Continuing Education: Gastrointestinal Motility
Part 2: Small Bowel and Colon transit

Alan H. Maurer, MD

Corresponding Author: Alan H. Maurer, M.D.,
Director Nuclear Medicine and Molecular Imaging
Temple University Hospital and School of Medicine
Broad and Ontario Streets, Philadelphia PA 19140
Email: amaurer@temple.edu
FAX: 215-707-2059

Running title: Small bowel and colon motility studies
Key Words: Gastrointestinal scintigraphy, small bowel transit scintigraphy, colon transit scintigraphy, whole gut transit scintigraphy
INTRODUCTION

Overview

Dyspeptic symptoms related to dysmotility originating from the small bowel or colon usually include abdominal pain, diarrhea or constipation. In many cases however symptoms overlap and it is difficult to differentiate whether symptoms originate in the upper or lower gastrointestinal (GI) tract or both. Studies of small bowel motility have shown a correlation between small bowel contractions and severity of symptoms in gastroparesis (1). Indications for small bowel and colon transit scintigraphy include but are not limited to dyspepsia, irritable bowel syndrome, chronic constipation, chronic diarrhea, chronic idiopathic intestinal pseudoobstruction, scleroderma, celiac disease, and malabsorption. Small and large-bowel motility is the result of complex GI contractions that promote the aboral movement of intestinal chyme and indigestible solids. It is recommended that GI transit studies be used to localize the potential site of disease and guide therapy (2). A final diagnosis of a primary motility disorder by scintigraphy should not be made until an anatomic or structural cause (e.g., tumor, stricture, malrotation) for abnormal transit has been excluded by imaging or endoscopy.

Non scintigraphic methods for measuring bowel transit include hydrogen breath tests for small bowel transit and radioopaque markers for colon transit. Wireless motility capsules measure pH, pressure, and temperature throughout the gastrointestinal tract and are capable of measuring gastric emptying, small bowel and colonic transit times. Indigestible solids such as radioopaque markers (4 mm) and the wireless motility capsule (27 x12 mm) do not move through the gastrointestinal tract in the same manner as a physiologic meal (3, 4). The American Neurogastroenterology and Motility Society task force on gastrointestinal transit has stated that “the scintigraphic method is the only one that reliably allows the determination of both total and regional transit times” for gastrointestinal and colon transit (2). In a more recent report this same organization together with the European Society of Neurogastroenterology and Motility have stated that scintigraphy is recommended for “detection of altered small-intestine transit in subjects with a suspected diffuse gastrointestinal motility disorder” and that colon transit scintigraphy “offers reproducible and accurate performance.” This report further states scintigraphy “is indicated to measure whole gut and regional colonic transit in patients with suspected colonic motility disorders or more diffuse disorders involving the stomach or small intestine” (5)

While scintigraphic methods for measuring small bowel and colon transit have been in use for at least 20 years they have not gained widespread clinical use, in large part, because of their lack of standardization. The recent published Society of Nuclear Medicine and Molecular Imaging(SNMMI) joint European Association of Nuclear Medicine(EANM) guideline has been recognized as an important “step towards standardization” (6). As an additional impediment to wider clinical use in the United States, there have been no Current Procedural Terminology (CPT) codes available for reporting and reimbursement. New CPT codes have been recently presented to and accepted by the American Medical Association CPT Panel. It is anticipated that these will soon be available.

General Methodology
As for the esophageal transit and gastric emptying studies described in Part 1, the two most commonly used radioisotopes for small bowel and colon gastrointestinal transit studies are $^{99m}$Tc and $^{111}$In. $^{67}$Ga complexes have also been used for colon transit studies which extend over several days(7).

The reader is referred to the recently published SNMMI and EANM Practice Guideline for Small-Bowel and Colon Transit for more in depth description of the technical details on performing these studies including patient preparation, image acquisition and processing (8). This CME review will highlight technical details for performing scintigraphic small bowel and colon transit studies and describe the normal and abnormal physiology and important imaging findings needed for clinical interpretation of these studies.

