

Motility and Transit in the Small Bowel

J. Barnert

Med. Klinik 3, Klinikum Augsburg, Germany

Introduction

The direct assessment of the myoneural function of the small bowel is not yet possible in the clinical setting. Present studies in this field are restricted to the measurement of the intraluminal pressure and the transport of material placed in the lumen using for example isotopes, radioopaque markers and hydrogen breath tests (using nonabsorbable carbohydrates as a marker).

Motility

Physiology of small bowel motility

Although the morphology of the alimentary tract can simplistically be described as a muscular tube extending from the mouth to the anus, the motility of the gastrointestinal tract is organized in a complex way. The contractions of the gastrointestinal tract can be divided into two types:

- **Tonic contractions** are long lasting. Tone is a state of stable and protracted contraction of the smooth muscle. Tonic contractions form sphincters and haustral indentations of the colon. They are prominent in the proximal stomach and the gallbladder.
- **Phasic contractions** are short and (more and less) rhythmic. They predominate in the tubular esophagus, the distal stomach and the small intestine. Peristaltic phasic contractions transport a bolus aborally, simultaneous contractions mix and grind the intestinal content.

In clinical practice manometry mainly measures phasic contractions. For measurement of tonic contractions in scientific studies a barostat device must be used.

The **motility pattern** in the small intestine in the fasting state is different from that after a meal (postprandial):

In the **fasting (interdigestive) state** the small intestine exhibits a recurring cycle of motor phenomena, the so called migrating motor complex (MMC). Periods alternate with periods of quiescence. It cycles every 50–220 minutes. The fasting (interdigestive) motility is divided into three distinct phases (Fig. 1):

- **Phase 1** exhibits no or little motor activity lasting 40–60% of the cycle length.
- **Phase 2**, occupying 20 to 30% of the cycle length. It exhibits random and irregular phasic contractions. Phase 2 leads to phase 3.
- **Phase 3** is the most distinct phase, characterized by a band of regular contractions ('activity front'). It cycles every 50 – 220 minutes. The maximal contractile frequency is determined by the slow wave frequency (i.e. 11/min in the duodenum, 7-8/min in the ileum). The band of contractions lasts for about 6-8 minutes and migrates aborally with 10% reaching the ileum. The velocity of migration of the phase 3 complex is 6-8 cm/min in the upper jejunum and about 1 to 2 cm/min in the ileum. Phase 3 complexes propagate over longer distances
- an phase 2 contractions. Two thirds of the phase 3 complexes originate in the stomach. Origin of phase 3 in the duodenum is observed in less than one third of the cycles and only rarely in the proximal jejunum.

