 40% of administered activity has progressed into the terminal ileum or passed into the cecum and ascending colon at 6 h. Small-bowel transit is delayed if activity persists in multiple loops of small bowel at 6 h and if little activity (<40%) arrives in the terminal ileum reservoir. The amount of colon filling at 6 h has also been used as an index of small-bowel transit. The wireless motility capsule has been shown to correlate well with scintigraphy for measuring small-bowel transit *(1)*.

Indications for small-bowel transit testing have been proposed in prior consensus publications. Authors of a review article by the American and European Neurogastroenterology and Motility societies proposed that small-bowel transit testing should be considered for those with unexplained nausea, vomiting, bloating, distention, or other manifestations of small intestinal bacterial overgrowth (SIBO) or dysmotility *(2)*. The authors of an older review commented that symptoms of small-bowel dysmotility are similar to those of gastroparesis and that small-bowel transit testing could be considered for those patients with persistent symptoms despite normal GE rates *(79)*.

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of nuclear medicine and final AUC scores in small-bowel transit are presented in Table 4.

Scenario 1: Symptoms of small-bowel dysmotility (e.g., symptoms of nausea, vomiting, bloating, constipation, diarrhea, abdominal distention) (Score 7 – Appropriate). Scintigraphy has been used to measure small-bowel transit in several retrospective studies with varying designs related to patient symptom profiles. In one study of 55 patients undergoing whole-gut transit scintigraphy (WGTS), small-bowel transit was abnormal in 3 of 14 (21%) with dyspepsia, and delays in small-bowel transit were found in 7 of 27 (26%) with constipation and in 3 of 14 (21%) with diarrhea *(80)*. In a second investigation of 108 patients with functional symptoms, 4 of 35 (11%) with dyspepsia exhibited small-bowel transit delays, and 5 of 69 (7%) with constipation had small-bowel delays *(77)*. Changes in management were directed by WGTS, which combines GE, small-bowel, and colon transit measurements, in 74% of patients with dyspepsia and 64% of those with constipation, although no mention was made of the specific impact of small-bowel transit findings on management decisions. A third report focused on concerns of unexplained constipation in 212 patients *(81)*. Nine individuals (10%) with slow-transit constipation had delayed small-bowel transit, and 2 of 25 (8%) with dyssynergic defecation had associated small-bowel delays. Seven of 53 (13%) with combined slow-transit constipation and dyssynergia and 2 of 43 (5%) with normal results of coloanal testing exhibited slowing of small-bowel transit. The authors postulated that the extracolonic transit delays could be a potential explanation for failed responses to appropriate therapies for constipation. In another study, small-bowel transit was delayed in 2 of 8 (25%) patients with constipation *(82)*. Moderately high intra- and intersubject variability in scintigraphic small-bowel transit times has been proposed by some investigators to limit discrimination of transit delays in some patients with small intestinal motility disorders *(79,83)*.

Small-bowel scintigraphy was used to document responsiveness to treatment in one study of patients with functional GI disorders *(84)*. The percentage of scintigraphic colonic filling at 6 h (reflecting orocecal transit) was significantly accelerated by oral administration of the serotonin 5-HT4 receptor agonist prokinetic medication tegaserod in 24 patients with constipation-predominant irritable bowel syndrome (IBS).

Other tests, including barium contrast radiography, radiopaque markers, video capsule endoscopy, and magnetic resonance imaging, have been proposed to quantify small-bowel transit; however, no case series that used these methods to document transit delays have been published *(2,85)*. This indication was considered appropriate by unanimous agreement of the panel.

Scenario 2: Suspected SIBO (Score 5 – May be Appropriate). The literature on the use of scintigraphy to document small-bowel transit delays in patients with SIBO is limited. In a study of patients undergoing concurrent lactulose breath testing and WGTS, there were no differences in breath test positivity overall in those with and without small-bowel transit delays *(86)*. However, patients with positive methane production results exhibited slower small intestinal transit compared with that of hydrogen producers. A second investigation that used simultaneous lactulose breath testing and scintigraphy conferred a diagnosis of SIBO when the hydrogen rise from bacterial fermentation of the substrate was detected before 5% of the radiolabeled tracer passed into the cecum *(87)*. Use of these rigorous criteria from combined testing showed that those with SIBO reported significantly better symptom responses to antibiotic treatment with rifaximin than did those who did not meet these criteria.

With lactulose breath tests, prolonged orocecal transit has been observed in patients with inflammatory bowel disease, acromegaly, diabetes, and scleroderma in association with SIBO (88–90). Wireless motility capsule testing and small intestinal manometry are also useful for demonstrating abnormal small-bowel transit associated with SIBO. Patients with SIBO diagnosed by lactulose breath testing exhibit delayed small-bowel transit on wireless motility capsule testing compared with patients who have negative breath test results (88,90).

From the above evidence, the committee concluded that small-bowel scintigraphy may be appropriate to measure transit in patients with suspected SIBO. It must be emphasized that, although documentation of transit delays cannot establish a diagnosis of SIBO, such testing may offer insight into the pathogenesis of SIBO and may stratify

TABLE 4

Clinical Scenarios for Small-Bowel Transit

Scenario no.	Description	Appropriateness	Score
1	Symptoms of small bowel dysmotility (e.g., symptoms of nausea, vomiting, bloating, constipation, diarrhea, abdominal distention)	Appropriate	7
2	Suspected SIBO	May be appropriate	5
3	Suspected generalized GI motility disorder (e.g., drug-induced, idiopathic, or genetic)	Appropriate	8
4	Suspected intestinal pseudo-obstruction (e.g., unexplained small-bowel dilation)	Appropriate	8

patients into those who may need different treatments. Documentation of delayed transit with scintigraphy may direct the use of prokinetic medications with the intention of expelling organisms trapped in a sluggish intestine. This indication was considered as may be appropriate by unanimous agreement of the panel.

