

Clinical Review

Esophageal & Gastric Disorders

Multichannel Intraluminal Impedance in Esophageal Function Testing and Gastroesophageal Reflux Monitoring

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Abstract

Multichannel intraluminal impedance (MII) is a new technique for evaluating esophageal function and gastroesophageal reflux. This technique depends on changes in resistance to alternating current between two metal electrodes produced by the presence of bolus inside the esophageal lumen. Combined MII and manometry (MII-EM) provides simultaneous information on intraluminal pressure changes and bolus movement, whereas combined MII and pH (MII-pH) allows detection of pH episodes irrespective of their pH values (ie, acid and non-acid reflux). Combined MII-EM studies are performed very similarly to standard manometry. Based on studies in healthy volunteers and patients, combined MII-EM challenges current existing criteria that define the effectiveness of esophageal body function. Combined MII-pH testing brings a shift in gastroesophageal reflux testing paradigm. In MII-pH studies, reflux events are no longer detected by pH. Refluxate presence, distribution, and clearing are primarily detected by MII and simply characterized as acid versus non-acid based on pH change and as liquid, gas, or mixed based on MII. MII determines refluxate clearance time, whereas pH measures acid clearance time. MII-pH shows promise to become an important clinical tool, particularly to assess gastroesophageal reflux in the postprandial period and in patients with persistent symptoms on therapy and with atypical symptoms.

Key Words: multichannel intraluminal impedance (MII), acid and non-acid gastroesophageal reflux, esophageal function testing, gastroesophageal reflux testing

Multichannel intraluminal impedance (MII) is a new technique for evaluating esophageal function and gastroesophageal reflux (GER). Esophageal function testing is an important step in evaluating patients with possible esophageal symptoms. This is currently performed using a combination of esophageal manometry and barium or radioisotope esophagram. In terms of GER testing, the cur-

rent "gold standard" is ambulatory pH-metry, a method that is based on detection of changes in acid content in the esophageal lumen. Even though the pathophysiologic role of acid in gastroesophageal (GER) lesions has been well established by a number of studies in both animals and humans,¹ GER symptoms often persist despite treatment with medications that decrease gastric acid secretion. It has been suggested that these symptoms may be due to reflux having pH > 4.0 (ie, non-acid reflux),² a type of reflux that is difficult to identify with conventional pH-metry.

The current article will review the principles of impedance testing, the use of combined MII and manometry (MII-EM) to evaluate esophageal function, and the use of combined MII and pH (MII-pH) to monitor GER.

BASIC PRINCIPLES OF IMPEDANCE TESTING

The principles of this technique were first described in 1991 by Silny³ and depend on changes in resistance to alternating current (ie, impedance) between two metal electrodes (ie, impedance-measuring segment) produced by the presence of bolus inside the esophageal lumen. Electric conductivity (the opposite of resistance or impedance) is directly related to the ionic concentration of the intraluminal content. Intraluminal content with high ionic concentrations (ie, refluxate, food) have a relative low resistance (high conductivity) compared with the esophageal lining or air.

Simultaneous video-fluoroscopic and impedance measurements have validated the following changes observed with bolus entry, presence, and clearing in the impedance-measuring segment^{3,4} shown in Figure 1. In the absence of bolus, impedance is determined by the electric conductivity of the esophageal lining. Upon arrival of bolus between the electrodes, impedance will often rise abruptly due to the presence of air in front of the head of the bolus. Intraluminal impedance then rapidly decreases as high ionic content of the bolus provides good electric conductivity. While the bolus is present in the impedance-measuring segment intraluminal impedance remains low. Esophageal contractions clearing the intraluminal content increase the impedance

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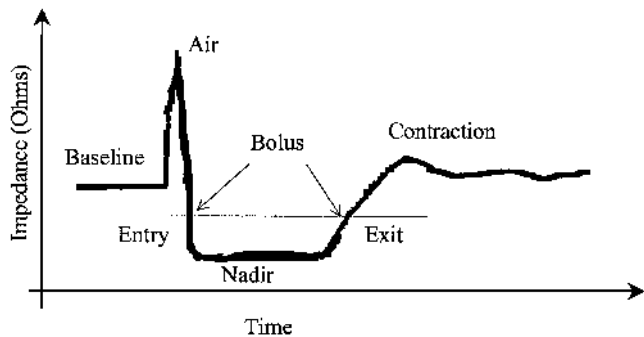


FIGURE 1. Impedance changes observed during bolus transit over a single pair of measurement rings separated by 2 cm. A rapid raise in resistance is noted when air traveling in front of the bolus head reaches the impedance-measuring segment followed by a drop in impedance once higher conductive bolus material passes the measuring site. Bolus entry is considered at the 50% drop in impedance from baseline relative to nadir and bolus exit at the 50% recovery point from nadir to baseline. Lumen narrowing produced by the contraction transiently increases the impedance above baseline.

with a slight “overshoot” due to a decrease in esophageal cross section during contraction before returning to baseline.

Multiple impedance-measuring segments within the esophagus allow determination of direction of bolus movement within the esophagus (ie, MII) (Figure 2). Antegrade (ie, swallows) bolus movement (Figure 3) is detected by impedance changes of bolus presence progressing proximal to distal. Retrograde (ie, reflux) bolus movement is detected by changes in impedance progressing distal to proximal followed by proximal to distal clearance of bolus by either a primary or secondary contraction wave (Figure 4).

The ability of MII to detect intraesophageal bolus movement by changes in electric resistance as well as mounting of the impedance-measuring segments on standard manometry or pH catheters allows MII to complement traditional manometry or pH testing. Combined MII and manometry

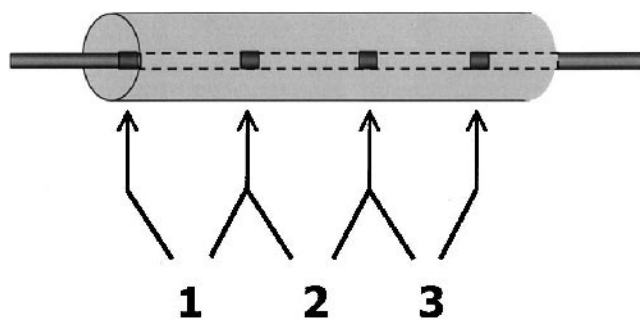


FIGURE 2. Multiple impedance-measuring segments within the esophagus allow determination of direction of bolus movement within the esophagus (ie, multichannel intraluminal impedance, MII).