Small-bowel and colon transit scintigraphy are typically performed alone or, with minor modifications, as a continuation of a gastric emptying study. Three methods have been reported. The most commonly employed method uses a mixed solid–liquid gastric-emptying meal(7,8). This method involves radiolabeling the liquid phase of a gastric-emptying meal with $^{111}$In-DTPA. As the liquid mixes with the intestinal chyme, transit of the radiopharmaceutical is used to assess small-bowel and colon transit. If the solid phase gastric emptying study is not requested the solid meal is administered but without radiolabeling to maintain the standardized meal content. A second method uses a specially prepared, delayed-release, methacrylate resin-coated capsule containing $^{111}$In -labeled activated charcoal particles. The coated capsule dissolves on reaching the alkaline terminal ileum, releasing the radioisotope into the lumen for subsequent measurement of colon transit (9). The third uses $^{67}$Ga-complexes to substitute for $^{111}$In -DTPA as part of a mixed solid-liquid meal (10,11).

**Small Bowel Transit Studies**

Measurement of small bowel transit is complex because the input of a meal into the small intestine is dependent on gastric emptying and small intestinal chyme spreads out over a large distance as it progresses toward the colon. The function of the small bowel is to transport food as it empties from the stomach and to mix it with bile, pancreatic and intestinal secretions to facilitate absorption over the bowel mucosal surface. 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(9). This process, although irregular, results in a net overall progression of chyme towards the colon. Periodic more organized peristaltic contractions occur which originate in the stomach and propagate throughout the small intestine. These specialized contractions called the migrating motor complex serve a housekeeping role to sweep undigested material through the intestines. While more rapid peristalsis and transit occur in the duodenum and jejunum it has been observed that small intestinal contents slow particularly in the terminal ileum before passing the ileocecal valve and moving into the colon. This results in a buildup of radiotracer activity in the terminal ileum which functions as a reservoir for chyme before it passes into the colon(10). (Figure 1)

The ileocolonic junction between the terminal ileal reservoir and the cecum regulates the flow of intestinal chime from the small bowel into the colon. (Figure 2A) Studies in animals and humans have confirmed that pulsatile filling of the cecum occurs associated with propagating ileal
contractions. The daily flow of chyme across the ileocolonic junction is estimated at 1-2 liters with increased flow seen postprandially (11). Early scintigraphic studies which demonstrated discrete bolus transfers of intestinal chyme across the ileocolonic junction also showed that such bolus transfers are more frequent within the first hour after a meal than during the fasting state (12). More recently scintigraphy has been combined with manometric pressure recordings to measure flow across the iliocolic valve. By direct instillation of radioisotope through a nasocolonic catheter that has multiple recording sites extending from the terminal ileum to the proximal colon discrete episodic movements of luminal flow have been recorded (13). (Figure 2B) Such studies have further demonstrated the role that the terminal ileum plays in initial storage of intestinal chyme before permitting flow into the colon.

The simplest conceptual 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. Accurate definition of the leading edge (first visualized arrival of activity in the cecum) however requires frequent imaging (every 10 to 15 minutes) and prolonged imaging time because of the stasis that occurs in the terminal ileum. Hydrogen breath testing which measures leading edge transit does correlate well with scintigraphy. In one study orocecal transit times were 56 4 minutes for lactulose breath testing and 43 4 minutes for simultaneously performed scintigraphy. Lactulose however itself speeds small bowel transit and accelerates orocecal transit. Without lactulose, the scintigraphic orocecal transit time was 231 37 minutes (14).

Small-bowel orocecal transit time will vary depending on the meal administered. Using resin pellets mixed with a meal, orocecal transit time in healthy individuals ranged from 151 to 290 min (18). Using the liquid phase of a mixed solid–liquid meal, small-bowel transit time ranged from 72 to 392 min in normal individuals(15). In some cases, there may be prolonged stasis of activity in the terminal ileal reservoir particularly when no second meal is administered. This results in the need for prolonged imaging beyond 6 hours to see progression of activity into the cecum or ascending colon which makes orocecal transit time measurements impractical.