Scenario 3: Suspected generalized GI motility disorder (e.g., drug-induced, idiopathic, or genetic) (Score 8 – Appropriate). WGTS permits quantification of GE, small-bowel transit, and colon transit in a single test. Some literature reports the utility of small-bowel scintigraphy in confirming or refuting the presence of generalized dysmotility disorder with abnormal transit in at least 2 of these 3 GI organs. In the previously described study of 108 patients with functional GI symptoms, 3 of the 4 patients with dyspepsia and delayed small-bowel transit also exhibited delayed GE by scintigraphy *(74)*. All 5 patients with constipation and delayed small-bowel transit also showed GE delays. In another investigation of 212 constipated patients, 9 individuals with slow-transit constipation and delayed small-bowel transit also had slow GE, confirming generalized impairments throughout the alimentary tract *(81)*. Findings of these scintigraphy studies parallel investigations that use the wireless motility capsule, which is also able to measure whole-gut transit in a single diagnostic test. Small-bowel transit delays were observed in 16% of 209 patients with suspected gastroparesis *(91)*.

These findings support the unanimous endorsement of the committee for use of small-bowel transit scintigraphy as an appropriate diagnostic test in patients with a suspected generalized GI motility disorder. The evidence is convincing that scintigraphy can document small-bowel transit delays in combination with delays in other gut regions. However, it is again uncertain as to whether such capability will have a significant impact on defining management decisions or determining outcomes from treatments directed by documenting small-bowel transit delays. Few prokinetic therapies are available to correct small intestinal motor impairments. Agents that act in the small bowel include erythromycin, pyridostigmine, prucalopride, and octreotide, but the benefits of any of these agents to specifically treat small-bowel transit delays in patients with functional symptoms without pseudo-obstruction are unproved. This indication was considered appropriate by unanimous agreement of the panel.

Scenario 4: Suspected intestinal pseudo-obstruction (e.g., unexplained small-bowel dilation) (Score 8 – Appropriate). Chronic intestinal pseudo-obstruction presents with symptoms that mimic mechanical obstruction with generalized dilation of small-bowel (and usually colon) loops in the absence of physical blockage. The diagnosis is usually made with plain or cross-sectional radiography with or without documentation of contractile abnormalities on intestinal manometry. Small-bowel transit measurements can be informative in cases in which luminal dilation is minimal and when motor impairments in this gut region are uncertain. In an early report of 8 patients with chronic intestinal pseudo-obstruction established by small-bowel manometry, transit in this gut region on scintigraphy was delayed compared with that in healthy controls for both solid (131I-fiber) and liquid (^{99m}Tc-diethylene triamine pentaacetic acid [DTPA]-water) meals The prokinetic drug cisapride normalized small-bowel transit delays for both solid and liquids in these patients. *(92)*. In another study of 14 patients who had undergone small intestinal manometry to confirm dysmotility, including documentation of neuropathic findings in 8 of them and myopathic patterns in 6, scintigraphic small-bowel transit was markedly prolonged compared with that in healthy controls (median 328 vs. 218 min, $P < 0.01$) *(93)*.

Regional transit abnormalities have also been documented by scintigraphy in the distal small intestine in chronic intestinal pseudo-obstruction. In a comparative study of patients with pseudo-obstruction and healthy controls, 6 patients with myopathic findings on intestinal manometry exhibited passage of solid radiolabeled boluses from the ileum into the colon that were smaller and occurred less frequently than they did in 14 patients with neuropathic disease and 10 healthy volunteers *(94)*.

These observations support the unanimous endorsement of the committee for use of small-bowel scintigraphy as an appropriate diagnostic test in patients with suspected intestinal pseudo-obstruction. Scintigraphic measures of small intestinal transit can clearly demonstrate delays in this patient population. The regional bolus findings suggest the potential to provide pathophysiological information that distinguishes neuropathic from myopathic variants. Although the method can detect treatment responses, information is inadequate for showing that performance of small-bowel scintigraphy can alter treatment decisions, predict outcomes from prokinetic therapy, or provide prognostic information to determine whether a given patient should be considered for parenteral nutrition.

Summary of Recommendations

The investigations cited in this systematic review support the endorsement of the panel for use of small-bowel scintigraphy as an appropriate diagnostic test in patients with symptoms of small-bowel dysmotility and SIBO. The available data suggest that a subset of patients with symptoms of presumed upper and/or lower gut origin will exhibit delayed small-bowel transit. However, there is not yet convincing literature that specifically documents that small-bowel transit delays will influence additional management decisions or affect outcomes of any treatments for patients with functional GI disorders.

COLON TRANSIT

Introduction/Background

Colonic motility regulates slow mixing and movement of its contents so that the colon can absorb water and electrolytes and transform liquid chyme into semisolids or solids in the sigmoid colon. Rhythmic phasic contractions aided by tonic contractions cause slow distal propulsion and mixing of colonic contents. In addition, infrequent high-amplitude (>100 mm Hg) propagating contractions produce mass movements that deliver a large column of stool into the rectum.

TABLE 5

Clinical Scenarios for Colon Transit

Scenario no.	Description	Appropriateness	Score
1	Symptoms of large-bowel (colon) dysmotility (e.g., symptoms of constipation, bloating, abdominal pain, non-diarrhea-dominant IBS)	Appropriate	8
2	Suspected generalized GI motility disorder	Appropriate	8
3	Suspected intestinal pseudo-obstruction (e.g., unexplained megacolon)	Appropriate	8

Thereafter, in healthy individuals, controlled evacuation of stool normally occurs between once in 3 d and up to 2 to 3 times a day. A key question in patients with chronic constipation is to identify whether there is colonic inertia, generalized slow colon transit, pelvic floor dysfunction, functional outlet obstruction, or IBS *(95)*. Colonic motility and transit time are tested to determine whether a patient with symptoms of constipation has abnormal colonic transit and whether a specific area of the colon is involved.

Colon transit can be imaged by using serial radiographs after ingestion of radiopaque markers with a meal.

Radiographs are obtained for several days (up to 7) to count the number of markers remaining in segments of the colon (right, left, and rectosigmoid regions) or throughout the colon. The radiopaque marker test is not physiological, however, for the assessment of transit of intestinal chime. In contrast, 2 scintigraphic methods that have been most commonly applied to provide a more dynamic assessment of colonic transit use oral ^{111}In-DTPA. These methods are described in detail in a consensus practice guideline *(67)*. The wireless motility capsule is a newer technique that has been shown to correlate well with scintigraphy and radiopaque markers for measuring colon transit *(1)*.

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of nuclear medicine and final AUC scores in colon transit are presented in Table 5.