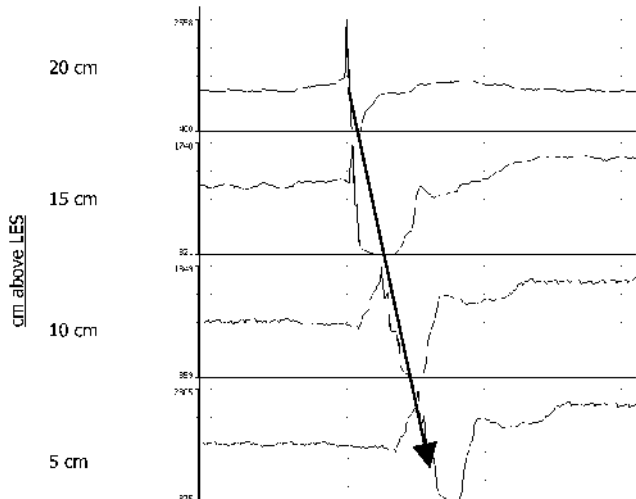


FIGURE 3. Antegrade (ie, swallows) bolus movement detected by impedance changes of bolus presence progressing proximal to distal.

(MII-EM) provides simultaneous information on intraluminal pressure changes and bolus movement, whereas combined MII and pH (MII-pH) allow detection of pH episodes irrespective of their pH values (ie, acid and non-acid reflux).

ESOPHAGEAL FUNCTION TESTING USING COMBINED MII-EM

Combined MII-EM is a new technique using two complementary methods of esophageal function testing: esophageal manometry provides information about intraluminal pressures generated during swallowing, whereas MII simultaneously assesses bolus movement. Although it does not provide the anatomic details offered by radiographic

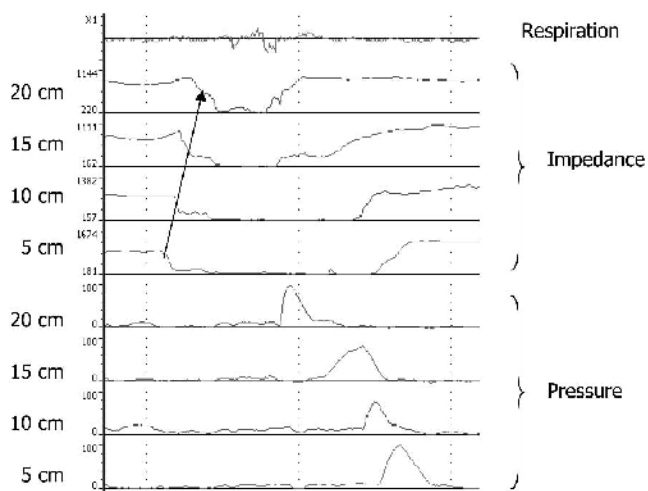


FIGURE 4. Combined MII-EM tracing in which retrograde bolus movement is detected by changes in impedance (MII) progressing distal to proximal followed by proximal to distal clearance of bolus a contraction wave.

barium swallow, MII has the advantage of not requiring radiation exposure in evaluating bolus movement, thus allowing safe testing of multiple swallows. Furthermore, bolus transit and pressures are obtained during a single test procedure.

The indications for combined MII-EM are the same as for esophageal manometry: evaluation of dysphagia, non-cardiac chest pain, and GER disease (GERD), including preoperative evaluation before antireflux surgery or endoscopic antireflux procedures.

Initial studies performed in our laboratory on normal subjects indicated that MII could detect the presence of small volumes of swallowed liquid (ie, 1 mL) and confirmed known pharmacologic effects of cholinergic medication on esophageal peristalsis and bolus movement.⁵

Combined MII-EM Equipment

The esophageal function testing catheter is a specially designed, flexible tube incorporating pressure sensors and impedance-measuring rings. Currently available as a 9-channel esophageal function testing catheter (Sandhill Scientific Inc., Highlands Ranch, CO), it incorporates five pressure (two circumferential and three unidirectional) sensors and four impedance-measuring segments (Figure 5). The two circumferential solid-state pressure sensors are located at 5 cm and 10 cm from the tip and three unidirectional pressure sensors at 15 cm, 20 cm, and 25 cm. Impedance-measuring segments consist of pairs of metal rings placed 2 cm apart, centered at 10, 15, 20, and 25 cm from the tip, thus straddling the four proximal pressure transducers. The signal from the catheter is transferred to an amplifying and digitizing interface (SensorPAC-Z, Sandhill Scientific Inc.) and then recorded and stored using dedicated software (Insight Acquisition, Sandhill Scientific Inc.). Upon completion of data acquisition, tracings are edited and analyzed using a second dedicated software program (BioView Analysis, Sandhill Scientific Inc.). The analysis software will report manometric (contraction amplitude, duration and velocity, lower esophageal sphincter [LES] resting, and residual pressure) and impedance (bolus presence time, bolus head advance time, total and segmental bolus transit times) parameters. Based on predefined criteria, the software will determine bolus entry, presence, and clearing parameters assessing completion of bolus transit. The summary generated will report the percent of manometric normal peristaltic, ineffective, and simultaneous contractions, percent of swallows with complete and incomplete bolus transit.

Combined MII-EM Parameters

Combined MII-EM offers simultaneous evaluation of both esophageal contraction characteristics and bolus transit.