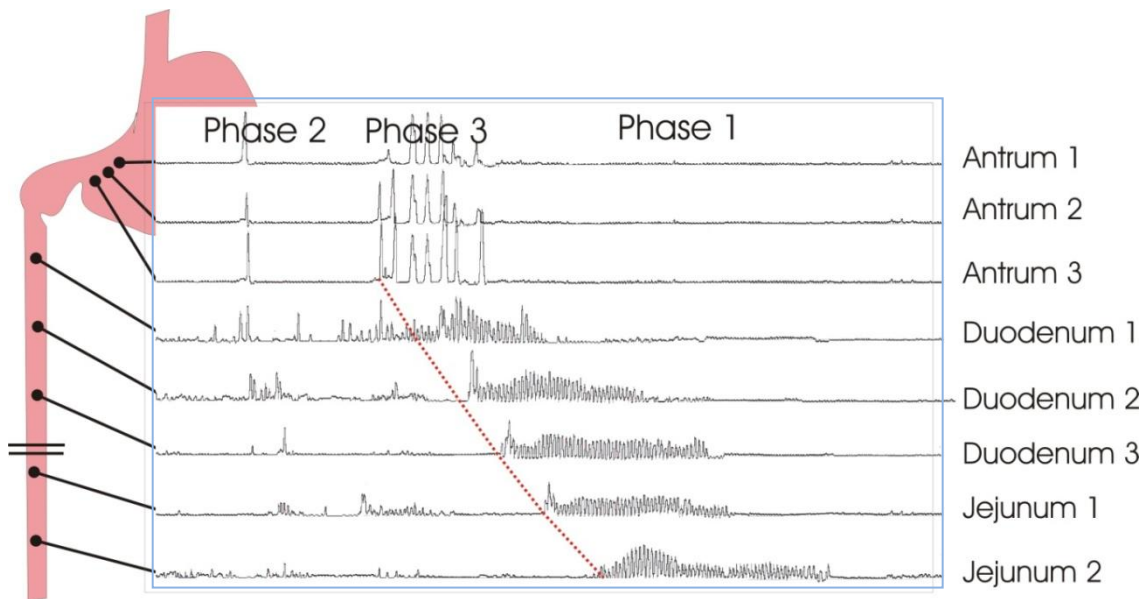


Fig. 1. *Intraluminal pressure recordings (manometry) of the fasting motility from the stomach (antrum), duodenum and jejunum of a healthy person. Phases 1 to 3 are indicated. The propagation front of phase 3 is shown by a dashed line (--).*

If food is ingested, the cyclic fasting (interdigestive) pattern is abolished for 3-10 hours and replaced by a band of random contractions called *fed pattern* (Fig. 2). It resembles phase 2 contractions of the fasting pattern. The duration of this fed pattern depends on the caloric value of the food and the type of food components. The contractions observed in the fed pattern are both stationary / segmental and propulsive. The stationary / segmental contractions squeeze the small food particles against the villi to increase absorption. The propulsive contractions transport the chyme over short segments.

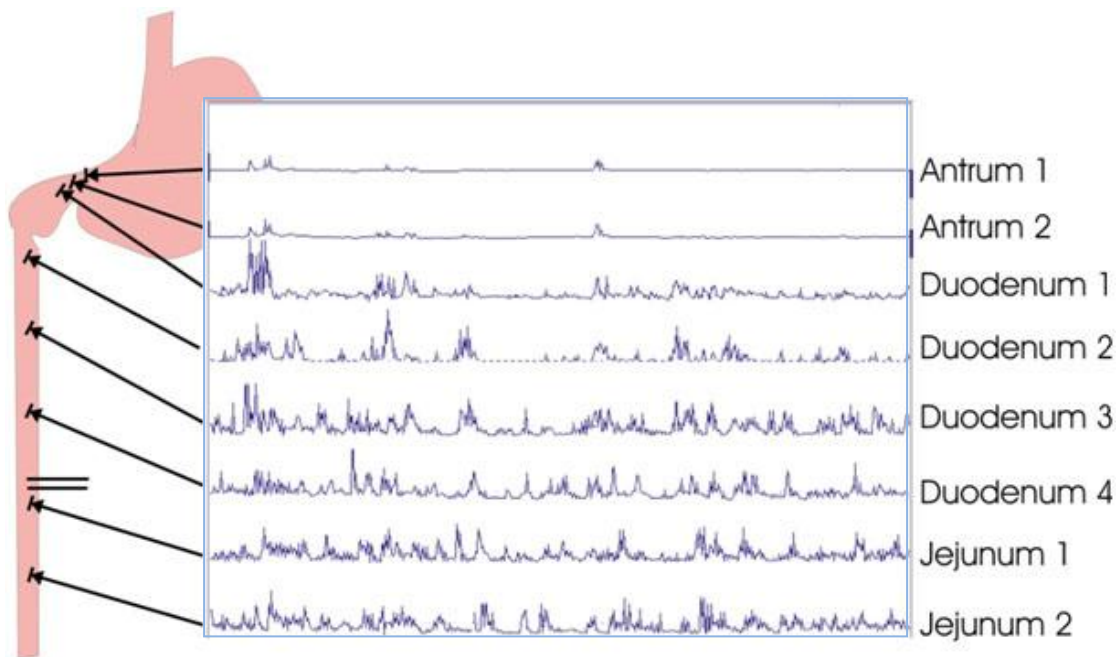


Fig. 2. *Intraluminal pressure recordings (manometry) of a typical fed (postprandial) motility from the gastric antrum, duodenum and jejunum of a healthy person. Note the irregular but persistent phasic pressure activity.*

