Clinical Application of Impedance-Manometry for Motility Testing and Impedance-pH for Reflux Monitoring

a report by

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Esophageal function testing and monitoring are important clinical tests in patients presenting with esophageal symptoms. Many clinicians and investigators consider esophageal manometry the gold standard to evaluate the motor function of the esophagus, and esophageal pH monitoring the gold standard to diagnose gastroesophageal reflux. As these techniques offer only indirect information about intraesophageal bolus movement and presence, videofluoroscopic or radioisotopic imaging have been used to evaluate bolus transit. Multichannel intraluminal impedance (MII) is a relatively new technique first developed a little over a decade ago at the Helmholz Institute in Aachen, Germany.[1] This new technology offers the opportunity to evaluate bolus movement in the esophagus without the use of radiation and, combined with manometry or pH, expands the information collected by these modalities.[2]

Principles of Multichannel Intraluminal Impedance

Impedance is a measurement of the opposition to electric current flow in an alternating current circuit. Placed inside a hollow organ (i.e. the esophagus) impedance is inversely related to the conductivity of the wall and content of the esophagus. The basic component of this technology is the impedance circuit. Two metal (steel) rings separated by an isolator (i.e. the body of the catheter) are connected to an alternating current (AC) generator. In order for the circuit to be closed, electric charges between the two metal rings have to travel in the area surrounding the isolator. When surrounded by air there is almost no current flow between the two rings and therefore the impedance measured between the electrodes is very high. When placed within the esophagus, current flow between the two metal rings is enabled by the electric charges within the esophageal mucosa. Any other material present within the esophagus will produce characteristic changes due to:

- the electric conductivity (directly related with ionic concentration); and
- the cross-section (i.e. the lower the cross-section the higher the impedance).

The electrical impedance, being the opposite of conductivity, decreases from air, to mucosal lining, to saliva/swallowed material to refluxed gastric contents (lowest impedance).

The presence of a liquid bolus between the two impedance rings is identified by following changes:

- a drop in impedance when the current flow is enhanced by the bolus; followed by
- a rise in impedance as the bolus is cleared from this segment by a peristaltic wave;
- an 'overshoot' in impedance corresponding to decreased luminal cross-section during muscle contraction; and
- return to baseline (see *Figure 1a*).

The presence of air between the two impedance rings is identified by a rapid rise in impedance (typically above 5,000Ohm) with a rapid return to baseline (see *Figure 1b*). The presence of mixed (gas–liquid or liquid–gas) boluses is characterized by a combination of both liquid and air changes (see *Figure 1c*).

Current conventions consider the bolus entry point at the 50% drop from baseline to nadir and bolus exit at the recovery of impedance to this 50% value. Studies using combined MII and fluoroscopy have validated these impedance parameters. Simren et al.[3] reported on combined MII-videofluroscopy studies and found a good correlation between impedance and videofluoroscopy of determining bolus head (r^2=0.89) and bolus tail (r^2=0.79) transit times. In another study, Inman et al.[4] reported very good correlation (97%) between impedance and fluoroscopy to identify swallows with complete and incomplete bolus transit.

The use of serial impedance measuring sites on a single catheter (i.e. multichannel intraluminal impedance; MII) allows determining not only bolus presence at various levels in the esophagus, but the direction of bolus movement in the esophagus. Progression of impedance changes from proximal to distal indicate an antegrade bolus movement as observed during swallowing (see *Figure 2a*) while

Figure 1: Impedance Changes Produced by Liquid (a), Gas (b), or Mixed (c) Boluses

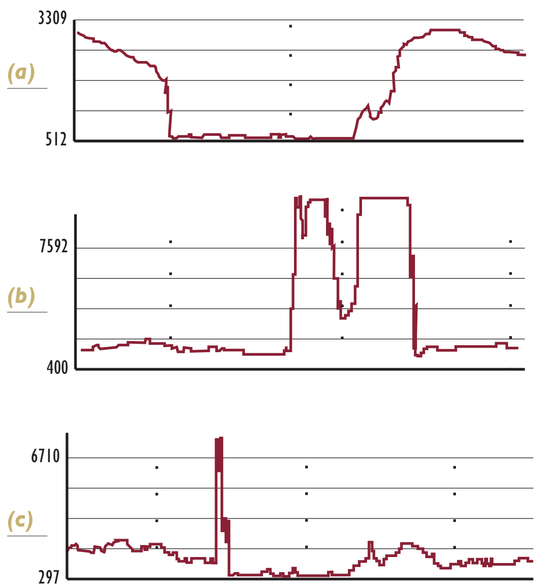
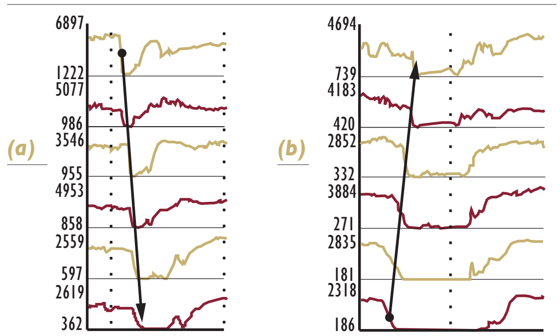