Scenario 1: Symptoms of large bowel (colon) dysmotility (e.g., symptoms of constipation, bloating, abdominal pain, non-diarrhea-dominant IBS) (Score 8 – Appropriate). Chronic constipation is a prevalent condition. From studies that use validated questionnaires, it is estimated to affect approximately 14% of the global population. Ruling out structural problems with colonoscopy or radiological imaging is of primary importance, particularly for colonic malignancy or extrinsic luminal obstruction. Three types of constipation have been identified: normal transit, slow transit (colonic inertia or chronic colonic pseudo-obstruction), and evacuation disorders. Considerable overlap exists between the 3 groups *(95)*. Normal-transit constipation includes individuals with IBS with constipation and IBS with mixed symptoms; in these patients, abdominal pain and bloating is associated with constipation. Some patients with mixed constipation and diarrhea have underlying constipation and the diarrhea is caused by overflow of stool material around hard impacted stool in the rectosigmoid region (overflow incontinence). Therefore, assessing large bowel motility is helpful to determine an approach to treatment in all of these patient groups, after obstructive lesions have been ruled out. It is also important to assess pelvic floor function, as this relates to constipation before performing scintigraphy. Pelvic floor dysfunction, especially dyssynergic defecation, has been shown to affect colonic transit (i.e., secondary slowing of colonic transit from distal functional obstruction) *(96)*. After obstruction and pelvic floor dysfunction have been eliminated, colon transit scintigraphy is indicated and has proven to be a reliable test to distinguish slow-transit from normal-transit constipation *(97)*. In addition to distinguishing constipated patients with slow-transit constipation, it can also differentiate patients who have delayed transit isolated to the rectosigmoid area. This indication was considered appropriate by unanimous agreement of the panel.

Scenario 2: Suspected generalized GI motility disorder (Score 8 – Appropriate). The discussion and evidence supporting the use of colon transit imaging for this indication is essentially the same as those supporting the use of WGTS, which includes GE, small-bowel, and colon transit studies (see Scenario 3: Suspected Generalized GI Motility Disorder in the Small-Bowel Transit section; Scenario 3: Suspected Intestinal Pseudo-Obstruction in the present section; and Scenario 1: Suspected Pan GI Motility Disorder in the Whole-Gut Transit section).

Scenario 3: Suspected intestinal pseudo-obstruction (e.g., unexplained megacolon) (Score 8 – Appropriate). Intestinal pseudo-obstruction is a severe motility disorder in which patients present with clinical signs of bowel obstruction. Radiographs will show dilated loops of bowel and air fluid levels suggesting an obstruction, but no mechanical occluding lesion can be found. As discussed under Scenario 6: Suspected Generalized GI Motility Disorder (Intestinal Pseudo-Obstruction) in the GE of Solids section, intestinal pseudo-obstruction is commonly seen with systemic sclerosis, in which the esophagus, stomach, small intestine, and colon are typically affected *(52)*. The presence of slow colon transit confirmed with WGTS, as well as the demonstration of delayed GE and delayed small-bowel transit, helps to establish a diagnosis of intestinal pseudo-obstruction *(98)*. This indication was considered appropriate by unanimous agreement of the panel.

Summary of Recommendations

Colonic transit scintigraphy can be used to distinguish motility disorders that affect colonic transit from those that affect the whole gut. Disorders of colonic transit that cause constipation can be further differentiated into slow-intestinal-transit and normal-transit constipation. In addition, this test may identify patients who have intestinal pseudo-obstruction and distal colonic disorders such as delayed rectosigmoid transit or dysfunction and disorders of the pelvic floor.

WHOLE-GUT TRANSIT

Introduction/Background

WGTS refers to a combined study that includes measurement of GE, small-bowel, and colonic transit after administration of a dual-isotope, solid-liquid meal *(73,74,99)*. These studies are helpful for evaluating patients whose symptoms cannot be classified as either upper or lower GI in origin, or where a functional and not an organic cause is suspected *(100)*. The wireless motility capsule has been shown to correlate well with scintigraphy for measuring whole-gut transit *(1)*.

Clinical Scenarios and AUC Scores

Clinical scenarios for the use of nuclear medicine and final AUC scores in whole-gut transit are presented in Table 6.

Scenario 1: Suspected pan GI motility disorder (e.g., unable to differentiate upper from lower GI motility disorder) (Score 8 – Appropriate). As discussed in both of the previous sections on small-bowel and colon transit, it is often difficult to determine whether a patient's symptoms are functional or organic and, if organic, whether caused by upper

TABLE 6
Clinical Scenarios for Whole-Gut Transit

Scenario no.	Description	Appropriateness	Score
1	Suspected pan GI motility disorder (e.g., unable to differentiate upper from lower GI motility disorder)	Appropriate	8
2	Presurgical evaluation of colonic inertia	Appropriate	8

or lower GI tract dysmotility. WGTS is therefore appropriate for use in such patients. In a study of patients referred for upper GI symptoms, constipation, or diarrhea, 40% were found to have an organic cause of symptoms, but 60% were diagnosed as functional *(99)*. In a study to evaluate the clinical utility of WGTS, organic disease was found in many patients with an initial suspected functional disorder; the initial diagnosis was changed in 45% of patients and patient management was changed in 67% of patients *(74)*.

Patients with diarrhea-predominant IBS have faster small-bowel transit and rapid colonic filling, whereas constipated patients have slower small-bowel transit and delayed colonic filling *(73,74,99,101)*. GI symptoms in patients with untreated celiac disease is associated with a wide range of dysmotility involving esophageal transit, gastric and gallbladder emptying, orocecal transit (small bowel), and colon transit *(102)*. WGTS therefore can play an important role in evaluating patients with suspected symptoms of celiac disease.

Many patients with severe idiopathic constipation may have prominent upper GI symptoms. WGTS is most helpful for evaluating patients with constipation. Colon transit is slowed more commonly in patients with organic disease and normal in patients with functional constipation. It is important to exclude significant upper GI dysmotility in such patients before surgery because subtotal colectomy may not correct their symptoms *(103)*. In a study of patients with severe idiopathic constipation with upper GI symptoms, 3 of 4 with upper GI symptoms had abnormal GE and small-bowel transit in addition to delayed colon transit *(104)*. Another study of patients with chronic diverse GI symptoms over a 5-y period who were referred for WGTS documented delayed colon transit in 63% of patients with constipation compared with only 29% with dyspepsia *(80)*. This indication was considered appropriate by unanimous agreement of the panel.