Motility and transit

Phase 3 of the *interdigestive (fasting) motility* was said to sweep the fasting gut clear of accumulated debris and was compared to a ‘house-keeper’. But observations in animal experiments [1] suggested that transit rates are maximal just before phase 3, in late phase 2. It was hypothesized by the authors of this animal study that phase 3 may function as a ‘back stop’ serving as a barrier to prevent backflow of luminal content into the quiescent part of the intestine. The intestinal transit time in dogs were shorter in the fed state than in phase 2 of the interdigestive state, the beginning of phase 3 and in phase 1 (Fig. 3). In this experiment the propagation of phase 3 of the MMC correlated in a almost linear way with the velocity of a fluid bolus injected just before the beginning of the activity front of phase 3. In humans Sarna et al. [2] observed that the contractions in phase 3 propagate over longer distances than phase 2 (5.2 cm vs. 2.6 cm). Kerlin et al. [3] observed in healthy controls that approximately 50% of flow in the interdigestive state occurred during periods associated with the phase 3 of the MMC.

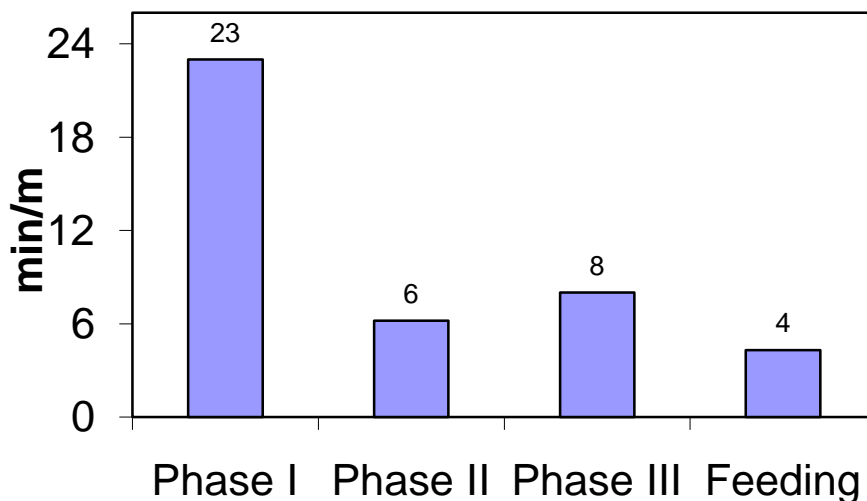


Fig. 3. Relations between the flow and the different motility pattern (assessed by electrical activity) in the fasting (phase 1 to phase 3) and fed state in dogs. Note that flow is fastest in phase 2 of the interdigestive motility and in the fed state (from Bueno et al. [1]).

In dogs the flow rates of the digesta in the *fed state* were threefold higher (333 ml/hr) than in phase 1 (104 ml/h) of the interdigestive MMC [1]. In the canine jejunum the propagation of intestinal contents was most of all influenced by the length of spread of contraction waves [4]. The propagation velocity of the contraction waves and the frequency of contractions exhibited a smaller effect. In this study a formula diet (Meritene^R, 1 kcal/ml) produced the slowest transit time and the shortest spreading waves in the small intestine compared to meals with oleic acid (0.15 kcal/ml), glucose (0,5 kcal/ml) and casein-hydrolysate (0,5 kcal/ml). Compared to a noncaloric control meal (cellulose) oleic acid, glucose and casein-hydrolysate caused a 50% reduction of the transit time, and the formula diet (Meritene^R) caused a reduction of 70% .

Small bowel manometry

The direct measurement of pressure activity in the small bowel, i.e. small bowel manometry, has entered clinical practice, although it remains confined to specialized centres. In most institutions, a perfused multilumen catheter assembly is used and the assembly is customized. For antroduodenal recordings, the assembly should include an array of closely spaced sensors to straddle the pylorus as well as recording sites in the duodenum and proximal jejunum. For small intestinal recordings, several widely spaced recording sites are more appropriate. These assemblies are placed under fluoroscopic guidance and recordings are typically performed for several hours during fasting and following the ingestion of a standardized liquid or solid meal. Recordings are analyzed for the various parameters of the MMC, for the presence and nature of the motor response to the meal, and for abnormal patterns. Ambulatory systems have been developed that combine solid-state miniaturized strain gauges, data loggers and appropriate computer software.

