

# Use of Multichannel Intraluminal Impedance to Document Proximal Esophageal and Pharyngeal Nonacidic Reflux Episodes

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**Recent studies in adults and children suggest that combined multichannel intraluminal impedance and pH measurement (MII-pH) has the potential to become the new “gold standard” for gastroesophageal reflux testing. In combined MII-pH, reflux is detected by changes in resistance to alternating current induced by the presence of intraluminal materials with different conductivities, and is characterized as acid or nonacid reflux based on concomitant pH measurements. Proximal distribution and duration of nonacid reflux events, predominantly in postprandial periods and during acid-suppressive therapy, can now be quantified. The ability to associate symptoms with nonacid reflux events will help guide therapy in select groups of patients, such as patients with ongoing symptoms on acid-suppressive therapy as well as in the pediatric population. *Am J Med.* 2003;115(3A): 119S–123S. © 2003 by Excerpta Medica, Inc.**

**A**mbulatory intraesophageal pH measurement is the “gold standard” for documenting gastroesophageal reflux disease (GERD). This test is based on the premise that persons with GERD but not on acid-suppressive therapy will reflux acid content into the esophagus when lower esophageal sphincter (LES) pressure is decreased. Acid-suppressive therapy and antireflux surgery are accepted standard treatments for GERD. The response to therapy of classic GERD symptoms and findings (i.e., heartburn, regurgitation, erosive esophagitis) shows a good correlation with the percentage of time that intraesophageal pH is  $<4$ , whereas “atypical” or “supraesophageal” symptoms (e.g., sore throat, hoarseness, asthma) show a weaker correlation. It has been suggested that nonacid reflux (mainly in the postprandial period), short acid reflux episodes ( $<5$  seconds), or repeated volume reflux during periods when intraesophageal pH is  $<4$  (i.e., acid rereflux) might contribute to the pathogenesis of supraesophageal manifestations of gastroesophageal reflux (GER).

Through its ability to identify GER independently of pH at various levels in the esophagus, combined multichannel intraluminal impedance (MII) and pH measurement (MII-pH) is able to detect both acid and nonacid reflux, as well as the proximal extent of the refluxate. We have previously reported on the potential applications of this technique.<sup>1</sup> This article describes the evolution of MII-pH monitoring and its current clinical applications.

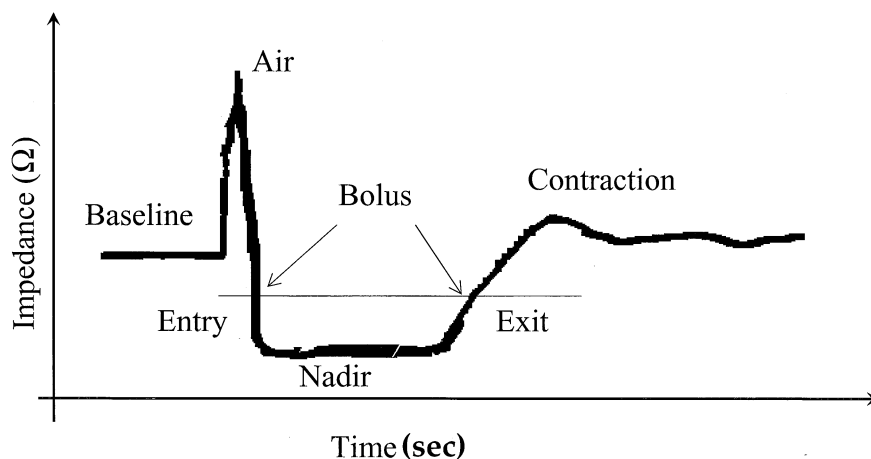
## **SIMULTANEOUS INTRALUMINAL IMPEDANCE AND pH MEASUREMENT**

Silny<sup>2</sup> first described the technique for measuring intraluminal impedance in 1991. It was proposed that the presence of fluid inside the esophagus can be identified based on the different resistance (impedance) of air, muscle, and fluids to alternating current measured between 2 electrodes. Intraluminal impedance is increased in the presence of air and decreased in the presence of fluid compared with the baseline impedance of the esophageal wall (**Figure 1**). Using a series of electrodes on 1 catheter, changes in temporal–spatial patterns in impedance are identified at various levels within the esophagus, allowing differentiation between antegrade (i.e., swallow) (**Figure**

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**Figure 1.** Graphic depiction of intraluminal impedance of the esophageal wall in ohms, starting at baseline and progressing through the presence of air and the presence of a bolus of fluid. Impedance is increased in the presence of air and decreased in the presence of fluid.