An alternative scintigraphic measurement of small bowel transit does not attempt to characterize either the complex temporal or spatial peristaltic small bowel patterns or leading edge transit but rather simply measures the overall bulk movement of radiotracer as it moves distally into the terminal ileum. Typically the orally administered radiolabeled meal collects in the terminal ileal reservoir area which is identified as an area of progressive increasing counts before visualization of the cecum or ascending colon. (Figure 3) This region is also referred to as the ileocolonic junction (16, 17). The progressive buildup of activity in the terminal ileum can easily be measured and used as an index of small bowel motility(18). The recent SNMMI/EANM guideline on small bowel transit recommends use of the percentage of administered liquid meal that has accumulated in the terminal ileum at 6 hours after meal ingestion as a simple index of small bowel transit. Normal small bowel transit will show that > 40% of administered activity has progress into the terminal ileum and/or passed into the cecum and ascending colon at 6 hours(19). (Figure 1) Delayed small bowel transit typically shows multiple loops of small bowel persisting at 6 hours with little (< 40%) or no arrival of activity in the terminal ilium reservoir area. (Figure 3)

The amount of colon filling at 6 hours has also been used as an index of small-bowel transit. The range for normal filling of the colon at 6 hours using nondigestible particles is 11%– 70%. The range for digestible solids is 43%–95% with rapid small-bowel transit defined as a cecal arrival time of < 90 minutes(20).
Deconvolution analysis of bowel transit was first introduced by Malagelada in 1984 to correct for how the rate of gastric emptying affects small bowel transit measurement (21). A modified approach was later proposed by Brinch in 1999(22). These methods yield an expected small intestine time–activity curve based on instantaneous gastric emptying. The curve can be used to calculate a mean transit time for the bulk of radiolabeled material. Deconvolution methods however require frequent(every 30 min) imaging and lengthy acquisitions until all tracer has passed into the colon. A further simplification to deconvolution was proposed by Read in 1986 and is based on subtraction of 50% gastric-emptying time from the time to 50% colon filling (23).

Colon Transit Studies

As discussed above the ileocolonic junction controls how liquid small bowel contents enter the colon. The motility of the colon controls slow mixing and movement of its contents to accomplish absorption of water and transformation of liquid to semisolid/solids in the sigmoid colon. Ultimately controlled defecation occurs 1-2 times daily in normal individuals. Three distinct colon contraction patterns with different spatiotemporal patterns have been described. Rhythmic phasic contractions aided by tonic contractions cause slow distal propulsion and mixing. Infrequent giant migrating contractions produce mass movements.

Therapy for patients with chronic constipation depends on identifying whether there is colonic inertia, generalized slow colon transit, pelvic floor dysfunction, functional outlet obstruction or irritable bowel syndrome. Colonic motility testing is used to determine if a patient with symptoms of constipation has abnormal colon transit and whether a specific area of the colon is involved (24, 25). Invasive manometric and myoelectric devices for studying colon transit are inconsistent, difficult to use, and have a limited number of recording sites. Imaging of colon transit can be performed using serial radiographs and radiopaque markers. Radiographic markers are ingested with a meal and radiographs are obtained to count the number of markers in segments of the colon. Such markers however are not physiologic compared to transit of intestinal chyme. The rate of transit of solid particles is size dependent, and intracolonic visualization and localization can be difficult given limited anatomic landmarks. Radiopaque markers however have been shown to correlate well with scintigraphic measurement of colon transit (26, 27). The wireless motility capsule is also used to measure colon transit. The colon transit time is the time from entry of the capsule into the cecum, determined by a sudden drop of pH, until the time the capsule passes out of the colon which can be determined by a sudden drop in the temperature reading accompanied by loss of pressure recording. In a large multicenter study of constipated patients comparing the wireless motility capsule to radiopaque markers, there was an overall agreement of 87% for classifying patients as either slow or normal colon transit (28). Colon transit scintigraphy is indicated for measuring colon transit in patients with constipation or diarrhea and can be used as a marker to validate new treatments and to direct patient care (19, 29).

Both 111In-DTPA(2.8 day half-life) and 67Ga-citrate(3.2 day half-life) when given orally for colon transit scintigraphy are non absorbable and have half-lives long enough to permit several days of imaging. 111In-DTPA is typically available as a sterile, single-use vial for intrathecal administration. Most centers which perform colon transit studies administer it orally in divided doses to keep unit dose expenses low. Ga-67 citrate has been used as an alternative because of
lower cost and availability and lower whole body radiation exposure (Table 1) which is of particular concern for pediatric use (30).