Bolus entry at a specific level measured by impedance is considered to occur at the 50% point between 3-second

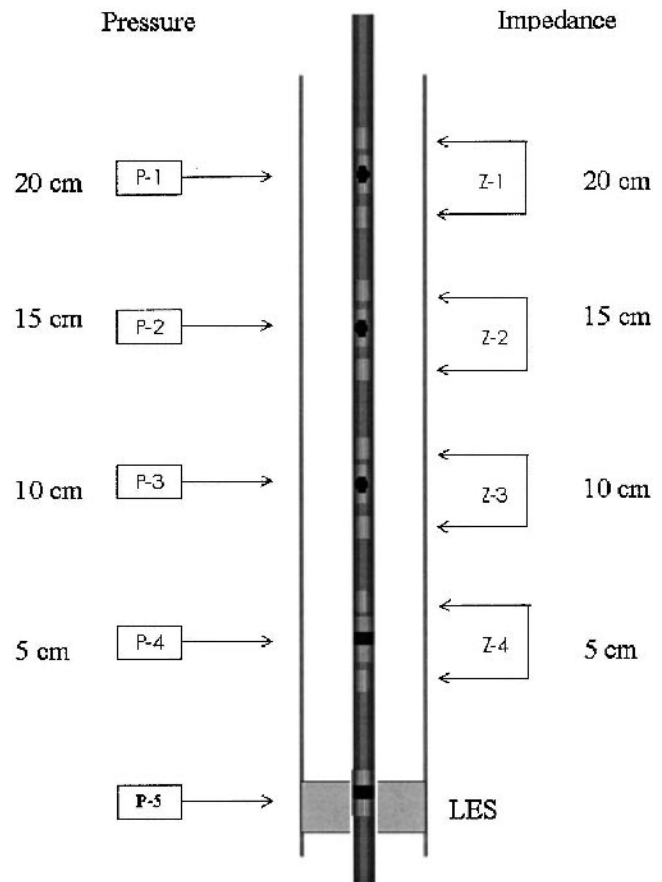


FIGURE 5. Nine-channel combined multichannel intraluminal impedance (MII) and manometry (EM) catheter. Circumferential solid-state pressure sensors located in LES high-pressure zone (P5) and 5 cm above it (P4), unidirectional solid-state pressure sensors located 10 cm (P3), 15 cm (P2), and 20 cm (P1) above LES. Impedance measuring segments centered at 5 cm (Z4), 10 cm (Z3), 15 cm (Z2), and 20 cm (Z1) above LES.

pre-swallow impedance baseline and impedance nadir during bolus presence. Bolus exit is determined as return to this 50% point on the impedance recovery curve (Figure 1). Simultaneous MII and barium swallow^{3,4} have validated these relationships. Impedance parameters calculated are shown in Figure 6: 1) total bolus transit time as time elapsed between bolus entry at 20 cm above LES and bolus exit at 5 cm above LES, 2) bolus head advance time as time elapsed between bolus entry at 20 cm above LES and bolus entry at 15, 10, and 5 cm above LES, 3) bolus presence time as time elapsed between bolus entry and bolus exit at each impedance-measuring site (5, 10, 15, and 20 cm above LES), and 4) segmental transit times as time elapsed between bolus entry at a given level above LES and bolus exit at the next lower level.

Classification of Swallows Using Combined MII-EM

Swallows are manometrically classified⁶ as follows: 1) normal if contraction amplitudes at 5 and 10 cm above the