But it must be kept in mind that manometry only measures lumen-occluding contractions. If contractions are not lumen-occlusive the contractile force is dissipated by the lumen contents.

Abnormalities in small bowel manometry can be divided into two varieties:

- *Uncoordination of the small bowel motility* refers to abnormalities of the enteric nervous system. In the fasting state abnormalities of phase 3 of the MMC are here the most prominent feature. Absence of any phase 3 complex in a six hour fasting study and abnormalities in the propagation of phase 3 complexes are important signs of intestinal dysmotility as are intense bursts of phasic pressure activity. Inability of a meal to induce a fed (postprandial) pattern or to interrupt fasting motor activity is a just as important characteristic of intestinal dysmotility.
- *Abnormal low contraction amplitudes* (<10 mmHg) refer to diseases of the small muscle of the gastrointestinal tract.

Dysmotility disorders

Two causes of intestinal dysmotility are known:

- *Visceral myopathy*, a disorder of the smooth muscle.
- *Intestinal neuropathy*, a disorder of the nerve cells of the gastrointestinal tract.

Both forms can only reliably be diagnosed and differentiated by microscopic examination of full-thickness biopsy specimens containing all layers of the intestinal wall. Careful pathological examinations for abnormalities in the smooth muscle and the myenteric plexus with special stains must then be carried out. In clinical practice this will be made only in few special patients, because such specimens can only be obtained by laparotomy. Subsequent to biopsy manometry is a suitable tool in diagnosing and differentiating the two forms. In intestinal neuropathy the contractions are uncoordinated but their amplitude is normal (Fig.4). In myopathy the converse is seen: the contractions are mostly coordinated but their amplitude is diminished. But manometry is not able to differentiate the idiopathic from secondary forms in which the intestinal is involved in systemic diseases of the nervous system (central nervous system diseases, paraneoplastic neuropathy, autonomic neuropathy) or the muscles (amyloidosis, scleroderma, dermatomyositis, myopathies).

The most important clinical manifestation of intestinal dysmotility disorders is the chronic intestinal pseudo-obstruction (CIPO). Primary forms of this disorder are called chronic idiopathic intestinal pseudo-obstruction (CIPO). These expressions are used regardless of cause. These patients exhibit the symptoms of an obstruction of the small intestine in the absence of a mechanical blockage. The symptoms are those of an ileus with repeated episodes of nausea, vomiting, abdominal pain and distension. Many are subjected to more than one diagnostic laparotomy before the correct diagnosis

is considered. The most commonly used and available diagnostic technique is radiography. Findings on plain films may include a picture of paralytic ileus or one which mimics mechanical obstruction.