2A) and retrograde (i.e., reflux) (Figure 2B) bolus movement.

Simultaneous intraesophageal MII-pH detects GER by impedance and characterizes it by pH (i.e., acid if  $\text{pH} < 4$  and nonacid if  $\text{pH} \geq 4$ ).<sup>3</sup> Besides acid and nonacid reflux, MII-pH can further identify sequential reflux events occurring while intraesophageal pH is  $< 4.0$  (i.e., acid rereflux).

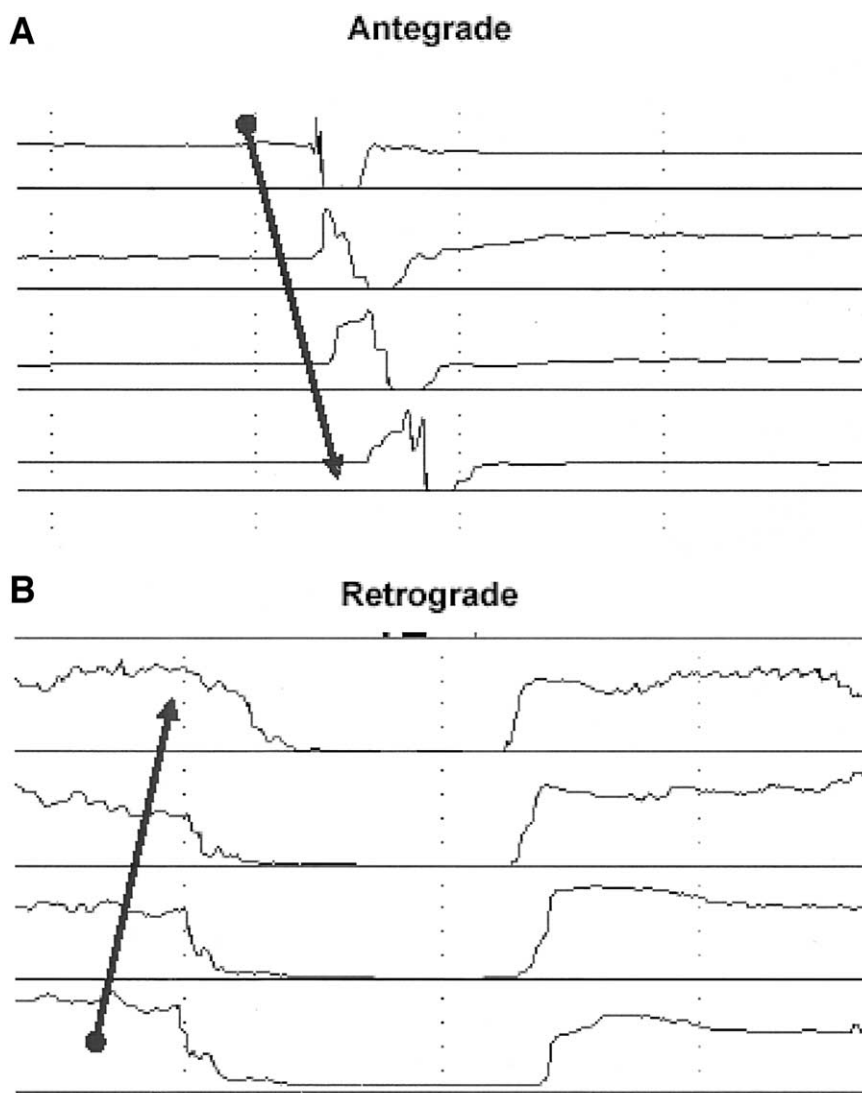
Different MII-pH catheters can be used depending on the clinical scenario. The classic 6MII-1pH assembly (Figure 3A) can be used to detect acid and nonacid reflux. Normative data for this design have recently been established in a multicenter study.<sup>4</sup> A modified design is the 6MII-2pH (Figure 3B), which is an esophageal plus gastric catheter that will concomitantly assess esophageal reflux and intragastric acid control in patients on therapy. Studies establishing normative data for patients on therapy are currently being conducted. A bifurcated 4MII-1pH plus 2MII-1pH adjustable catheter (Figure 3C) may be the preferred design to evaluate pharyngeal reflux concomitantly with distal esophageal reflux. Normative data for this technique have yet to be established, although our previous experience with bifurcated pH probes reveals that acid reflux rarely reaches the pharynx in normal volunteers.<sup>4</sup>

### COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE AND pH MEASUREMENT FINDINGS IN NORMAL ADULT VOLUNTEERS

Normative data for the 6MII-1pH catheter have been established in a multicenter study<sup>5</sup> involving Graduate Hospital (Philadelphia, PA), the Cleveland Clinic (Cleve-

land, OH), the Mayo Clinic (Rochester, MN), University of Southern California (Los Angeles, CA), and Catholic University (Leuven, Belgium). Healthy adult volunteers ( $N = 45$ ) underwent 24-hour MII-pH studies. These results indicate that normal volunteers have less nonacid reflux than acid reflux; MII-detected acid refluxate presence time (percent time) is significantly less than the percent time that intraesophageal pH is  $< 4$ , and minor amounts of nonacid refluxate and small numbers of nonacid reflux events occur at nighttime in the supine position. Furthermore, 37% of distal (5 cm above the LES) reflux episodes, either acid or nonacid, reach the proximal (15 cm above the LES) esophagus in normal volunteers.

We are currently conducting MII-pH studies in adult patients with persistent symptoms on therapy and patients with supraesophageal symptoms. In 1 patient with persistent regurgitation on maximal acid-suppressive therapy, we documented normal percent time intraesophageal pH  $< 4$  and MII-detected acid reflux events, but highly abnormal nonacid reflux, with increased nonacid reflux episodes and refluxate percent time in the proximal esophagus (Figure 4). Note the contrast between this individual and the reflux patterns reported in the normal volunteers. In addition, this patient had a 100% symptom index (19 of 19) of regurgitation with nonacid reflux episodes. This case demonstrates the ability of MII-pH to detect the proximal extent of nonacid reflux and the specific relation of the reflux to persistent symptoms with acid-suppressive therapy. Analysis of combined MII-pH is being refined, and algorithms for automatic reading of these studies are being developed.<sup>6</sup>



**Figure 2.** Changes in temporal-spatial patterns of impedance are identified at various levels within the esophagus, depicting the difference between swallow (antegrade) and reflux (retrograde) bolus movements. (A) Temporal-spatial patterns of impedance for antegrade bolus movement. (B) Temporal-spatial patterns of impedance for retrograde bolus movement.