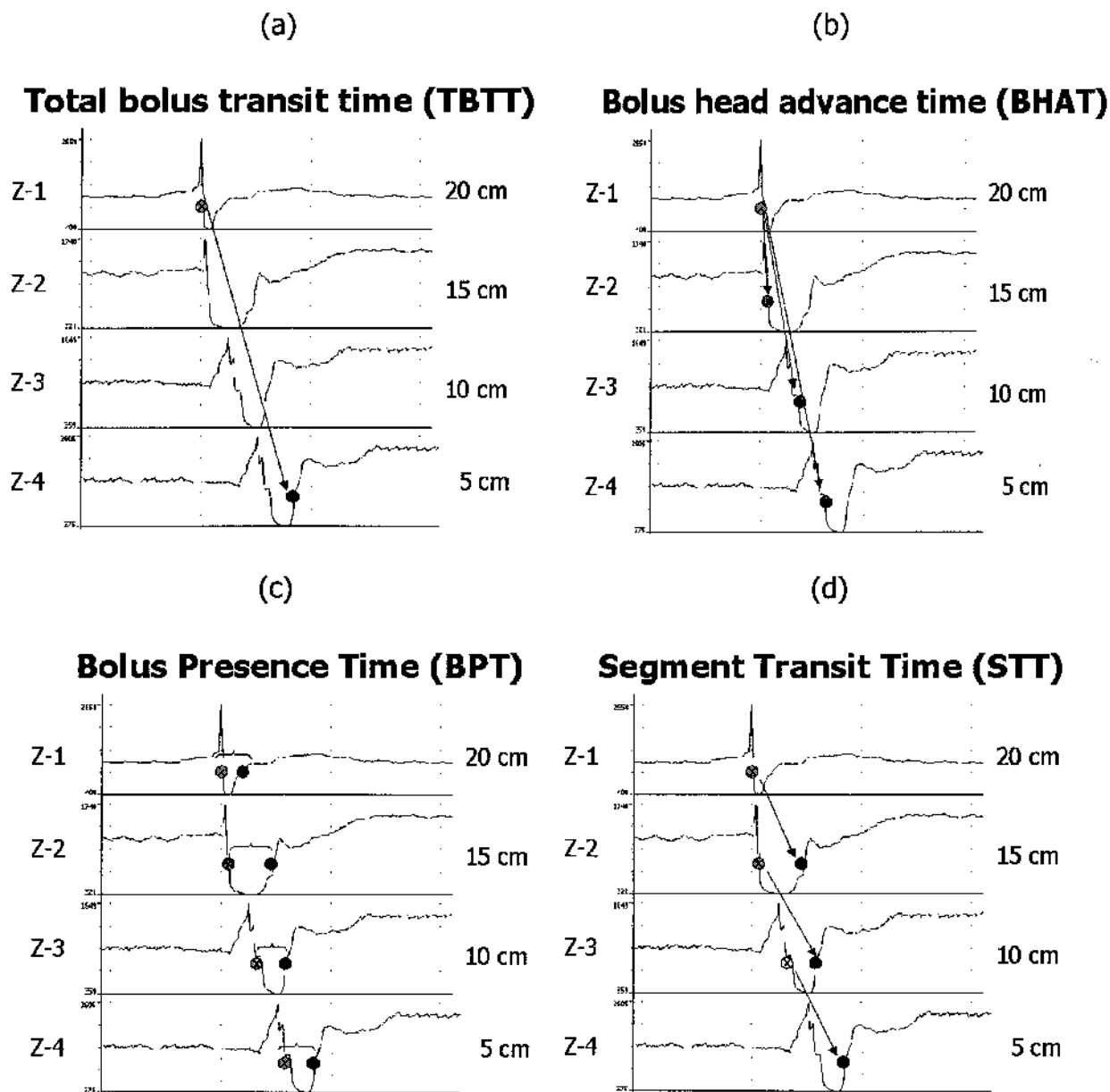


FIGURE 6. Definitions of impedance parameters. **a:** Total bolus transit time (TBTT) as time elapsed between bolus entry at 20 cm above LES and bolus exit at 5 cm above LES. **b:** Bolus head advance time as time elapsed between bolus entry at 20 cm above LES and bolus entry at 15, 10, and 5 cm above LES. **c:** Bolus presence time (BPT) as time elapsed between bolus entry and bolus exit at each impedance-measuring site (5, 10, 15, and 20 cm above LES). **d:** Segmental transit times (STT) as time elapsed between bolus entry at a given level above LES and bolus exit at the next lower level.

LES are each ≥ 30 mmHg and distal onset velocity is < 8 cm/s; 2) ineffective if either of the contraction amplitudes at 5 and 10 cm above the LES is < 30 mmHg; and 3) simultaneous if contraction amplitudes at 5 and 10 cm above the LES are each ≥ 30 mmHg and distal onset velocity is > 8 cm/s. These criteria are based on studies in normal volunteers⁷ and simultaneous video-fluoromanometry.⁸

Swallows are classified by MII as showing: complete bolus transit (Figure 7A) if bolus entry is seen at the most

proximal site (20 cm above LES) and bolus exit points are recorded in all three distal impedance-measuring sites (ie, 15, 10, and 5 cm above the LES) and incomplete bolus transit (Figure 7B) if bolus exit is not identified at any one of the three distal impedance-measuring sites.

Overall Study Interpretation

The combined MII-EM study is performed very similarly to standard manometry. The two variations are the 5 mL of

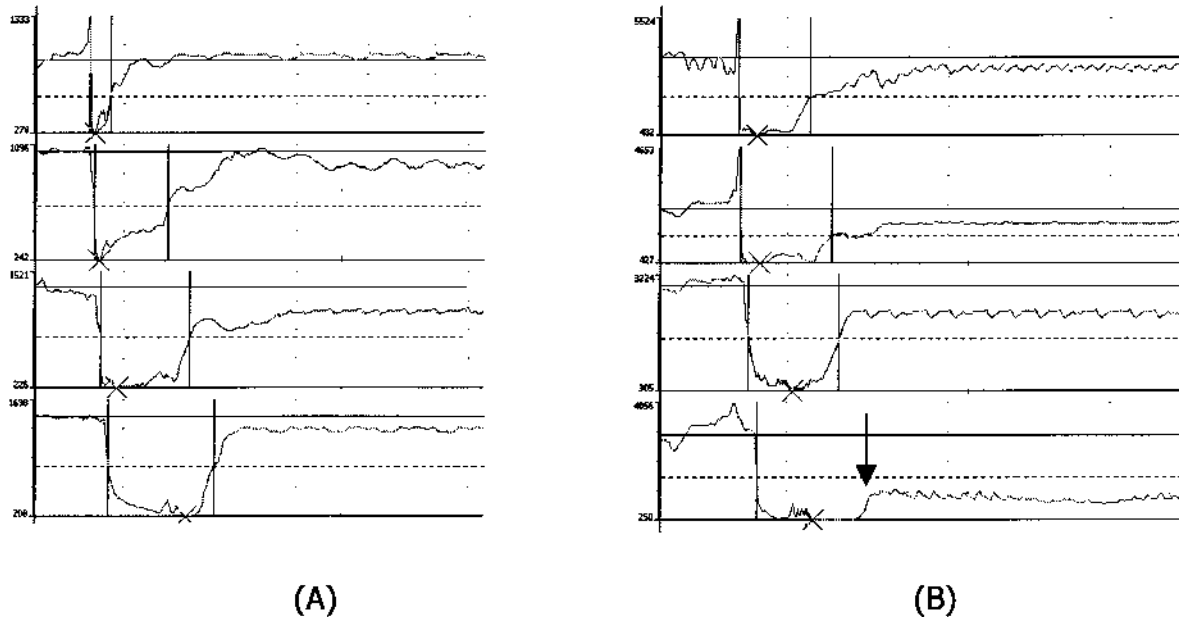


FIGURE 7. Classification of swallows by MII criteria: complete bolus transit (**A**), if bolus entry is seen at the most proximal site (20 cm above LES) and bolus exit points are recorded in all three distal impedance-measuring sites (ie, 15 cm, 10 cm, and 5 cm above the LES) and incomplete bolus transit (**B**) if bolus exit is not identified at any one of the three distal impedance-measuring sites.

normal saline replaces the water swallows to provide a more standard impedance solution and an additional set of 10 viscous swallows (apple sauce like). Normal esophageal function testing parameters have been recently determined in a multicenter study.⁹ Normal values for impedance parameters were proposed based on the 95th percentile in 43 healthy volunteers (Table 1).