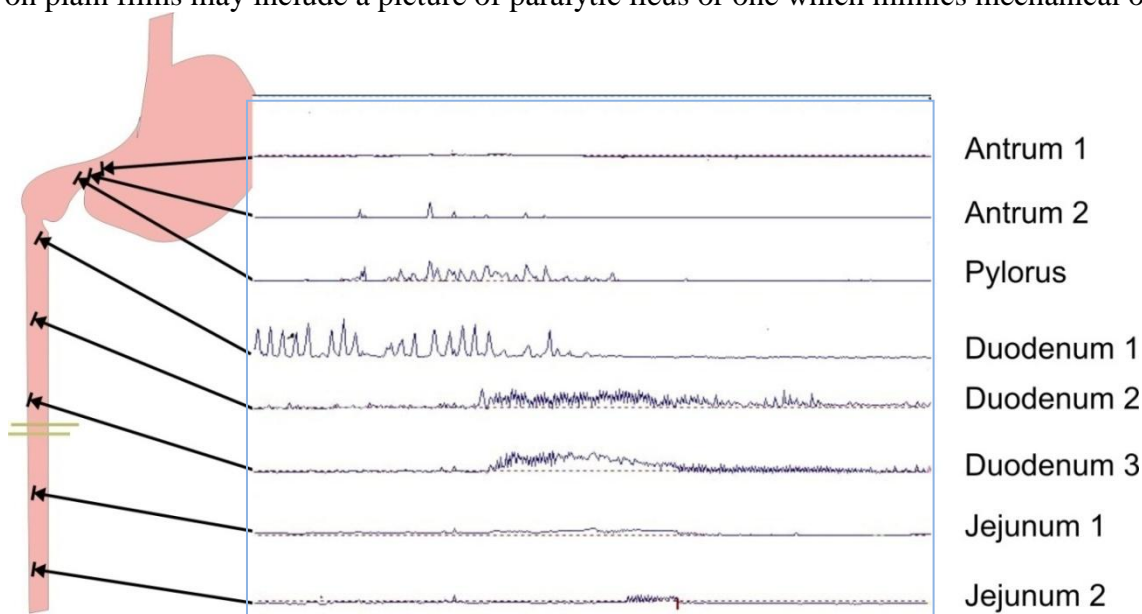


Fig. 4. Intraluminal pressure recordings (manometry) of fasting motility from the gastric antrum, duodenum and jejunum of a patient with neuropathic chronic intestinal pseudo-obstruction (CIPO). Fasting tracing shows a simultaneous phase 3 activity in the duodenum with failure to migrate into the jejunum.

Transit measurement

Radiology

For many years, the sole technique for the assessment of intestinal motor function was the radiologic observation of the passage of barium through the gut. Cinefluorography can well describe wall contractions and barium flow through the small intestine, but its periods of observation are limited and the barium filling represents a situation different from either the fasting or the postprandial state. In chronic intestinal pseudo-obstruction (CIPO) relevant observation can be already made on a plain film of the abdomen. When performing a small-bowel-follow-through with barium enteroclysis (small bowel barium enema) is useful to detect lesions in the small intestine and to rule out a mechanical obstruction of the small intestine. The most striking features in CIPO are the presence of a mega-duodenum and dilated small bowel loops in addition to a delayed transit of barium through the small intestine. But this technique is too insensitive, subjective, and extremely difficult to assess small bowel motility disorders.

Hydrogen (H_2) breath test

The small intestine in humans is unable to break down some carbohydrates like lactulose, a synthetic disaccharide comprised of the sugars D-galactose and D-fructose. Bacteria in the large intestine are able to ferment lactulose, releasing hydrogen (H_2) as one of the final products. The gaseous hydrogen is quickly absorbed into the blood and exhaled from the lungs. After ingestion of lactulose and measurement of hydrogen in the exhaled breath, we can assess how long it takes for the test meal to

reach the cecum. After reaching the colon a sharp peak of hydrogen concentration will appear in the exhaled breath (Fig.5). Alternatively a test meal may be used containing unabsorbable carbohydrates such as baked beans. Their fermentation by colonic bacteria is producing a sufficient amount of hydrogen as a rule.

Most clinical studies are done using an iso-osmotic solution of lactulose which reaches the cecum in about 90 minutes. The *oro-cecal transit time* was said a good indicator for the speed of the small intestine passage [5]. LaBrooy et al. [6] (1983), however, found a considerable intra- and intersubject variation using aqueous test solutions with doses of 10, 15 and 20g lactulose. In this study oro-cecal transit time tended to decrease with increasing doses of lactulose. The addition of lactulose to a liquid meal containing carbohydrate, fat, and protein decreased the coefficient of variation of the test results. Similar observations were reported in another study [7]. The considerable acceleration of the oro-cecal transit time by lactulose was also shown in a study comparing the lactulose breath test with the sulphalsalazine/sulphapyridine (SLZ/SP) method. The mean oro-cecal transit time was assessed in this study using a semisolid test meal (rice pudding) to which lactulose or SLZ/SP were admixed. The mean oro-cecal transit time was 2.92 hours by the lactulose/breath test and 4.84 hours by the SLZ/SP method. Admixing both markers to the test meal showed that the oro-cecal transit assessed by the lactulose/breath test correlate well with transit simultaneously assessed by the SLZ/SP method. Read et al. [8] compared the lactulose/breath test and scintigraphy in measuring small bowel transit time. They used a solid test meal containing sausages, mashed potatoes, baked beans and pineapple custard. Admixing lactulose to the test meals shortened the transit time through the small bowel. In addition, increasing doses of lactulose shortened more and more the small bowel transit time. It was also shown that transit times assessed with 10g of lactulose admixed to water were much shorter (0.8 hr) compared to the same dose in the standard meal (4.2 hr.).