Two methods that use oral $^{111}$In-DTPA to measure colon transit have been in most common use. The reader is referred to the recent SNMMI and EANM Practice Guideline for Small-Bowel and Colon Transit 1.0 for more complete technical details (8). One method (Mayo Clinic, Rochester, Minnesota) requires preparation of a resin-coated capsule which is designed to dissolve at a pH between 7.2 and 7.4 in the environment of the ileum (pH 7.4) (31). An alternate method (Temple University, Philadelphia, Pennsylvania) which does not require fabrication of a special capsule is to give the $^{111}$In-DTPA as a part of a standard solid-liquid GE meal (18). To quantitate colon transit, a geometric center has been defined as a measure of the progression of colonic radiotracer activity. To calculate the geometric center, the colon is divided into anatomic regions each with a numerical value. Using the solid-liquid meal method, a seven segment analysis includes: cecum–ascending colon (1), hepatic flexure (2), transverse colon (3), splenic flexure (4), descending colon (5), rectosigmoid colon (6), and excreted stool (7). The geometric center is a weighted average of the counts in each region (Figure 4). A low geometric center (1 to 2) indicates that the center of the activity is in the proximal colon, and a higher geometric center (5 to 7) indicates that it has progressed to the left side of the colon or has been eliminated in the stool. A simpler five segment region analysis has also been described (8). Using the geometric center, a simple single numerical value is used to measure the transit of activity through the colon.

Using the mixed solid-liquid meal method, colon images are acquired at 24, 48, and 72 hours. If the geometric center at 48 hours is less than 4.1 (proximal to the splenic flexure), no further imaging is needed because colon transit is delayed. If the geometric center is greater than 4.1 but less than 6.4, an image at 72 hours should be obtained to exclude functional outlet obstruction. The normal mean (± 1 SD) geometric center values are 4.6 ± 1.5 at 24 hours, 6.1 ± 1.0 at 48 hours, and 6.6 ± 0.19 at 72 hours.

There are three major patterns of slow colon transit: generalized slow transit with diffuse retention throughout the length of the colon; marked right sided retention proximal to the splenic flexure (colonic inertia), and retention in the rectosigmoid (functional rectosigmoid obstruction) (32) (Figure 5). In adults with diarrhea, accelerated colon transit can be confirmed with a geometric center greater than 6.1 (at or beyond the rectosigmoid colon) at 24 hours. Colon transit studies in pediatric patients with chronic constipation show a subgroup who have rapid proximal colon transit (> 25% of the tracer beyond the hepatic flexure at 6 hours and/or > 25% beyond the end of the descending colon at 24 hours) (33).

**Whole Gut Transit Studies (Combined solid-liquid gastric emptying with small bowel and colon transit study)**

Whole gut transit scintigraphy refers to a combined study which includes measurement of gastric emptying, small bowel and colon transit after administration of a dual-isotope, solid-liquid meal. 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 (e.g., structural, metabolic, myopathic or neuropathic) is suspected. In a study at the Mayo Clinic, 40% of patients
referred for upper GI symptoms, constipation, or diarrhea were found to have an organic cause of symptoms but 60% were diagnosed as functional (34). Colon transit is slowed more commonly in patients with organic disease and normal in many patients with functional complaints of constipation. In a study to evaluate the clinical utility of whole gut transit scintigraphy, organic disease was found in many patients with an initial suspected functional disorder and the initial diagnosis was changed in 45% patients and patient management was changed in 67% patients (19).

As noted above whole gut transit scintigraphy “is indicated to measure whole gut and regional colonic transit in patients with suspected colonic motility disorders or more diffuse disorders involving the stomach or small intestine” (5).

Patients with diarrhea-predominant irritable bowel syndrome have shorter small bowel transit and rapid colonic filling whereas constipated patients have slower small bowel transit and delayed colonic filling (17). Gastrointesinal 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 (35). Whole gut scintigraphy therefore can play an important role in evaluating patients with suspected symptoms from celiac disease.

Whole gut transit scintigraphy is most helpful for evaluating patients with constipation. Many patients with severe idiopathic constipation have prominent upper GI symptoms. It is important to exclude significant upper GI dysmotility in such patients before surgery because subtotal colectomy may not correct their symptoms (36). Colectomy should be performed only if a transit abnormality is limited to the colon. In a study of patients with severe idiopathic constipation with upper gastrointestinal symptoms (12 constipated patients), 3 of 4 with upper gastrointestinal symptoms had abnormal gastric emptying and small bowel transit in addition to delayed colon transit (37).