Manometric parameters define a study as being normal if it does not contain >20% ineffective and 10% simultaneous liquid swallows.⁶

Impedance parameters define a study as normal if at least 80% of liquid and at least 70% of viscous swallows showed complete MII-detected bolus transit.⁹ When using viscous testing substances a study is considered normal if it does not contain >20% ineffective and 10% simultaneous swallows.⁹

Clinical Applications of Combined MII-EM

Currently, studies using combined MII-EM in patients with manometric defined motility abnormalities are in prog-

ress. These studies should provide a better understanding of bolus transit of various categories of motility abnormalities. Preliminary observations in our laboratory suggest that more than half of patients with manometric defined distal esophageal spasm or ineffective esophageal motility have complete bolus transit measured by MII. Patients with nutcracker esophagus or isolated LES abnormalities (ie, hypertensive LES, hypotensive, poor relaxing LES) have complete bolus transit during swallowing, whereas patients with achalasia or scleroderma have consistently incomplete bolus transit during swallowing.

Combined MII-EM studies in healthy volunteers and patients with various manometric abnormalities suggest a new classification for esophageal motility abnormalities into those associated with bolus transit defects (ie, achalasia, scleroderma, ineffective esophageal motility, and distal esophageal spasm) and those that appear to be only pressure defects (ie, nutcracker esophagus, hypertensive LES, hypotensive LES, and poorly relaxing LES) as shown in Figure 8.

Incorporating two complementary techniques combined MII-EM provides a more detailed evaluation of both aspects of esophageal function: esophageal contractility and bolus transit. Given differences in transit pattern of liquid and viscous bolus transit identified by MII-EM, we recommend using both testing substances for a more refined characterization of esophageal function. In summary, the availability of simultaneous assessment of esophageal contractions and

TABLE 1. Proposed normal values (based on 95th percentile) for MII parameters for liquid and viscous swallows

	Liquid	Viscous
Total bolus head advance time 20, 5 cm (sec)	5.0	7.5
Total bolus transit time (sec)	12.5	12.5
Smooth muscle transit time 10, 5 cm (sec)	10.5	8.5
% complete bolus transit	≥80	≥70

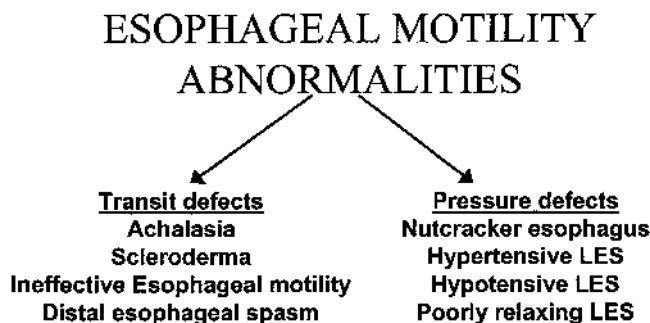


FIGURE 8. New separation of esophageal motility abnormalities into bolus transit defects and pressure defects based on MII-EM findings.

bolus transit using combined MII-EM challenges current existing criteria that define the effectiveness of esophageal body function. Future outcome studies are warranted to evaluate the prognostic values of pressure and bolus transit abnormalities.

GASTROESOPHAGEAL REFLUX MONITORING USING COMBINED MII-pH

The currently accepted gold standard for the assessment of GER is distal esophageal pH recording,¹⁰ which bases detection of reflux of acidic material into the esophagus on changes in hydrogen ion concentration. Conventional pH recording has difficulties detecting non-acid reflux, although some authors have proposed that reflux can be detected by pH-metry even when intraesophageal pH remains above 4.0 but show a definite fall >1 pH unit.¹¹ Currently available techniques for the study of non-acid or alkaline reflux have several limitations: aspiration techniques¹² allow for only short analysis periods and the accuracy of enzymatic determination of the contents of the aspirates has been questioned¹³; scintigraphic methods^{14,15} are expensive, involve radiation exposure, and are limited to short monitoring periods; and ambulatory combined pH monitoring and bilirubin monitoring (Bilitec)¹⁶ require the presence of bilirubin and is therefore incapable of measuring bile-free non-acid reflux, which accounts for >90% of non-acid reflux.¹⁷ Furthermore, the Bilitec device requires special liquid diets during the monitoring period to avoid false-positive readings.¹⁸

MII used in combination with pH-metry (MII-pH) has been shown to allow accurate recording of GER at all pH levels and is emerging as a useful tool to study both acid and non-acid reflux.^{19,20} The technique has been validated fluoroscopically and manometrically to detect bolus movement in the esophagus both in the oral and aboral direction,²¹ and thus enable measurement of and distinction between swallows and reflux. Because MII records retrograde flow of gastric contents into the esophagus in a pH-independent

fashion, combining the technique with pH-metry enables detection of non-acid reflux as well as acid reflux. Additionally, MII-pH provides detailed characterization of the reflux episode, including determination of the composition (gas, liquid, or mixed) and the height reached by the refluxate.^{19,20,22}

Combined MII-pH Equipment

The combined MII-pH catheter is similar to standard 2-mm flexible pH catheters. The “classic” 6MII-1pH assembly (Figure 9) has four impedance-measuring sites (Z1–Z4) in the distal esophagus and two impedance-measuring sites in the proximal esophagus (Z5–Z6). The pH sensor on this assembly is at the same level as the center of the second impedance-measuring segment. The catheter is placed transnasally into the esophagus and positioned so that the pH sensor is located 5 cm above the proximal border of the lower esophageal sphincter (LES). The impedance-measuring segments will be located at 3, 5, 7, and 9 cm above the LES in the distal esophagus and at 15 cm and 17 cm above the LES in the proximal esophagus. Initial studies using MII-pH were done with stationary setups and over relatively short periods of time (2- to 3-hour recording sessions). More recently, equipment to perform ambulatory MII-pH studies over prolonged periods of time has become available (Sleuth; Sandhill Scientific Inc.). Upon completion of data acquisition, tracings are edited and analyzed using a second dedicated software program (BioView Analysis, Sandhill Scientific Inc.).