Figure 2: Using multiple impedance measuring sites MII can detect direction of bolus movement



Progression of impedance changes from proximal to distal (a) are indicative of antegrade bolus movement as observed during swallowing while progression of impedance changes from distal to proximal (b) are indicative for retrograde bolus movement as observed in reflux.

progression of impedance changes from distal to proximal indicate a retrograde bolus movement as observed in reflux (see *Figure 2b*). In order to detect these changes, MII systems sample impedance data at high frequencies (50–1,000Hz). Evaluating various sampling rates, Bredenoord et al[5] reported that sample rates as low as 8Hz are sufficient to identify bolus transit during swallowing but sampling rates of at least 50Hz are required for an accurate detection of reflux episodes.

Combined with manometry (MII-EM) impedance offers the opportunity to evaluate pressure changes and bolus transit during the same swallow hereby providing information on the functionality of esophageal peristalsis. Combined with pH (MII-pH) impedance offers the opportunity to detect all types of reflux episodes, independent of the pH of the refluxate.

Combined Multichannel Intraluminal Impedance and Manometry

Impedance measuring capabilities can be added to both water-perfused and solid-state manometry systems. The design of currently available catheters allows collecting impedance and pressure data at the same levels in the esophagus. The 9-channel combined MII-EM catheter (see *Figure 3*) provides information on pressure and bolus presence at five, 10, 15, and 20cm above the lower esophageal sphincter (LES) and the LES residual pressure during swallowing. Combined MII-EM testing is performed in a very similar way to conventional manometry. After successful esophageal intubation and positioning of the catheter using station pull-through technique, subjects are given 10 liquid and 10 viscous single swallows in 20–30 seconds intervals.

Normal values for combined MII-EM testing have been established in a multicenter study including 43 normal volunteers.[6] Normal values for bolus presence and transit in the esophagus were defined based on the 5th–95th percentile values recorded in these healthy volunteers. In addition, this study found that more than 90% of normal healthy volunteers clear more than 80% of individual liquid swallows and more than 70% of individual viscous swallows.

The additional information obtained from the impedance data has been described in a study in 350 patients with various manometric findings.[7] While all patients with achalasia and scleroderma were found to have abnormal bolus transit, the majority (>95%) of patients with normal esophageal manometry, nutcracker esophagus, and isolated LES abnormalities (i.e. poorly relaxing LES, hypertensive LES, and hypotensive LES) was found to have normal bolus transit. Approximately 50% of patients with manometric features of ineffective esophageal motility (IEM) or distal esophageal spasm (DES) were found to have normal bolus transit for liquid (see *Figure 4*).

Evaluating patients with IEM in more detail, it was found that there is no perfect (i.e. highly sensitive and highly specific) manometric cut-off that would predict complete bolus transit, and the current manometric criteria for diagnosing IEM (i.e. 30% or more manometric ineffective swallows) is too sensitive and lacks the specificity of identifying patients with abnormal bolus transit. The study also found that approximately one-third of patients with IEM had normal bolus transit for liquid and viscous, approximately one-third had abnormal bolus transit for either liquid or viscous, and the remaining third of IEM patients had abnormal bolus transit for both liquid and viscous.[8] Based on these findings, a grading scale of esophageal function defect in patients with IEM has been proposed:

1. Mild defect for patients with normal bolus transit for both liquid and viscous.
2. Moderate defect for patients with abnormal bolus transit for either liquid or viscous.
3. Severe defect for patients with abnormal bolus transit for liquid and viscous.

A similar detailed analysis was performed for patients with manometric DES.[9] In this group of patients, it was found that the onset of contraction in the distal esophagus and the contraction amplitude in the distal esophagus influence bolus transit. In contrast to the results in patients with IEM it was found that approximately 50% of DES patients have normal bolus transit for both liquid and viscous, approximately 25% have normal bolus transit for liquid or viscous and the remaining 25% have abnormal bolus transit for both liquid and viscous.

