Published in final edited form as:

Neurogastroenterol Motil. 2012 January ; 24(1): 40–e2. doi:10.1111/j.1365-2982.2011.01816.x.

Ambulatory High Resolution Manometry, Lower Esophageal Sphincter Lift and Transient Lower Esophageal Sphincter Relaxation

Ravinder K. Mittal, MD, Anna Karstens, BS, Eric Leslie, BA, Arash Babaei, MD, and Valmik Bhargava, PhD

Division of Gastroenterology, San Diego VA Health Care System & University of California, San Diego, CA, USA

Abstract

Introduction—Lower esophageal sphincter (LES) lift seen on high resolution manometry (HRM) is a possible surrogate marker of the longitudinal muscle contraction of the esophagus. Recent studies suggest that longitudinal muscle contraction of the esophagus induces LES relaxation.

Aim—Our goal was to determine, 1) the feasibility of prolonged ambulatory HRM and 2) to detect LES lift with LES relaxation using ambulatory HRM color isobaric contour plots.

Methods—*In vitro* validation studies were performed to determine the accuracy of HRM technique in detecting axial movement of the LES. Eight healthy normal volunteers were studied using a custom designed HRM catheter and a 16 channel data recorder, in the ambulatory setting of subject's home environment. Color HRM plots were analyzed to determine the LES lift during swallow-induced LES relaxation as well as during complete and incomplete transient LES relaxations.

Results—Satisfactory recordings were obtained for 16 hours in all subjects. LES lift was small (2 mm) in association with swallow-induced LES relaxation. LES lift could not be measured during complete transient LES relaxations (TLESRs) because the LES is not identified on the HRM color isobaric contour plot once it is fully relaxed. On the other hand, LES lift, mean 7.6 ± 1.4 mm, range 6–12 mm was seen with incomplete TLESRs (n = 80).

Conclusions—Our study demonstrates the feasibility of prolonged ambulatory HRM recordings. Similar to a complete TLESR, longitudinal muscle contraction of the distal esophagus occurs during incomplete TLESRs, which can be detected by the HRM. Using prolonged ambulatory HRM, future studies may investigate the temporal correlation between abnormal longitudinal muscle contraction and esophageal symptoms.

Address correspondence to: Dr. R.K. Mittal, Division of Gastroenterology (111D), San Diego VA Medical Center and University of California San Diego, 3350 La Jolla Village Drive, San Diego, CA 92161, rmittal@ucsd.edu.

Conflict of Interest: No conflicts of interest exists for all of the authors.

Contribution of Each Author:

Ravinder K. Mittal: Design of equipment, design of experiment, supervise data acquisition, write and edit the manuscript.

Anna Karstens: Initial testing of equipment, recruiting subjects for the study, data acquisition and data analysis.

Eric Leslie: Recruiting subjects for the study, data acquisition, data analysis and help with writing the manuscript.

Arash Babaei: Recruiting subjects for the study, data acquisition and analysis.

Valmik Bhargava: Initial testing of equipment, software development, data analysis, creating figures, and writing of the manuscript

Keywords

Longitudinal Muscle Contraction; Mechanosensitive Motor Neurons

INTRODUCTION

Longitudinal muscle contraction of the esophagus plays an important role in the physiology and pathophysiology of esophageal motor function and esophageal symptoms¹. Studies suggest that it may actually be the cause of lower esophageal sphincter (LES) relaxation^{2, 3}. Furthermore, heartburn and esophageal chest pain may be related to sustained contraction of longitudinal muscles of the esophagus^{4, 5}.

Several investigators have used catheter based, high frequency intra-luminal ultrasound imaging (HFIUS) to study longitudinal muscle contraction in the humans⁶⁻⁹. The problem with the HFIUS technique is that the US image analysis is extremely time consuming and labor intensive, which has prevented its wide-spread use. High resolution manometry (HRM) is an improved recording technique to study esophageal motility, but similar to other intra-luminal pressure recording techniques, it only measures circular muscle contractions of the esophagus. Several investigators have observed LES lift on routine HRM clinical manometry studies and suspect it to be a surrogate of longitudinal muscle contraction of the esophagus^{10, 11}. However, it is not clear if the HRM can accurately determine oral-aboral movements of the LES.

Esophageal symptoms occur infrequently and at unpredictable times. The equipment and technique of HRM are only available for recording esophageal motility in the non-ambulatory setting and only for short time intervals, which is not ideal to determine the temporal correlation between symptoms and motor events. Therefore, it would be advantageous to record HRM in the ambulatory setting for symptom correlation. The aim of our study was two-fold: 1) to study the feasibility of ambulatory, long term HRM recording in humans, 2) to determine if LES lift, as a marker of longitudinal muscle contraction can be detected during various types of LES relaxation in normal healthy subjects.