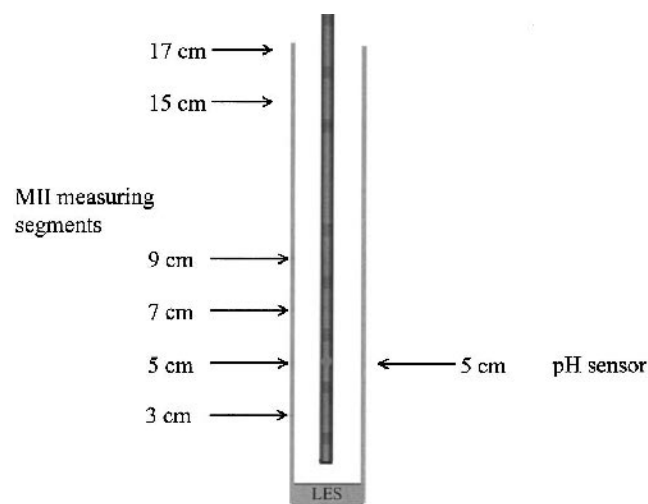


FIGURE 9. Schematic representation of the 2-mm-diameter MII-pH catheter with impedance electrodes (4 mm in length) set in pairs at 2-cm intervals, allowing for six impedance-measuring segments, as well as one pH electrode. Once properly positioned, this catheter allows recording of pH at 5 cm above the LES and impedance in six measuring segments, with their centers 3, 5, 7, 9, 15, and 17 cm above the LES.

Classification of GER Using Combined MII-pH

GER Composition and Height

Based on different impedance patterns, reflux episodes can be classified by MII as containing gas, liquid, or both. Air conducts electricity poorly and therefore has very high impedance, whereas liquid gastric contents have a low impedance. As illustrated in Figure 10, gas produces increases in intraluminal impedance and liquid gastric contents result in decreased impedance. Mixed reflux events are a combination of both a liquid and gas pattern. The height or a reflux event is defined by the most proximal impedance-measuring segment reached by the liquid component of the reflux episode. Gas reflux events are not assigned a height because, per definition, they penetrate the upper esophageal sphincter and are eliminated.

GER Content: Acid, Minor Acid, Non-Acid reflux and Acid Re-Reflux

An acid MII-GER event is an MII-detected reflux event in which a drop of pH from >4.0 to <4.0 is noted (Figure 11a). Non-acid reflux is an MII-detected event during which the pH stays above 4.0 and does not drop more than 1 pH unit (Figure 11b). Minor acid reflux is an MII-detected reflux event during which pH stays above 4.0 but the pH drops more than 1 unit (Figure 11c). An acid re-reflux event is another type of acid reflux that occurs while intraesophageal pH is already below 4.0. It is detected by MII, and the pH may or may not go further below 4.0 (Figure 11d).

Combined MII-pH Parameters

Combined MII-pH is a dual modality technique for detecting GER, and its parameters are more complex than just number of events and percent time pH <4 used by traditional pH monitoring. Besides these two pH parameters, combined MII-pH defines number of MII-GER events as the total number of MII-detected events. Refluxate presence time is defined as the total amount of liquid containing MII-refluxate presence time (absolute or percent of the study period) detected by the impedance-measuring segment located at 5 cm above the LES. Refluxate clearance time is defined as the average duration of liquid containing MII-refluxate presence at 5 cm above the LES. All of the aforementioned parameters could be further separated into acid, minor acid, non-acid, and re-reflux based on the pH changes recorded at the time when the reflux occurred. Based on the position of the subject at the time they occurred, these parameters are further separated into upright and recumbent.

OVERALL STUDY INTERPRETATION

Overall study interpretation is currently based on normative data proposed by Shay et al based on the 95th percentile of these parameters in 60 normal volunteers²³ (Table 2). While normal values on proton pump inhibitor (PPI) therapy still have to be established, at the present time the upper limit of normal on therapy for total number of reflux events can be extrapolated from the total number of MII-GER