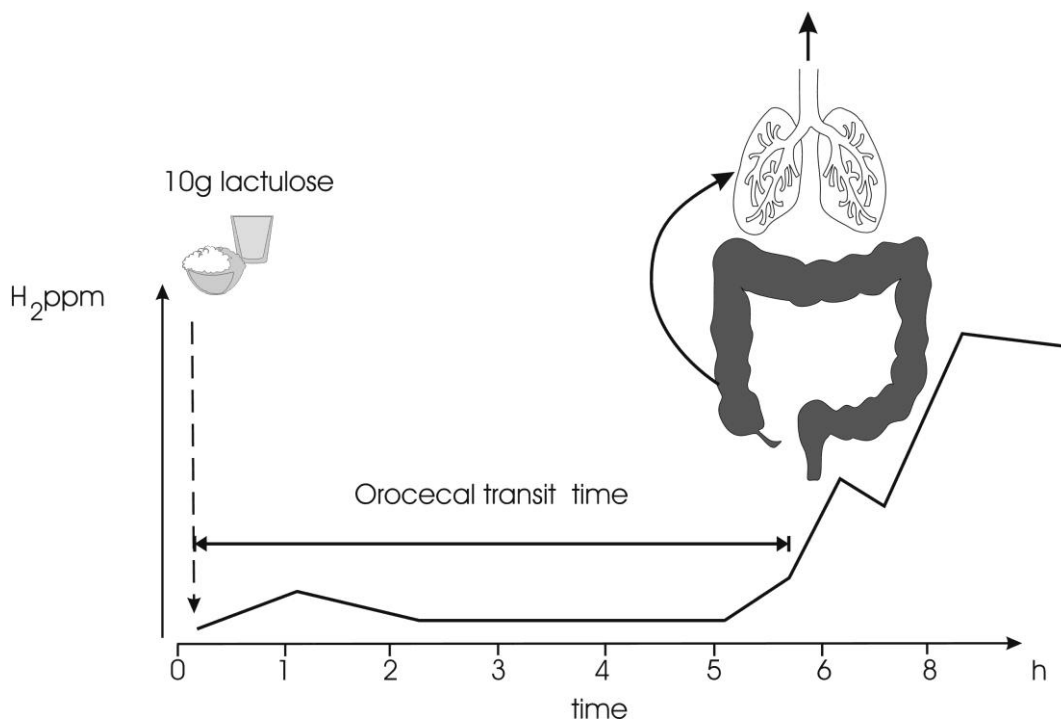


Fig 5. Measurement of oro-cecal transit time with the hydrogen breath test: The diagram illustrates the principle of this technique. In this case 10 g of lactulose has been mixed to a test meal and then ingested by the patient. About 6 hours later there is a sudden rise in the quantity (ppm) of hydrogen (H_2) in the exhaled breath. This is the time when the lactulose arrives in the cecum.

In conclusion it must be kept in mind that the lactulose/breath test provides only an estimate of small intestine transit time when using it in clinical practice. Although the lactulose/breath test used with a test meal gives more representative and reproducible results, a drink of lactulose is often used in clinical practice. Performing the test with a test meal is very time consuming and patients often break off the test. Other problems to be considered in the lactulose breath test are delayed gastric emptying and bacterial overgrowth of the small intestine. In 5-20% of the population the colonic bacteria do not form H₂ from unabsorbed carbohydrates ('non-producer').