METHODS

In-vitro studies

We determined if HRM and color contour plots can measure movement of the high pressure zone along the catheter accurately. A custom-made HRM catheter was used for these studies. The catheter was 3 mm in diameter and equipped with 16 solid-state, unidirectional pressure transducers spaced 1 cm apart, starting 5 cm from the tip of the catheter (from Unisensor, NH). A vascular occluder (from *In-Vivo* Metrics, CA) was used to create an artificial high pressure zone (HPZ). It was wrapped around a small cylinder made of 1% agar with a 2 mm diameter piezoelectric crystal embedded in it. Another piezoelectric crystal was glued to the HRM catheter (Figure 1A). The entire assembly was placed inside a tub filled with water so as to allow measurement of distance between the two piezoelectric crystals sonographically. The cuff was inflated with water to a pressure of 30 – 50 mmHg. To shift the cuff location (artificial HPZ) on the catheter, the cuff was gradually pulled in either direction over various distances. The exact distance moved by the catheter was recorded by piezoelectric crystals (measurement accuracy 0.01mm). HRM recordings were scored in a blinded fashion to determine the movement of the artificial HPZ on the catheter. The relationship between the distances detected by the piezoelectric crystal and HRM color isobaric contour plot was determined.

***In Vivo* Humans Studies**

The HRM catheter with 16 solid state pressure transducers, used for *in-vitro* studies, was also used for the *in-vivo* human recordings. Pressure transducers were calibrated in a pressure chamber and the catheter was soaked in the water at 37° for one half hour prior to placement in the subject. This procedure reduces the zero drift of the pressure transducers, which was determined to be less than 5mmHg during 24 hours. The protocol for these studies was approved by the “Human Subject Protection Committee of the University of California San Diego” and each subject signed a consent form prior to the beginning of the study. Eight normal healthy asymptomatic subjects participated in the study protocol. The age of subjects ranged from 22 – 50 years (mean, 34 years). The catheter was placed trans-nasally and positioned such that the 2 or 3 most distal transducers were located in the stomach and the remainder spanned across the LES and distal esophagus. The catheter was secured to the tip of the nose with tape and connected to a 16-channel ambulatory data recorder (from MMS, Netherlands). The data recorder weighs approximately 1.5 lbs and uses AA batteries as a power source. In addition to pressure signals, it has the ability to record events such as pain, meals etc. Data was captured at a sampling rate of 4 or 8 Hz. At the 8 Hz sampling rate, data could be acquired for 16 hours and at 4 Hz for 32 hours. After catheter placement, subjects returned home and ate regular meals during the recording period. The subjects documented meal times, time spent in the supine position and other events of interest by using the event marker on the recorder.

Data Analysis

Stomach, LES and esophageal pressure recordings were displayed as HRM color isobaric contour plots. Longitudinal muscle contraction occurs in association with swallow induced peristalsis and transient LES relaxation. Therefore, the following events were identified and marked for analysis in the HRM color isobaric contour plots: 10 randomly selected dry swallows, 10 complete transient LES relaxations, i.e., end-expiratory LES pressure of less than 2 mmHg at the peak of relaxation, and 10 incomplete transient LES relaxations. LES pressure was measured in reference to gastric pressure. Incomplete TLESRs were recognized when the end-expiratory LES pressure during relaxation was more than 5 mmHg. LES pressure was measured prior to and during LES relaxation to determine percent relaxation during all of the above events. The lower edge of the LES high pressure zone was also identified, where it transitioned to the stomach pressure. For each event, vertical displacement of the lower edge of the LES was measured prior to and during relaxation. Maximum, minimum, and average esophageal pressures were measured over a 10s interval before and during TLESRs. All esophageal pressures were measured relative to the atmospheric pressure.

Recordings obtained during a previously published study were also analyzed¹². In that study, we simultaneously recorded esophageal pressures using a stationary, HRM system (Sierra Scientific Inc, Los Angeles, CA) and HFIUS images of the esophagus at 3 cm above the LES (Hewlett Packard, Sonos 100, MA). These recordings were obtained in 8 subjects, following ingestion of a 1000 kcal meal. We identified 10 complete and 10 incomplete TLESRs in these studies. Ultrasound images before and during TLESRs were analyzed, as described previously¹². Briefly, from the tomographic ultrasound images, m-mode images were developed using custom software and temporally aligned with the pressure data. Change in muscle thickness, as a marker of longitudinal muscle contraction was determined during complete and incomplete TLESRs. The goal of these measurements was to verify if longitudinal muscle contraction of the esophagus (as detected by HFIUS imaging) occurs during incomplete TLESR.

Statistical Analysis

Data are reported as mean and standard error of mean, unless otherwise stated. Paired and unpaired student's t-tests were used for statistical comparison. Pearson's product-moment correlation coefficient was used to estimate correlation coefficients. P-value < 0.05 was considered statistically significant.