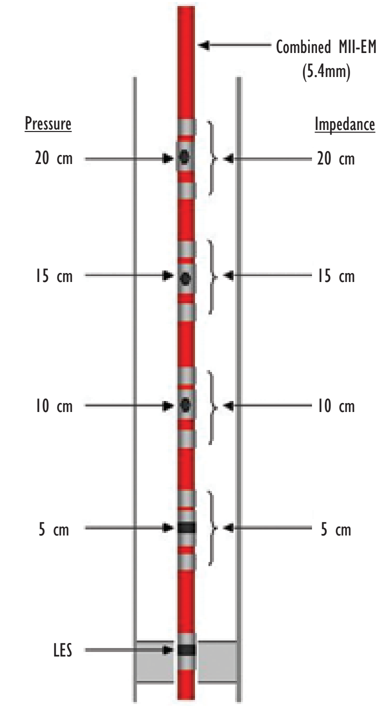
Outcome studies are warranted to evaluate if grading of esophageal function defect in patients with manometric IEM and DES has the potential of identifying patients at risk for developing post-operative dysphagia (i.e. those with severe functional defect).

Combined MII-EM provides better information about bolus transit in patients with post-fundoplication dysphagia.[10] Combined impedance-manometry and videofluoroscopy studies in patients with post-fundoplication dysphagia indicate the ability of MII-EM to identify intraesophageal bolus pooling proximal to the fundoplication and retrograde escape of the bolus into the proximal esophagus after the completion of an otherwise normal peristaltic contraction. These studies underscore the potential of combined MII to evaluate patients with esophageal symptoms after fundoplication.

Combined Multichannel Intraluminal Impedance and pH (MII-pH)

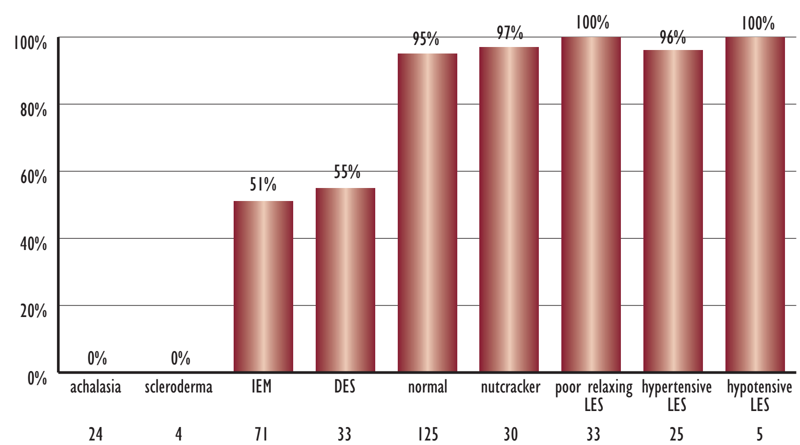
Combined MII-pH represents a shift in the reflux-testing paradigm. Gastroesophageal reflux (GER) of all types is detected by MII and is only characterized as acid or non-acid by its pH. Simultaneous measurements of manometry and impedance have been used to validate reflux detection by MII when reflux was identified by the presence of a manometrically defined 'common cavity'.[11] Combined MII-pH classifies GER (1) by the content of the refluxate into liquid, gas, and mixed reflux events and (2) by the pH characteristics of the content into acid and non-acid. Using multiple impedance measuring sites MII can also identify the height of the refluxate (i.e. most proximal impedance channel in which GER impedance changes are noted). Bredenoord et al.[12] have studied the reproducibility of combined MII-pH monitoring and reported high concordances between impedance data recorded in 20 healthy volunteers on two separate days.

Figure 3: 9-channel esophageal function catheter.



Circumferential solid-state pressure sensors located in LES high-pressure zone (P5) and 5cm above it (P4), unidirectional solid-state pressure sensors located 10cm (P3), 15cm (P2) and 20cm (P1) above LES. Impedance measuring segments centered at 5cm (Z4), 10cm (Z3), 15cm (Z2), and 20cm (Z1) above LES.

Figure 4: Percentage of 350 patients with normal bolus transit for liquid based on manometric diagnoses (IEM – ineffective esophageal motility; DES – distal esophageal spasm)



Currently available systems using combined MII-pH employ impedance rings mounted on pH catheters (Sandhill Scientific Inc., Highlands Ranch, CO). The dimensions of combined MII-pH catheters are similar to those of traditional pH catheters (2.1 mm diameter) and therefore do not change patient comfort compared with traditional pH testing (see *Figure 5*).