Scintigraphy

The technique of labelling food with a small amount of radio-isotope and plotting its progress through the small intestine by means of a gamma camera placed over the abdomen allows quantitative data to be obtained for gastric emptying, the residence of the meal in the small intestine and for the rate of entry of residues of the meal into the colon. The most common problem with the scintigraphic technique is the poor resolution, which makes it difficult or impossible definitely to ascribe radioactivity in the gamma camera image to a specific organ, especially in cases where overlap between the abdominal organs is present. In small bowel transit studies ileal loops are often superimposed on the cecum and ascending colon. Special care has to be used in analyzing the temporal pattern and differential counting in the carefully outlined regions of interest. The gastric emptying curve and the colonic filling curve must be subtracted to obtain the small intestinal curve. Another problem in small bowel scintigraphy is to define the transit time. The question is for example whether the head of the meal should be taken as reference point or if one should subtract the half-time for the gastric emptying from the half-time of colonic filling.

An interesting study was performed by Greydanus et al. [9]. They assessed small bowel transit of a test meal (labelled with ¹¹¹Indium) in patients with intestinal neuropathy and myopathy and compared these data with healthy controls. In health, the ileocolonic transit of the test meal was characterized by intermittent bolus transfers. Bolus filling of the colon was less frequent and less effective in those with intestinal myopathy, whereas bolus transfer was still preserved in patients with neuro-pathic dysmotility.

In clinical practice the scintigraphic method is not used to assess small bowel transit .

Impedance measurement

Impedance measurement is currently in clinical practice used to assess movements in the esophageal lumen to investigate non-acid reflux and transit problems in dysphagia. Multichannel impedance is a new technique designed to detect intraluminal bolus movement. The principle is based on measurement of changes in resistance to alternating electrical current when a bolus passes by a pair of metallic rings mounted on a catheter. Liquid boluses contain an increased number of ions exhibiting a higher conductivity. Thus they will lower the impedance. The impedance stays at its nadir as long as the bolus is present in the segment, returning to baseline once the bolus is cleared by a contraction (Fig.6). In contrast gas will show a high impedance. In consequence gas passing will produce a transient rapid rise in the impedance since it has a poor electrical conductance. The direction of bolus movement can be seen by temporal differences in bolus entry and exit. A bolus progressing from proximal to distal indicates an antegrade movement whereas bolus entries progressing from distal to proximal indicate retrograde movement.

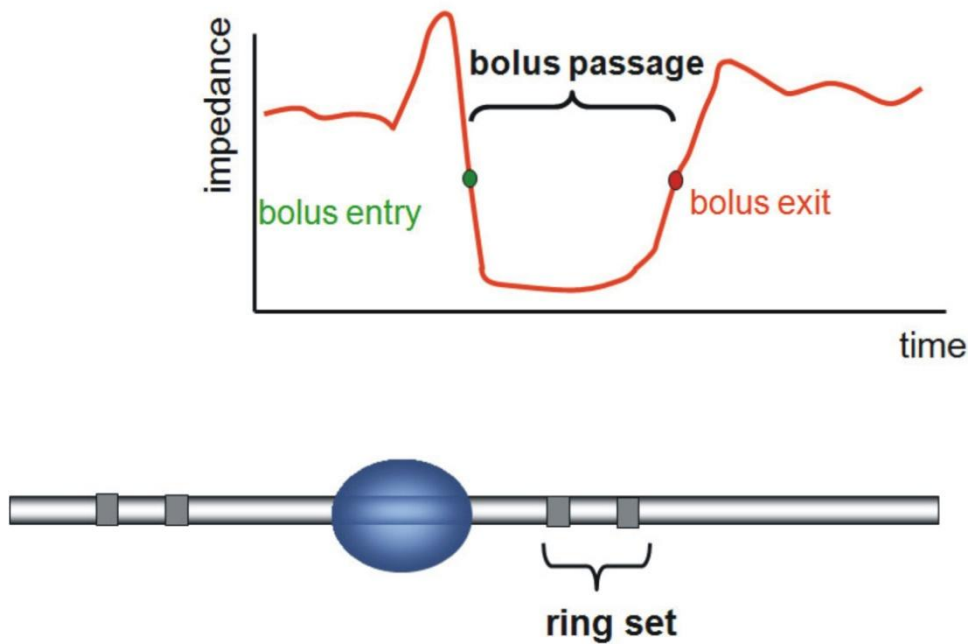


Fig 6. Impedance measurement: This diagram illustrates the principle of impedance measurement: A bolus with a high conductivity (many ions) is passing the impedance ring set mounted on a catheter. As a consequence impedance between the two rings will be lowered. When the bolus has passed the ring set impedance will increase again.