Scenario 2: *Presurgical evaluation of colonic inertia (Score 8 – Appropriate).* In patients with chronic constipation, WGTS is useful to identify whether there are abnormalities of GE and small-bowel transit. These upper GI transit delays may be playing a role in the symptoms of constipation. For patients being considered for surgical treatment of chronic refractory constipation, such as total colectomy, obtaining WGTS is useful to ensure that colonic transit is delayed and that transit of the upper GI tract is relatively normal. Pelvic floor dysfunction should also be excluded. Better outcomes are achieved for total colectomy if there is isolated colonic inertia *(105)*. This indication was considered appropriate by unanimous agreement of the panel.

Summary of Recommendations

Substantial evidence exists that WGTS helps in localizing a site or sites of abnormal GI motility, thus helping yield a diagnosis and directing therapy in patients with a wide range of both upper and lower GI tract symptoms.

BENEFITS AND HARMS OF IMPLEMENTING THE AUC GUIDANCE

The goal of this document is to aid and benefit referring physicians in using clinical decision support (CDS) tools so that they may achieve efficient and cost-effective use of scintigraphic GI motility studies for the wide range of clinical scenarios described in this report. The recommendations presented are not meant to replace clinical judgment, but rather are presented so that they can be incorporated into CDS tools to both educate referring physicians about the appropriate use of these studies and permit efficient ordering of scintigraphic GI motility studies.

It is not possible to cover all patient symptom scenarios where GI scintigraphy studies may aid the referring physician in diagnosis and treatment. There are instances where no literature is available to support the use of such studies in a particular clinical scenario. Thus, there is concern that reliance on CDS tools may diminish the appropriate use of an imaging study for a clinical indication not described in this document. At this time, the future impact on patient outcomes of CDS tools based on use of AUC is unknown.

QUALIFYING STATEMENTS

Study/Evidence Limitations

A limitation of the literature on GI transit studies is the lack of a gold standard to establish sensitivity and specificity values. Much of the literature, especially on measurement of GE and small and large-bowel transit, was established without comparison to another standard because no other methodology was available to investigate solid and liquid transit of a physiological meal within the GI tract.

IMPLEMENTATION OF THE AUC GUIDANCE

To develop broad-based multidisciplinary clinical guidance documents, SNMMI has been working with several other medical specialty societies. It is hoped that this collaboration will foster the acceptance and adoption of this guidance by other specialties. SNMMI has developed a multipronged approach to disseminate AUC for GI transit scintigraphy to all relevant stakeholders, including referring physicians, nuclear medicine physicians, and patients. The dissemination and implementation tactics will include a mix of outreach and educational activities targeted to each of these audiences. SNMMI will create case studies for its members, as well as for referring physicians, and make them available via online modules and webinars. These cases will cover the appropriate clinical scenarios for the use of GI transit scintigraphy studies. Related resources such as the systematic review supporting the development of these AUC, a list of upcoming education events on the AUC, factsheets, and other didactic materials will be made available on the SNMMI website. Live sessions will be held at the SNMMI annual and midwinter meetings, as well as at other relevant professional society meetings of referring physicians to highlight the importance and application of these AUC. SNMMI also aims to create a mobile application for these AUC for both Apple and Android platforms.

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APPENDIX A: WORKGROUP MEMBERS AND EXTERNAL REVIEWERS

Workgroup members: The members of the workgroup are Alan Maurer, MD (Chair), Temple University Hospital, Philadelphia, PA (SNMMI); Thomas L. Abell, MD, University of Louisville, Louisville, KY (AGA); Paige Bennett, MD, Wake Forest University Baptist Medical Center, Winston-Salem, NC (SNMMI); Jesus R. Diaz, MD, Texas Tech University Health Sciences Center, El Paso, TX (SNMMI); Lucinda A. Harris, MD, Mayo Clinic, Scottsdale, AZ (ACP); William Hasler, MD, University of Michigan Health System, Ann Arbor, MI (AGA); Andrei Iagaru, MD, FACNM, Stanford University, Stanford, CA (SNMMI); Kenneth L. Koch, MD, Wake Forest University Baptist Medical Center, Winston-Salem, NC (AGA); Richard McCallum, MD, Texas Tech University Health Sciences Center, El Paso, TX; Henry Parkman, MD, Temple University School of Medicine, Philadelphia, PA; Satish S. C. Rao, MD, Augusta University, Augusta, GA; Mark Tulchinsky, MD, FACNM, CCD, Milton S. Hershey Medical Center, Hershey, PA (ACNM).

TABLE 7
Relationships with Industry and Other Entities

Workgroup member	Reported Relationships
Abell, Thomas	ADEPT-GI
Bennett, Paige	None
Diaz, Jesus	None
Harris, Lucinda	Allergan
Hasler, William	None
Iagaru, Andrei	None
Koch, Kenneth	GSK
Maurer, Alan	Icon Medical, Part-time employee DraxImage Bayer Pharma Temple University
McCallum, Richard	Allergan Pharmaceuticals, Consulting/Speaking, Irritable Bowel San-X Pharmaceuticals, Consulting/Speaking, Irritable Bowel Synergy Pharmaceuticals, Consulting/Speaking, Irritable Bowel
Parkman, Henry	None
Rao, Satish	Forest Laboratories, Honorarium, Advisory Board/Consultant, Linaclotide, Constipation Progenity, Honorarium, Advisory Board/Consultant, Capsule Device, SIBO Ironwood Pharmaceuticals, Honorarium, Advisory Board/Consultant, Linaclotide, Constipation Sucampo Pharmaceuticals, Honorarium, Advisory Board/Consultant, Linaclotide, Constipation & IB In Control Medical, Stock, Advisory Board/Consultant, Lubiprostone, Constipation & IB In Control Medical, Stock, Advisory Board/Consultant, Biofeedback Device, Biofeedback Vibrant, Honorarium, Advisory Board, Vibrant Capsule, Constipation Synergy Pharmaceuticals, Honorarium, Advisory Board, Placanatide, Constipatoin & IBS Quin-Tron, Honorarium, Advisory Board, Breath Test Device, SIBO Valeant Pharmaceuticals, Honorarium, Advisory Board, Rifaximin, SIBO/IBS Progenity, Research Grant, Investigator, Capsule Device, SIBO Valeant Pharmaceuticals, Research Grant Investigator, Rifaximin, IBS Vibrant, Research Grant, Investigator, Vibrant Capsule, Constipation
Tulchinsky, Mark	None

External Reviewers: The external (peer) reviewers are Harvey A. Ziessman, MD, Johns Hopkins University, Baltimore, MD (SNMMI); Giuliano Mariani, MD, University of Pisa, Pisa, Italy; Michael J. Camilleri, MD, Mayo Clinic, Rochester, MN.