Figure 6: Revised diagnostic algorithm for GERD

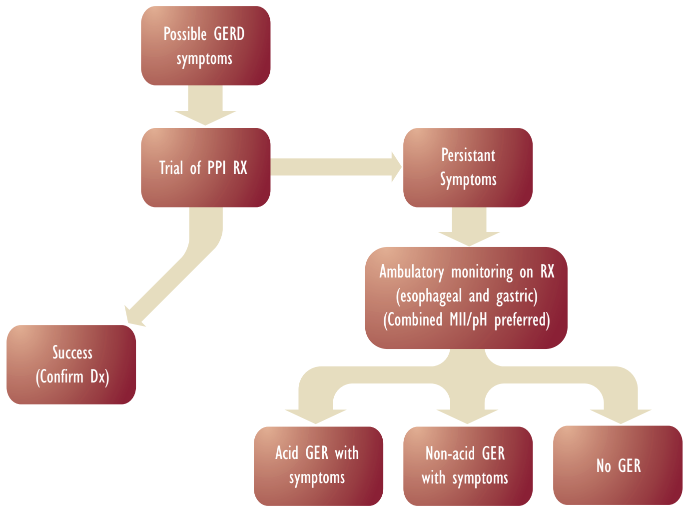
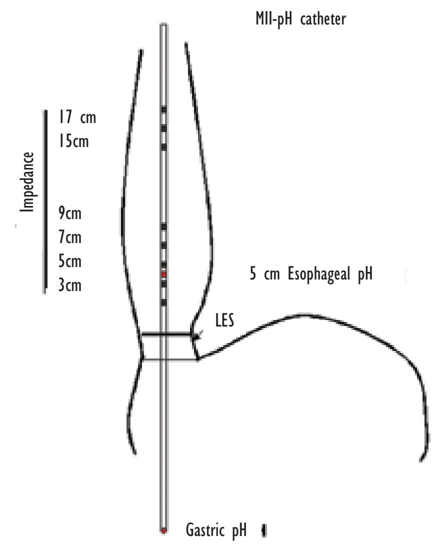


Figure 5: Combined multichannel intraluminal impedance and pH catheter



During reflux monitoring the esophageal sensor is located 5cm above the proximal border of the lower esophageal sphincter (LES). Impedance measuring segments are centered at three, five, seven, and 9cm above the LES in the distal esophagus and around 15 and 17cm above the LES in the proximal esophagus. This catheter also allows monitoring gastric pH (10cm below the LES).

Normal values for combined MII-pH monitoring have been established in a multicenter study in 60 healthy volunteers.[13] Data in normal volunteers suggest that in the absence of acid suppressive therapy the vast majority of GER episodes are acidic, with non-acid GER episodes limited primarily to post-prandial periods. Of particular interest in this study is the observation that the time that intraesophageal pH is below four (detected by pH) is much longer compared with the actual acid bolus presence time (detected by impedance), underscoring the observation that acid clearance requires not only removal of the bolus but neutralization of the mucosal acid. These data confirm prior scintigraphic-pH data by Helm et al. that demonstrated that esophageal acid clearance time (assessed by pH) was much longer compared with the time the radiolabeled hydrochloric acid (HCl) bolus was present in the esophagus.[14]

Preliminary data from a multicenter study evaluating the relationship between residual symptoms on PPI therapy and acid and non-acid reflux suggest that persistent acid reflux is associated with symptoms in only 20% of patients on PPI therapy. In approximately 40% of patients, the residual symptoms are due to non-acid reflux while in the remaining 40% of patients the symptoms are not related to GER episodes.[15] These percentages are dependent on the type (typical or atypical) of GERD symptoms.[16]

Combined MII-pH monitoring is an important addition to the clinical armamentarium for diagnosing and managing GERD. Because GER episodes are detected independent of their pH, combined MII-pH allows detection of all types of reflux events providing information not only about their chemical (pH) composition but about their physical properties (liquid, gas, mixed). By its ability to separate bolus clearance from acid clearance and identify acid re-reflux episodes, combined MII-pH improves our understanding regarding the mechanisms of long pH-detected acid reflux episodes.

The most important addition is the ability to identify the mechanism of residual GERD symptoms on acid suppressive therapy as due to persistent acid reflux, non-acid reflux or no reflux. In the authors' experience, combined MII-pH has revised the diagnostic algorithm for GERD (see *Figure 6*). ■

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