Nguyen et al. [10] published in 1995 data about the transport of duodenal content in the fasting and fed state. They observed different transport patterns in phase 2 of the fasting motility compared with the postprandial period. Long distance (>16 cm) propulsive bolus transports could be separated from those spanning only short-distances. Short distance bolus transports were predominating during fasting (72%), whereas propulsive bolus transport predominated after a meal (76%). Retrograde transport of a bolus was seen as well in the fasting period (4%) as postprandially (8%). Using simultaneously manometry and impedance measurement the same group [11] observed that short distance bolus transport after a meal is predominantly associated with stationary or contractions propagated only over a short distance. In contrast long-spanned transport of duodenal content was associated with propulsive contractions over a longer distance. The latter often exhibited a double-wave or clustered contraction pattern. In diabetic patients duodenal impedance measurement [12] exhibited a significantly lower number of propulsive bolus transports and a higher proportion of retrograde and so called complex chyme movements.

Intraluminal electrical impedance measurement in the small bowel is at the moment used only in scientific studies. This method is a very promising investigative tool and it gives new insights in the complex relationship between contractions and transport not only in animals but in humans, too. On the other side this new methods is time consuming and requires much experience. In addition a quite expensive laboratory equipment is necessary to do such studies in the duodenum and small bowel.

Methodical problems seem to be caused by the presence of a lot of liquid contents in the small intestine secreted by stomach, pancreas and biliary tract.

References

1. Bueno, L., J. Fioramonti, and Y. Ruckebusch, Rate of flow of digesta and electrical activity of the small intestine in dogs and sheep. *J Physiol (Lond)*, 1975; 249: 69-85.
2. Sarna, S.K., et al., Spatial and temporal patterns of human jejunal contractions. *Am J Physiol*, 1989; 257: G423-32.
3. Kerlin, P. and S. Phillips, *Variability of motility of the ileum and jejunum in healthy humans*. *Gastroenterology*, 1982; 82: 694-700.
4. Schemann, M. and H.J. Ehrlein, *Postprandial patterns of canine jejunal motility and transit of luminal content*. *Gastroenterology*, 1986; 90: 991-1000.
5. Bond, J.H., Jr., M.D. Levitt, and R. Prentiss, Investigation of small bowel transit time in man utilizing pulmonary hydrogen (H₂) measurements. *J Lab Clin Med*, 1975; 85: 546-55.
6. La Brooy, S.J., et al., Assessment of the reproducibility of the lactulose H₂ breath test as a measure of mouth to caecum transit time. *Gut*, 1983; 24: 893-6.
7. Staniforth, D.H., Comparison of oro-caecal transit times assessed by the lactulose/breath hydrogen and the sulphasalazine/sulphapyridine methods. *Gut*, 1989; 30: 978-82.
8. Read, N.W., et al., Transit of a meal through the stomach, small intestine, and colon in normal subjects and its role in the pathogenesis of diarrhea. *Gastroenterology*, 1980; 79: 1276-82.
9. Greydanus, M.P., et al., Ileocolonic transfer of solid chyme in small intestinal neuropathies and myopathies. *Gastroenterology*, 1990; 99: 158-64.
10. Nguyen, H.N., et al., Chyme transport patterns in human duodenum, determined by multiple intraluminal impedancometry. *Am J Physiol*, 1995; 268: G700-8.
11. Nguyen, H.N., et al., Postprandial transduodenal bolus transport is regulated by complex peristaltic sequence. *World J Gastroenterol*, 2006; 12: 6008-16.
12. Nguyen, H.N., et al., Abnormal postprandial duodenal chyme transport in patients with long standing insulin dependent diabetes mellitus. *Gut*, 1997; 41: 624-31.

Published in: Current Topics In Neurogastroenterology. Proceedings of the 2nd International Symposium of Neurogastroenterology. Cluj-Napoca, Romania 4-7 October 2007.

Editor: D.L. Dumitrascu

Editura Medicala Universitara "Iuliu Hatieganu" Cluj-Napoca. 2007