SNMMI staff support: The supporting staff from SNMMI are Sukhjeet Ahuja, MD, MPH, Director, Health Policy & Quality Department; Teresa Ellmer, MIS, CNMT, Senior Program Manager, Health Policy & Quality Department; Julie Kauffman, Program Manager, Health Policy & Quality Department.

APPENDIX B: DEFINITION OF TERMS AND ACRONYMS

ACNM: American College of Nuclear Medicine

ACP: American College of Physicians

AGA: American Gastroenterological Association

AUC: appropriate use criteria

CDS: clinical decision support

COI: conflict of interest

CVS: cyclic vomiting syndrome

DES: diffuse esophageal spasm

ETS: esophageal transit scintigraphy

FD: functional dyspepsia

GE: gastric emptying

GER: gastroesophageal reflux

GERD: gastroesophageal reflux disease

GES: gastric emptying scintigraphy

GI: gastrointestinal

IBS: irritable bowel syndrome

LES: lower esophageal sphincter

QUADAS-2: Quality Assessment of Diagnostic Accuracy-2

ReYGB: Roux-en-Y gastric bypass

SIBO: small intestinal bacterial overgrowth

SNMMI: Society of Nuclear Medicine and Molecular Imaging

SPECT: single-photon emission computed tomography

UCLA: University of California, Los Angeles

WGTS: whole-gut transit scintigraphy

APPENDIX C: DISCLOSURES AND CONFLICTS OF INTEREST

SNMMI rigorously attempted to avoid any actual, perceived, or potential conflicts of interest (COIs) that might have arisen as a result of an outside relationship or personal interest on the part of the workgroup members or external reviewers. Workgroup members were required to provide disclosure statements of all relationships that might be perceived as real or potential COIs. These statements were reviewed and discussed by the workgroup chair and SNMMI staff and were updated and reviewed by an objective third party at the beginning of every workgroup meeting or teleconference. The disclosures of the workgroup members can be found in Table 7. A COI was defined as a relationship with industry—including consulting, speaking, research, and nonresearch activities—that exceeds $5,000 in funding over the previous or upcoming 12-mo period. In addition, if an external reviewer was either the principal investigator of a study or another key member of the study personnel, that person's participation in the review was considered likely to present a COI. All reviewers were asked about any potential COI. A COI was also considered likely if an external reviewer or workgroup member was either the principal investigator or a key member of a study directly related to the content of this AUC document. All external reviewers were asked about any potential COI.

APPENDIX D: PUBLIC COMMENTARY

The workgroup solicited information from all communities through the SNMMI website and through direct solicitation of SNMMI members. The comments and input helped to shape the development of these AUC on the use of nuclear medicine in GI transit.