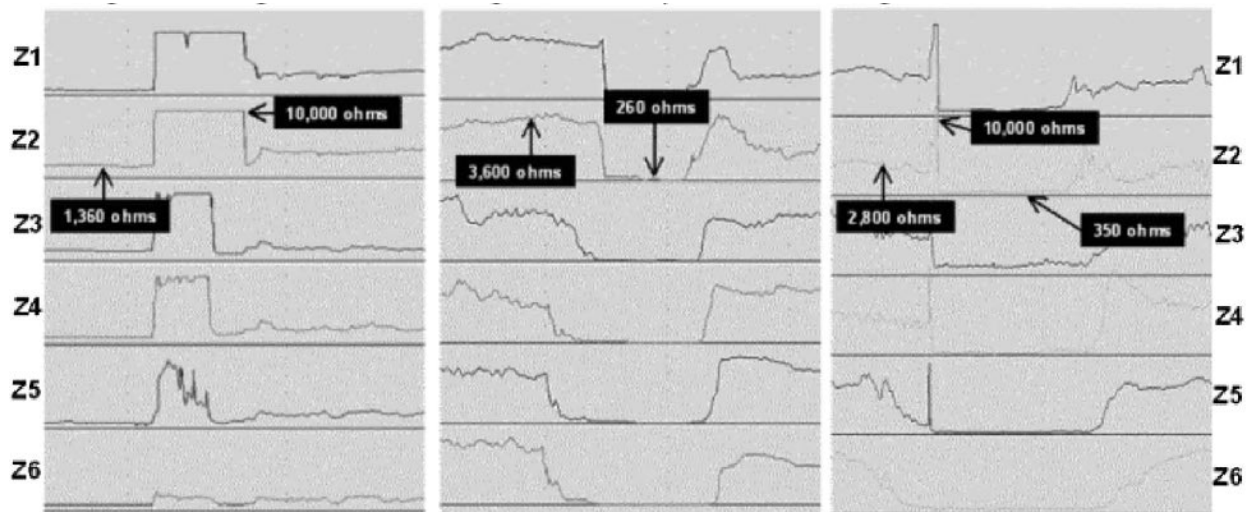


FIGURE 10. Impedance changes in ohms during reflux of gas, liquid, and mixed contents, obtained with a catheter incorporating six impedance-measuring segments (Z1 to Z6), which are shown in the “Y” axis. Impedance values for the second measuring segment (Z2) are shown for the three reflux episodes. **a:** Reflux of gas is characterized by sharp increases in impedance beginning in the most distal recording segment and rapidly progressing upwards toward the proximal esophagus. In Z2 impedance rises from a baseline of 1,360 ohms to a peak of 10,000 ohms. **b:** Reflux of liquid is characterized by sequential impedance falls starting in the distal esophagus and moving upwards toward the mouth. In Z2 impedance falls from a baseline of 3,600 ohms to a trough of 260 ohms. **c:** Reflux of gas mixed with liquid. In Z2 impedance rises from a baseline of 2,860 ohms to a peak of 10,000 ohms; this is followed by an impedance fall to a trough of 350 ohms.

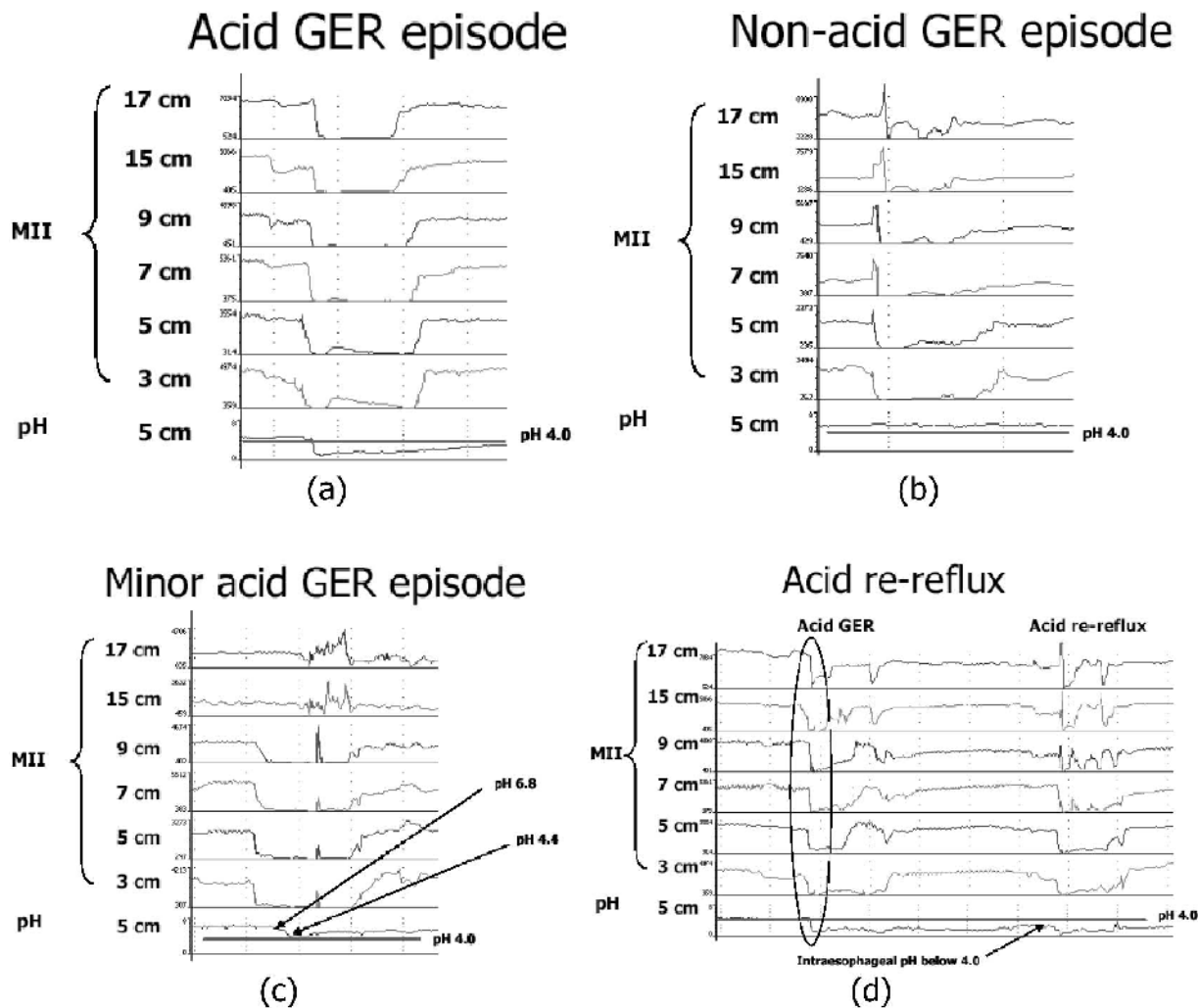


FIGURE 11. Various types of reflux events detected by MII-pH. An acid MII-GER reflux event is an MII-detected reflux event in which a drop of pH from above 4.0 to below 4.0 is noted (a). Non-acid reflux is an MII-detected reflux event during which the pH stays above 4.0 and does not drop more than 1 pH unit (b). Minor acid reflux is an MII-detected reflux event during which pH stays above 4.0 but the pH drops more than 1 unit (c). An acid re-reflux event is another type of acid reflux that occurs while intraesophageal pH is below 4.0 and the pH may go further below 4.0 (d).

TABLE 2. Twenty-four-hour MII-pH values 5 cm above the LES in 60 normal volunteers

	MII parameters						
	MII-GER (total)	MII-GER type and frequency			pH parameters		
		Acid	Non-acid	Acid re-reflux	% bolus exposure†	pH-only GER‡	% acid exposure
Total 24-hr	73	55	26	4	1.4	3	6.3
Upright	67	52	24	4	2.1	3	9.7
Recumbent	7	5	4	0	0.7	0	2.1

*MII-GER types are based on pH probe findings. Acid MII-GER and pH-GER: pH fall above to below 4; Non-acid, MII-GER while pH > 4; acid re-reflux, MII-GER while pH < 4.