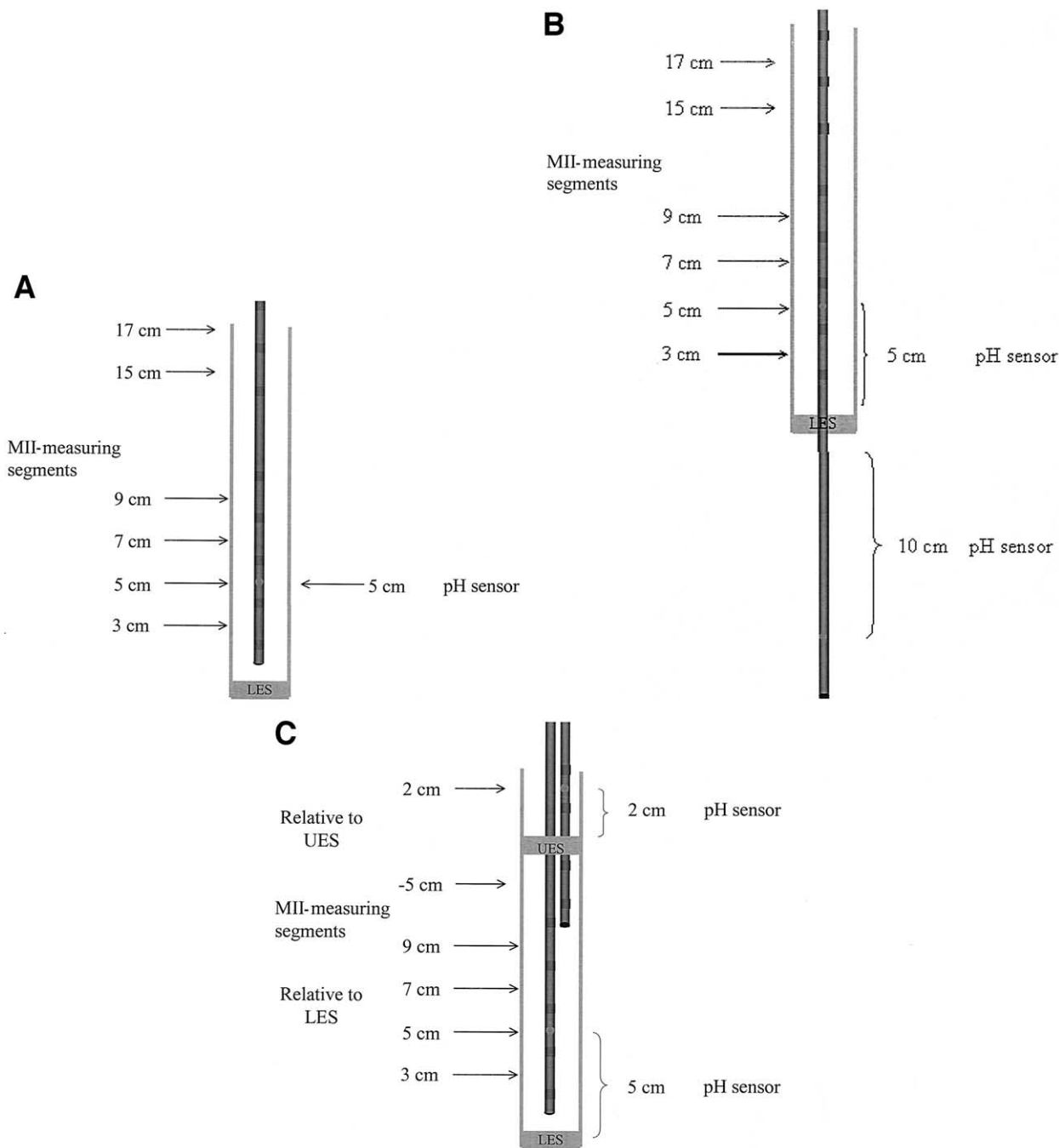
### COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE AND pH MEASUREMENT IN THE PEDIATRIC POPULATION

Before the MII technique became available, the association between pH-detected acid or nonacid reflux and respiratory symptoms in children was controversial.<sup>7,8</sup> Because normal intraesophageal pH is 5.0 to 6.8, a standard pH probe cannot reliably detect reflux episodes with pH >4.0.<sup>9</sup>

In 1996, Skopnik et al.<sup>10</sup> published a study on the ability to detect GER in children aged 1 to 6 months using combined MII-pH. In their analysis of 6-hour MII-pH studies in 17 infants with clinical symptoms of reflux dis-

ease, they found 596 MII-detected reflux episodes, of which only 185 (31%) were identified by pH. A total of 391 (65%) reflux episodes occurred in the 2-hour post-prandial period, and 356 (89%) of these had a pH >4. Another important finding was that 84% of all reflux episodes reached the most proximal MII-recording site (fluoroscopically located in the pharynx).