REFERENCES

1. Maqbool S, Parkman HP, Friedenberg FK. Wireless capsule motility: comparison of the SmartPill GI monitoring system with scintigraphy for measuring whole gut transit. *Dig Dis Sci.* 2009;54:2167–2174.
2. Rao SS, Mysore K, Attaluri A, Valestin J. Diagnostic utility of wireless motility capsule in gastrointestinal dysmotility. *J Clin Gastroenterol.* 2011;45:684–690.
3. Orthey P, Dadparvar S, Parkman HP, Maurer AH. Enhanced gastric emptying scintigraphy to assess fundic accommodation using intragastric meal distribution and antral contractility. *J Nucl Med Technol.* 2019;47:138–143.
4. Maurer AH, Parkman HP. Towards a fuller assessment of gastric motility in patients with upper GI dyspepsia: time to accommodate! *Am J Gastroenterol.* 2019;114:16–18.
5. Orthey P, Yu D, Van Natta ML, et al. Intragastric meal distribution during gastric emptying scintigraphy for assessment of fundic accommodation: correlation with symptoms of gastroparesis. *J Nucl Med.* 2018;59:691–697.
6. Fitch K, Bernstein SJ, Aguilar MD, Burnand B. *The RAND/UCLA Appropriateness Method User's Manual*. Santa Monica, CA: RAND; 2001.
7. Hendel RC, Patel MR, Allen JM, et al. Appropriate use of cardiovascular technology: 2013 ACCF appropriate use criteria methodology update: a report of the American College of Cardiology Foundation appropriate use criteria task force. *J Am Coll Cardiol.* 2013;61:1305–1317.
8. Institute of Medicine. *Clinical Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011.
9. Pacific Northwest Evidence-based Practice Center. *Systematic Review: Gastrointestinal Transit Imaging*. Portland, OR: Oregon Health and Science University; 2018.
10. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med.* 2011;155:529–536.
11. *AQA Principles for Appropriateness Criteria*. London, UK: Assessment and Qualifications Alliance; 2009.
12. Drane WE, Johnson DA, Hagan DP, Cattau EL, Jr. "Nutcracker" esophagus: diagnosis with radionuclide esophageal scintigraphy versus manometry. *Radiology.* 1987;163:33–37.
13. Jørgensen F, Hesse B, Tromholt N, Højgaard L, Stubgaard M. Esophageal scintigraphy: reproducibility and normal ranges. *J Nucl Med.* 1992;33:2106–2109.
14. Maurer AH, Parkman HP. Update on gastrointestinal scintigraphy. *Semin Nucl Med.* 2006;36:110–118.
15. Blackwell JN, Hannan WJ, Adam RD, Heading RC. Radionuclide transit studies in the detection of oesophageal dysmotility. *Gut.* 1983;24:421–426.
16. de Caestecker JS, Blackwell JN, Adam RD, Hannan WJ, Brown J, Heading RC. Clinical value of radionuclide oesophageal transit measurement. *Gut.* 1986;27:659–666.
17. Gilchrist AM, Laird JD, Ferguson WR. What is the significance of the abnormal oesophageal scintigram? *Clin Radiol.* 1987;38:509–511.
18. Mughal MM, Marples M, Bancewicz J. Scintigraphic assessment of oesophageal motility: what does it show and how reliable is it? *Gut.* 1986;27:946–953.
19. Parkman HP, Maurer AH, Caroline DF, Miller DL, Krevsky B, Fisher RS. Optimal evaluation of patients with nonobstructive esophageal dysphagia. Manometry, scintigraphy, or videoesophagography? *Dig Dis Sci.* 1996;41:1355–1368.
20. Tatsch K, Voderholzer WA, Weiss MJ, Schrottle W, Hahn K. Reappraisal of quantitative esophageal scintigraphy by optimizing results with ROC analyses. *J Nucl Med.* 1996;37:1799–1805.
21. Kochan P, Maurer AH, Parkman HP. Clinical role of esophageal and gastroesophageal reflux scintigraphy. *J Nucl Med.* 2002;43:162.
22. Isaacs PE, Martins JC, Edwards S, Fagg NL, Maisey MN, Sladen GE. Assessment of gastro-esophageal reflux disease: comparison of reflux scintigraphy with endoscopy biopsy and esophageal pH monitoring. *Hepatogastroenterology.* 1990;37:198–200.
23. Silver KH, Van Nostrand D. The use of scintigraphy in the management of patients with pulmonary aspiration. *Dysphagia.* 1994;9:107–115.
24. Kjellen G, Andersson P, Sandstrom S. Esophageal scintigraphy: a comparison with esophagoscopy. *Scand J Gastroenterol.* 1987;22:75–81.
25. Styles CB, Holt S, Bowes KL, Jewell L, Hooper HR. Gastroesophageal reflux and transit scintigraphy: a comparison with esophageal biopsy in patients with heartburn. *J Can Assoc Radiol.* 1984;35:124–127.
26. Falk GL, Beattie J, Ing A, et al. Scintigraphy in laryngopharyngeal and gastroesophageal reflux disease: a definitive diagnostic test? *World J Gastroenterol.* 2015;21:3619–3627.
27. Cuomo R, Sarnelli G, Grasso R, et al. Functional dyspepsia symptoms, gastric emptying and satiety provocative test: analysis of relationships. *Scand J Gastroenterol.* 2001;36:1030–1036.
28. Abell TL, Camilleri M, Donohoe K, et al. Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *Am J Gastroenterol.* 2008;103:753–763.
29. Donohoe KJ, Maurer AH, Ziessman HA, et al. Procedure guideline for adult solid-meal gastric-emptying study 3.0. *J Nucl Med Technol.* 2009;37:196–200.
30. Tougas G, Eaker EY, Abell TL, et al. Assessment of gastric emptying using a low fat meal: establishment of international control values. *Am J Gastroenterol.* 2000;95:1456–1462.
31. Sachdeva P, Kantor S, Knight LC, Maurer AH, Fisher RS, Parkman HP. Use of a high caloric liquid meal as an alternative to a solid meal for gastric emptying scintigraphy. *Dig Dis Sci.* 2013;58:2001–2006.
32. Solnes LB, Sheikhbahaei S, Ziessman HA. EnsurePlus as an alternative to the standardized egg gastric-emptying meal. *Clin Nucl Med.* 2019;44:459–461.
33. Somasundaram VH, Subramanyam P, Palaniswamy SS. A gluten-free vegan meal for gastric emptying scintigraphy: establishment of reference values and its utilization in the evaluation of diabetic gastroparesis. *Clin Nucl Med.* 2014;39:960–965.
34. Ziessman HA, Chander A, Clarke JO, Ramos A, Wahl RL. The added diagnostic value of liquid gastric emptying compared with solid emptying alone. *J Nucl Med.* 2009;50:726–731.
35. Ziessman HA, Okolo PI, Mullin GE, Chander A. Liquid gastric emptying is often abnormal when solid emptying is normal. *J Clin Gastroenterol.* 2009;43:639–643.
36. Camilleri M, Parkman HP, Shafi MA, Abell TL, Gerson L. Clinical guideline: management of gastroparesis. *Am J Gastroenterol.* 2013;108:18–37; quiz 38.

37. Bharucha AE, Kudva Y, Basu A, et al. Relationship between glycemic control and gastric emptying in poorly controlled type 2 diabetes. *Clin Gastroenterol Hepatol.* 2015;13:466–476.e461.

38. Fraser RJ, Horowitz M, Maddox AF, Harding PE, Chatterton BE, Dent J. Hyperglycaemia slows gastric emptying in type 1 (insulin-dependent) diabetes mellitus. *Diabetologia.* 1990;33:675–680.

39. Schvarcz E, Palmer M, Aman J, Horowitz M, Stridsberg M, Berne C. Physiological hyperglycemia slows gastric emptying in normal subjects and patients with insulin-dependent diabetes mellitus. *Gastroenterology.* 1997;113:60–66.

40. Sheik A, Anolik J, Maurer AH. Update on serum glucose and metabolic management of clinical nuclear medicine studies: current status and proposed future directions. *Sem Nuc Med.* 2019;49:411–421.

41. Pathikonda M, Sachdeva P, Malhotra N, Fisher RS, Maurer AH, Parkman HP. Gastric emptying scintigraphy: is four hours necessary? *J Clin Gastroenterol.* 2012;46:209–215.

42. Guo JP, Maurer AH, Fisher RS, Parkman HP. Extending gastric emptying scintigraphy from two to four hours detects more patients with gastroparesis. *Dig Dis Sci.* 2001;46:24–29.

43. Ziessman HA, Bonta DV, Goetze S, Ravich WJ. Experience with a simplified, standardized 4-hour gastric-emptying protocol. *J Nucl Med.* 2007;48:568–572.

44. Asano H, Tomita T, Nakamura K, et al. Prevalence of gastric motility disorders in patients with functional dyspepsia. *J Neurogastroenterol Motil.* 2017;23:392–399.

45. Farre R, Vanheel H, Vanuytsel T, et al. In functional dyspepsia, hypersensitivity to postprandial distention correlates with meal-related symptom severity. *Gastroenterology.* 2013;145:566–573.

46. Simren M, Tornblom H, Palsson OS, et al. Visceral hypersensitivity is associated with GI symptom severity in functional GI disorders: consistent findings from five different patient cohorts. *Gut.* 2018;67:255–262.

47. Quartero AO, de Wit NJ, Lodder AC, Numans ME, Smout AJ, Hoes AW. Disturbed solid-phase gastric emptying in functional dyspepsia: a meta-analysis. *Dig Dis Sci.* 1998;43:2028–2033.