Intestinal pseudo-obstruction is a severe motility disorder where 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. The presence of delayed gastric emptying, delayed small bowel transit, and slow colon transit seen with whole gut transit scintigraphy helps to establish a diagnosis of idiopathic intestinal pseudo-obstruction (38).

**Conclusion**

Because of the difficulty often encountered to decide if a patient’s symptoms originate in the upper or lower GI tract, GI transit scintigraphy is uniquely suited to provide a noninvasive, quantitative and physiologic method for determining if there is a motility disorder which affects the stomach, small bowel, or colon. Small bowel and colon transit studies can be obtained singularly or together with gastric emptying studies following oral administration of an appropriately radiolabeled meal. Newly published standards for performing these studies and the anticipated arrival of new CPT codes in the US for small bowel and colon transit will hopefully increase their availability and more widespread utilization.
REFERENCES


Figure 1. Normal small bowel transit following liquid $^{111}$In-DTPA meal (anterior views only). Sequential images from a liquid gastric emptying study are shown. Over time early diffuse small bowel activity demonstrates later progressive accumulation in the terminal ilium reservoir (oval region of interest). There is > 60% of total activity already in the terminal ileum by 4 hours (240 minutes). This is followed by activity further progressing into the cecum-ascending colon (arrow) at 6 hours (300 minutes). Following this, activity progresses to fill the ascending colon with 100% of activity having completed transit through the small bowel at 6 hours (360 minutes).
Figure 2A. These images demonstrate how the location of the ileocolonic junction is defined scintigraphically in relationship to the terminal ileum and proximal colon and how regions of interest have been defined to study the coordination of manometric pressure recordings with luminal flow shown in Figure 2B. (Reprinted with permission from (13))

Figure 2B. Serial images show how radiotracer activity in the terminal ileum and cecum can be linked to simultaneous pressure recordings. With this technique both antegrade and retrograde flow across the ileocolonic junction has been observed. Transient retrograde flow can occur across the
ileocecal valve but the ileum is capable of rapidly clearing any colonic reflux. Several studies have shown that ileal propagative waves are coordinated with cecal propagating waves. (Reprinted with permission from (13))
Figure 3. Delayed small bowel transit following liquid $^{111}$In-DTPA meal (anterior views only). In contrast to Figure 1 there is delayed small bowel transit with images showing persistent, diffuse activity within multiple proximal loops of small bowel and no arrival of activity in the terminal ileum reservoir or ileocolonic junction by 6 hours.
Geometric center = \( \text{sum} \left( \frac{\text{ROI}_i}{\text{total counts}} \right) \times i \) 
\[(i = 1-7)\]

**Regions of interest in 7-segment method**

- Hepatic flexure
- Ascending colon & cecum
- Transverse
- Descending colon
- Rectosigmoid colon
- Splenic flexure
- Excreted feces

(Calculated: total initial abdominal counts – amount retained)

Figure 4. Colon geometric center analysis. The 6 regions of interest used to define each segment and formula for calculation are shown.
Normal colon transit shows activity predominantly in the right colon at 24 hours with near complete emptying at 72 hours. Colonic inertia demonstrates failure of activity to progress beyond the splenic flexure at 48 and 72 hours. Functional rectosigmoid outlet obstruction shows normal progression from the right colon to the left side of the colon but with retention in the rectosigmoid colon at 72 hours. Generalized slow colon transit shows a diffuse pattern of colonic retention at 72 hours.

Figure 5. Normal and Abnormal Colon Transit Patterns. (Marker is placed on right iliac crest for reference)
Table 1 Comparison adult dose estimates for oral $^{111}$In-DTPA vs $^{67}$Ga-citrate

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Dose (MBq)</th>
<th>Effective dose (mSv)</th>
<th>Absorbed dose (mSv)</th>
<th>Absorbed dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower Large Intestine</td>
<td>Lower Large Intestine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Normal</td>
<td>Constipated</td>
</tr>
<tr>
<td>$^{111}$In - DTPA</td>
<td>4</td>
<td>1.20</td>
<td>6.4</td>
<td>11.6</td>
</tr>
<tr>
<td>$^{67}$Ga - citrate</td>
<td>4</td>
<td>0.74</td>
<td>6.5</td>
<td>11.8</td>
</tr>
</tbody>
</table>

Modified from (7).