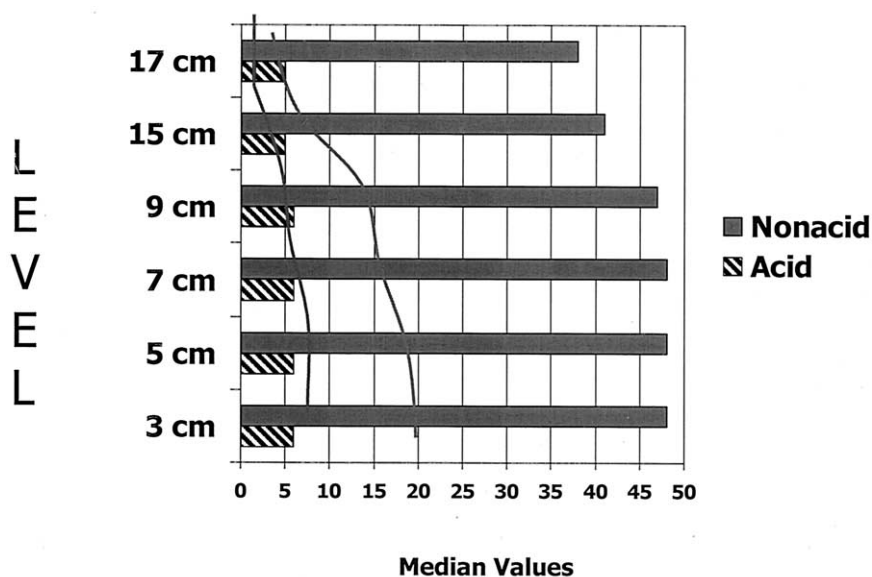
In another study published by Wenzl et al.,<sup>11</sup> 22 infants (9 girls, 13 boys; mean age, 2 ± 1 months) with recurrent regurgitation and respiratory problems underwent 6-hour MII-pH studies. A total of 364 MII-detected reflux episodes were found in all 22 subjects. Breathing irregularities accompanied 312 (85.7%) MII-GER episodes. Most reflux episodes (315 of 364; 86.5%) and most



**Figure 3.** (A) Multichannel intraluminal impedance (MII). Schematic of the classic 6MII-1pH adult esophageal pH probe. This instrument can be used to detect both acid and nonacid reflux. (B) Schematic of the 6MII-2pH esophageal and gastric pH probe. This probe concomitantly measures esophageal reflux and intragastric acid control for patients on antireflux therapy. (C) Schematic of the bifurcated 4MII-1pH + 2MII-1pH probe. This probe measures both pharyngeal and distal esophageal reflux. LES = lower esophageal sphincter; UES = upper esophageal sphincter.

episodes of GER associated with breathing irregularities (269 of 312; 86.2%) occurred during the first 2 postprandial hours. Only 21 (7.8%) of these episodes were acid events ( $\text{pH} < 4$ ). Most GER episodes (260 of 364; 71.4%) and most episodes associated with breathing irregulari-

ties (229 of 312; 73.4%) reached the most proximal recording site (hypopharynx). Only 26 (11.4%) of these were acid events ( $\text{pH} < 4$ ). In all, 19 subjects had a total of 165 episodes of apnea, with 29.7% of these being associated with MII-detected GER.



**Figure 4.** Graph showing the total number of multichannel intraluminal impedance (MII)-gastroesophageal reflux episodes at various levels of the esophagus as recorded by MII-pH probe for a single patient with persistent regurgitation on maximal acid-suppressive therapy. This patient had normal percent time intraesophageal pH <4 and MII-detected acid reflux events, but highly abnormal nonacid reflux, with increased nonacid reflux episodes and refluxate percent time in the proximal esophagus. Curves represent median number of acid (hatched bars) and nonacid (gray bars) reflux episodes based on studies in healthy volunteers.

## SUMMARY

Through its ability to detect both acid and nonacid GER as well as the proximal extent of the reflux, MII-pH promises to become the new gold standard for evaluating patients with supraesophageal symptoms of GERD, pediatric patients with reflux, and patients with persistent symptoms on acid-suppressive therapy.

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