48. Troncon LE, Herculano JR, Jr., Savoldelli RD, Moraes ER, Secaf M, Oliveira RB. Relationships between intragastric food maldistribution, disturbances of antral contractility, and symptoms in functional dyspepsia. *Dig Dis Sci.* 2006;51:517–526.

49. Berg P, McCallum RW. Dumping Syndrome. In: Rao SSC, Parkman HP, McCallum RW, eds. *Handbook of Gastrointestinal Motility and Functional Disorders*. Thorofare, NJ: SLACK; 2015:123–134.

50. McCallum RW SJ. Gastroparesis. In: PR McNally, ed. *GI/Liver Secrets Plus*. New Delhi, India: Saunders; 2015:87–94.

51. Buckles DC, Sarosiek I, McMillin C, McCallum RW. Delayed gastric emptying in gastroesophageal reflux disease: reassessment with new methods and symptomatic correlations. *Am J Med Sci.* 2004;327:1–4.

52. Sridhar KR, Lange RC, Magyar L, Soykan I, McCallum RW. Prevalence of impaired gastric emptying of solids in systemic sclerosis: diagnostic and therapeutic implications. *J Lab Clin Med.* 1998;132:541–546.

53. Marie I, Gourcerol G, Leroi AM, Menard JF, Levesque H, Ducrotte P. Delayed gastric emptying determined using the 13C-octanoic acid breath test in patients with systemic sclerosis. *Arthritis Rheum.* 2012;64:2346–2355.

54. Hejazi RA, Lavenbarg TH, McCallum RW. Spectrum of gastric emptying patterns in adult patients with cyclic vomiting syndrome. *Neurogastroenterol Motil.* 2010;22:1298–1302, e1338.

55. Pattathan MB, Hejazi RA, McCallum RW. Association of marijuana use and cyclic vomiting syndrome. *Pharmaceuticals (Basel).* 2012;5:719–726.

56. McCallum RW, Grill BB, Lange R, Planky M, Glass EE, Greenfeld DG. Definition of a gastric emptying abnormality in patients with anorexia nervosa. *Dig Dis Sci.* 1985;30:713–722.

57. Gonlachanvit S, Maurer AH, Fisher RS, Parkman HP. Regional gastric emptying abnormalities in functional dyspepsia and gastro-oesophageal reflux disease. *Neurogastroenterol Motil.* 2006;18:894–904.

58. Chedid V, Halawi H, Brander J, Burton D, Camilleri M. Gastric accommodation measurements by single photon emission computed tomography and two-dimensional scintigraphy in diabetic patients with upper gastrointestinal symptoms. *Neurogastroenterol Motil.* March 13, 2019 [Epub ahead of print].

59. Bouras EP, Delgado-Aros S, Camilleri M, et al. SPECT imaging of the stomach: comparison with barostat, and effects of sex, age, body mass index, and fundoplication. Single photon emission computed tomography. *Gut.* 2002;51:781–786.

60. Breen M, Camilleri M, Burton D, Zinsmeister AR. Performance characteristics of the measurement of gastric volume using single photon emission computed tomography. *Neurogastroenterol Motil.* 2011;23:308–315.

61. Lacy BE, Saito YA, Camilleri M, et al. Effects of antidepressants on gastric function in patients with functional dyspepsia. *Am J Gastroenterol.* 2018;113:216–224.

62. Ardila-Hani A, Soffer EE. Review article: the impact of bariatric surgery on gastrointestinal motility. *Aliment Pharmacol Ther.* 2011;34:825–831.

63. McCallum RW, Lin Z, Forster J, Roeser K, Hou Q, Sarosiek I. Gastric electrical stimulation improves outcomes of patients with gastroparesis for up to 10 years. *Clin Gastroenterol Hepatol.* 2011;9:314–319.e1.

64. Davis BR, Sarosiek I, Bashashati M, Alvarado B, McCallum RW. The long-term efficacy and safety of pyloroplasty combined with gastric electrical stimulation therapy in gastroparesis. *J Gastrointest Surg.* 2017;21:222–227.

65. Mekaroonkamol P, Dacha S, Wang L, et al. Gastric peroral endoscopic pyloromyotomy reduces symptoms, increases quality of life, and reduces health care use for patients with gastroparesis. *Clin Gastroenterol Hepatol.* 2019;17:82–89.

66. Deden LN, Cooiman MI, Aarts EO, et al. Gastric pouch emptying of solid food in patients with successful and unsuccessful weight loss after Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis.* 2017;13:1840–1846.

67. Vijgen GH, Schouten R, Bouvy ND, Greve JW. Salvage banding for failed Roux-en-Y gastric bypass. *Surg Obes Relat Dis.* 2012;8:803–808.

68. Sun WM, Doran SM, Jones KL, Davidson G, Dent J, Horowitz M. Long-term effects of pyloromyotomy on pyloric motility and gastric emptying in humans. *Am J Gastroenterol.* 2000;95:92–100.

69. McCallum RW, Polepalle SC, Schirmer B. Completion gastrectomy for refractory gastroparesis following surgery for peptic ulcer disease. Long-term follow-up with subjective and objective parameters. *Dig Dis Sci.* 1991;36:1556–1561.

70. Michiura T, Nakane Y, Kanbara T, et al. Assessment of the preserved function of the remnant stomach in pylorus-preserving gastrectomy by gastric emptying scintigraphy. *World J Surg.* 2006;30:1277–1283.

71. Takahashi T, Endo S, Nakajima K, Souma Y, Nishida T. Effect of rikkunshito, a Chinese herbal medicine, on stasis in patients after pylorus-preserving gastrectomy. *World J Surg.* 2009;33:296–302.

72. Knight LC. Update on gastrointestinal radiopharmaceuticals and dosimetry estimates. *Semin Nucl Med.* 2012;42:138–144.

73. Antoniou AJ, Raja S, El-Khouli R, et al. Comprehensive radionuclide esophagogastrointestinal transit study: methodology, reference values, and initial clinical experience. *J Nucl Med.* 2015;56:721–727.

74. Bonapace ES, Maurer AH, Davidoff S, Krevsky B, Fisher RS, Parkman HP. Whole gut transit scintigraphy in the clinical evaluation of patients with upper and lower gastrointestinal symptoms. *Am J Gastroenterol.* 2000;95:2838–2847.