†Duration of all MII-GER/time monitored.

‡GER detected by the pH probe but not by MII.

parameters off therapy because acid-suppressive therapy would be expected to change only the ratio of acid versus non-acid reflux events and not to alter the total number of events.¹⁸

APPLICATION OF MII-pH IN GERD

Pediatric Applications

Skopnik et al were the first ones to report using MII-pH to detect acid and non-acid reflux in the postprandial period in 17 infants with GERD.²⁴ They reported detection of a large number of non-acid reflux episodes that would otherwise be undetectable by conventional pH-metry.²⁴ Further reports in the pediatric literature have described the use of MII-pH to study the relationship between reflux (both acid and non-acid) and apnea in infants and premature babies.^{25,26}

Adult Applications

Several studies have examined different patterns of reflux using MII-pH in stationary conditions and over short periods of time.

Sifrim et al used the technique with concurrent manometry to study patterns of gas and liquid reflux during transient lower esophageal sphincter relaxations (TLESRs) in 11 normal volunteers in the postprandial period; their findings showed that in upright normal subjects, although belching can precipitate acid reflux, most acid reflux occurs as a primary event.²⁷ In a subsequent study,¹⁹ this group of investigators evaluated the composition of postprandial refluxate in 16 patients with GERD and 15 healthy controls and found that in the postprandial period, TLESRs and reflux of gastric contents are similarly frequent in patients with GERD and controls; however, GERD patients showed more acid reflux and less non-acid reflux. They postulated that differences in the air-liquid composition of the refluxate may contribute to higher rate of acid reflux in the patient group.

More recently, Shay et al²² used MII-pH in combination with manometry in 10 GERD patients and 10 normal volunteers to evaluate the accuracy of MII in detecting individual reflux events identified by pH probe and manometry. The subjects were studied fasting in both the left and right lateral decubitus position. Overall, patients had 30-fold more reflux episodes than normal volunteers; MII detected 95% of all reflux events identified by pH metry or manometry alone and showed that liquid reflux predominates in the right recumbent posture, with gas reflux being more common in the left recumbent position.

Two studies have used MII-pH to assess acid and non-acid reflux and their associated symptoms after pharmacologic manipulation. Vela et al¹⁹ reported, in a group of subjects with frequent heartburn studied in the postprandial period, that treatment with omeprazole resulted in a significant decrease in the number of acid reflux episodes; how-

ever, non-acid reflux continued to occur and was responsible for some symptoms. Thus, acid suppression did not result in a decrease in reflux episodes but rather in a shift from acid to non-acid reflux in the immediate postprandial period. This study also showed that taking all reflux episodes into account (both acid and non-acid reflux) results in a higher calculated symptom index. In a subsequent study of patients with heartburn, these investigators studied the effect of baclofen, a GABA B agonist, on acid and non-acid reflux and their associated symptoms.²⁸ By inhibiting TLESRs, this medication was able to both decrease acid and non-acid reflux as well as their associated symptoms in the postprandial period.

All of the studies described above were performed in stationary setups and over short periods of time (3 hours or less). The findings described by these investigators await confirmation in ambulatory conditions and over prolonged periods of time.

In the only published study using 24-hour ambulatory MII-pH, Sifrim et al²⁷ described acid, non-acid, and gas reflux in 30 patients with symptomatic GERD and erosive esophagitis and 28 healthy controls. Interestingly, they found that the total rate of reflux episodes was similar in the patients and the healthy controls. However, GERD patients had a higher proportion of acid reflux. One third of the reflux episodes were non-acid in both groups. In terms of reflux composition, mixed reflux (liquid and gas) was most frequent in both groups and GERD patients had more pure liquid reflux than the normal controls.

Preliminary data from a multicenter study using ambulatory combined MII-pH involving the Medical University of South Carolina, Cleveland Clinic, and Catholic University in Leuven, Belgium suggest that only 20% of patients with persistent symptoms on twice daily PPI therapy have symptoms associated with acid reflux. Combined MII-pH was able to evaluate the association of persistent symptoms in the remaining 80% of patients, finding that half of these patients had symptoms associated with non-acid reflux while the other half of the patients had neither acid nor non-acid preceding their symptoms. Based on this observation, we propose using the algorithm in Figure 12 for a more complete diagnosis of GERD.

In summary, MII-pH testing brings a shift in GER testing paradigm. In MII-pH studies, reflux events are no longer detected by pH. Refluxate presence, distribution, and clearing are primarily detected by MII and simply characterized as acid versus non-acid based on pH change and as liquid, gas, or mixed based on MII. MII determines refluxate clearance time, whereas pH measures acid clearance time. MII-pH shows promise to become an important clinical tool, particularly to assess GER in the postprandial period and in patients with persistent symptoms on therapy and with atypical symptoms. In these situations, it has great potential

GERD DIAGNOSTIC ALGORITHM

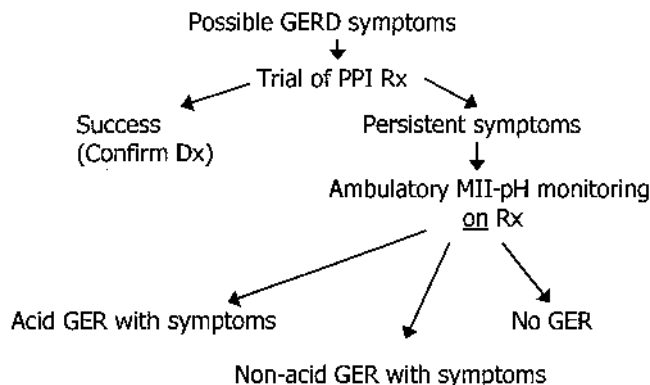


FIGURE 12. Proposed GERD diagnostic algorithm.

to direct therapy into additional pharmacologic approaches, surgery, or perhaps even endoscopic modification of reflux.

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