75. Maurer AH. Gastrointestinal motility, part 2: small-bowel and colon transit. *J Nucl Med Technol.* 2016;44:12–18.

76. Ning Y, Lou C, Huang Z, et al. Clinical value of radionuclide small intestine transit time measurement combined with lactulose hydrogen breath test for the diagnosis of bacterial overgrowth in irritable bowel syndrome. *Hell J Nucl Med.* 2016;19:124–129.

77. Seidl H, Gundling F, Pfeiffer A, Pehl C, Schepp W, Schmidt T. Comparison of small-bowel motility of the human jejunum and ileum. *Neurogastroenterol Motil.* 2012;24:e373–380.

78. Maurer AH, Camilleri M, Donohoe K, et al. The SNMMI and EANM practice guideline for small-bowel and colon transit 1.0. *J Nucl Med.* 2013;54:2004–2013.

79. Camilleri M, Hasler WL, Parkman HP, Quigley EM, Soffer E. Measurement of gastrointestinal motility in the GI laboratory. *Gastroenterology.* 1998;115:747–762.

80. Balan K, Alwis L, Sonoda LI, Pawaroo D, Parry-Jones DR, Middleton S. Utility of whole gut transit scintigraphy in patients with chronic gastrointestinal symptoms. *Nucl Med Commun.* 2010;31:328–333.

81. Shahid S, Ramzan Z, Maurer AH, Parkman HP, Fisher RS. Chronic idiopathic constipation: more than a simple colonic transit disorder. *J Clin Gastroenterol.* 2012;46:150–154.

82. Stivland T, Camilleri M, Vassallo M, et al. Scintigraphic measurement of regional gut transit in idiopathic constipation. *Gastroenterology.* 1991;101:107–115.

83. Miller MA, Parkman HP, Urbain JL, et al. Comparison of scintigraphy and lactulose breath hydrogen test for assessment of orocecal transit: lactulose accelerates small bowel transit. *Dig Dis Sci.* 1997;42:10–18.

84. Prather CM, Camilleri M, Zinsmeister AR, McKinzie S, Thomforde G. Tegaserod accelerates orocecal transit in patients with constipation-predominant irritable bowel syndrome. *Gastroenterology.* 2000;118:463–468.

85. Szarka LA, Camilleri M. Methods for the assessment of small-bowel and colonic transit. *Semin Nucl Med.* 2012;42:113–123.

86. Suri J, Kataria R, Malik Z, Parkman HP, Schey R. Elevated methane levels in small intestinal bacterial overgrowth suggests delayed small bowel and colonic transit. *Medicine (Baltimore).* 2018;97:e10554.

87. Zhao J, Zheng X, Chu H, et al. A study of the methodological and clinical validity of the combined lactulose hydrogen breath test with scintigraphic oro-cecal transit test for diagnosing small intestinal bacterial overgrowth in IBS patients. *Neurogastroenterol Motil.* 2014;26:794–802.

88. Cuoco L, Montalto M, Jorizzo RA, et al. Eradication of small intestinal bacterial overgrowth and oro-cecal transit in diabetics. *Hepatogastroenterology.* 2002;49:1582–1586.

89. Rana SV, Sharma S, Malik A, et al. Small intestinal bacterial overgrowth and orocecal transit time in patients of inflammatory bowel disease. *Dig Dis Sci.* 2013;58:2594–2598.

90. Wegener M, Adamek RJ, Wedmann B, Jergas M, Altmeyer P. Gastrointestinal transit through esophagus, stomach, small and large intestine in patients with progressive systemic sclerosis. *Dig Dis Sci.* 1994;39:2209–2215.

91. Hasler WL, May KP, Wilson LA, et al. Relating gastric scintigraphy and symptoms to motility capsule transit and pressure findings in suspected gastroparesis. *Neurogastroenterol Motil.* 2018;30.

92. Camilleri M, Brown ML, Malagelada JR. Impaired transit of chyme in chronic intestinal pseudoobstruction. Correction by cisapride. *Gastroenterology.* 1986;91:619–626.

93. Camilleri M, Zinsmeister AR, Greydanus MP, Brown ML, Proano M. Towards a less costly but accurate test of gastric emptying and small bowel transit. *Dig Dis Sci.* 1991;36:609–615.

94. Greydanus MP, Camilleri M, Colemont LJ, Phillips SF, Brown ML, Thomforde GM. Ileocolonic transfer of solid chyme in small intestinal neuropathies and myopathies. *Gastroenterology.* 1990;99:158–164.

95. Camilleri M, Ford AC, Mawe GM, et al. Chronic constipation. *Nat Rev Dis Primers.* 2017;3:17095.

96. Chitkara DK, Bredenoord AJ, Cremonini F, et al. The role of pelvic floor dysfunction and slow colonic transit in adolescents with refractory constipation. *Am J Gastroenterol.* 2004;99:1579–1584.

97. Camilleri M. Scintigraphic biomarkers for colonic dysmotility. *Clin Pharmacol Ther.* 2010;87:748–753.

98. Panganamamula KV, Parkman HP. Chronic intestinal pseudo-obstruction. *Curr Treat Options Gastroenterol.* 2005;8:3–11.

99. Charles F, Camilleri M, Phillips SF, Thomforde GM, Forstrom LA. Scintigraphy of the whole gut: clinical evaluation of transit disorders. *Mayo Clin Proc.* 1995;70:113–118.

100. Maurer AH, Krevsky B. Whole-gut transit scintigraphy in the evaluation of small-bowel and colon transit disorders. *Semin Nucl Med.* 1995;25:326–338.

101. Read NW, Al-Janabi MN, Holgate AM, Barber DC, Edwards CA. Simultaneous measurement of gastric emptying, small bowel residence and colonic filling of a solid meal by the use of the gamma camera. *Gut.* 1986;27:300–308.

102. Tursi A. Gastrointestinal motility disturbances in celiac disease. *J Clin Gastroenterol.* 2004;38:642–645.

103. Kamm MA, Hawley PR, Lennard-Jones JE. Outcome of colectomy for severe idiopathic constipation. *Gut.* 1988;29:969–973.

104. van der Sijp JR, Kamm MA, Nightingale JM, et al. Disturbed gastric and small bowel transit in severe idiopathic constipation. *Dig Dis Sci.* 1993;38:837–844.

105. McCoy JA, Beck DE. Surgical management of colonic inertia. *Clin Colon Rectal Surg.* 2012;25:20–23.