RESULTS

In-vitro Study

Figure 1 shows the design of the ambulatory HRM catheter and *in-vitro* recording technique to study the effects of movement of the artificial HPZ on the HRM catheter. Figure 1B shows the effect of movement of different distances of the artificial HPZ as recorded by piezoelectric crystals and by HRM color isobaric contour plot. Note that each of the movements of the HPZ is recorded sonographically as well as by the HRM color isobaric contour plot. The graph in figure 1C shows the relationship between distances moved, as monitored by the 2 techniques. There is a strong linear correlation between the HPZ movements recorded sonographically and by the HRM color isobaric contour plot, r value of 0.91. Further analysis revealed that if the distance moved was more than 5mm, the reliability of HRM to detect axial movement was even better with an r value of 0.99.

Human Studies

Studies were successfully conducted in all 8 subjects and the pressure measurements were converted into HRM color isobaric contour plots using MMS software. Adequate recording were obtained for a minimum of 16 hours duration in all subjects. Spontaneous swallow induced movement of the LES is shown in figure 2. Note, the elevation of the lower border of the LES high pressure zone (LES lift) in each of the two swallows. The LES lift was small and ranged from 2 to 4 mm (mean, 2.03 ± 0.21 mm). Figure 3 shows the relationship between percent LES relaxation and LES lift during spontaneous swallows; there is poor correlation between the two values ($r^2 = 0.001$). Similarly the correlation between LES lift and delta LES pressure was also poor with an r^2 of 0.018.

HRM recording during complete TLESRs is shown in figure 4A. LES relaxation occurs fairly quickly and completely. Once the LES is completely relaxed its location in the HRM color isobaric contour plot can't be identified. Therefore, LES lift during complete TLESRs cannot be measured with HRM. However, in some complete TLESRs, the onset of LES relaxation is relatively slow and during these events LES lift and LES relaxation are seen to occur concurrently at the onset of relaxation (Figure 4).

Figure 4B shows LES lifts of 7 mm and 17 mm during two incomplete TLESRs. The lower edge of LES in these records was marked as the transition zone between the LES HPZ and gastric pressure. A total of 80 incomplete TLESRs were scored (10 per subject in 8 subjects). The LES lift ranged from 4 to 18 mm (mean, 8.37 ± 0.60 mm). Figure 3 shows the relationship between change in LES pressure during LES relaxation, or delta LES pressure, and the amplitude of LES lift. There was poor correlation between the two values ($r^2 = 0.046$). Percent LES relaxation and LES lift also did not show significant correlation ($r^2 = 0.007$), (figure 3).

Changes in esophageal pressure during complete and incomplete TLESRs are shown in figure 5. The increase in esophageal pressure starts to occur with the onset of LES relaxation, and once the LES is fully relaxed, the esophagus and stomach become one cavity (common cavity). The average increase in esophageal pressure during complete TLESRs is 3.7 ± 0.9 mmHg (n = 8 subjects with 10 complete TLESRs for each subject). Interestingly,

the esophageal pressure also increases during incomplete TLESRs (Figure 5) (mean, 4.7 ± 0.6 mmHg ($n = 8$ subjects with 10 incomplete TLESRs for each subject). The amplitude of esophageal pressure increase during complete and incomplete TLESR is not different.

Figures 6A and 6B show m-mode US images and HRM during incomplete and complete TLESRs respectively. Muscle thickness is shown as an m-mode image at the bottom of the HRM plot. The changes in thickness are demonstrated more clearly when superimposed on the HRM plot (yellow line). During TLESR, an increase in muscle thickness is observed. This muscle thickening, a marker of longitudinal muscle contraction, returns to baseline upon termination of the TLESR. The peak increase in muscle thickness during complete TLESRs, 94 ± 30 % tended to be greater but not significantly different than with the incomplete TLESRs, 54 ± 8 % ($p > .05$).

DISCUSSION

In summary, our data show the following, 1) *in-vitro* recordings show that movements of an artificial HPZ along the length of HRM catheter are faithfully recorded by the HRM color isobaric contour plot, 2) swallow related LES relaxation is associated with a small LES lift. 3) LES lift can't be recognized during complete TLESRs because a fully relaxed LES is not seen on the HRM plot. 4) Incomplete TLESRs are associated with significant LES lift, which is greater than those associated with spontaneous swallow-induced LES relaxation. 5) There is an increase in esophageal pressure with the onset of complete as well as incomplete TLESRs, with no difference in the degree of increase in pressure between the two. 6) Ultrasound image analysis shows that, similar to complete TLESR, incomplete TLESRs are also associated with sustained longitudinal muscle contraction of the esophagus for the entire duration of the TLESR.

Since pressure transducers on the HRM catheter are located 1 cm apart (from center of one transducer to the center of other), one can be certain that LES movement on the HRM catheter of 1 cm or more would be easily and certainly detected. However, our *in-vitro* study shows that even less than 1 cm of HPZ movement can be detected by the HRM catheter. There may be several reasons for the above, 1) HRM color isobaric contour plot uses a computer algorithm (linear interpolation) to generate a seamless color plot between the actual pressure data obtained at every 1 cm. The LES is 3–4 cm in length and pressures along its length are distributed in the shape of a bell. Small movements of the LES shift the location of peak pressure as well as change the full length of the pressure profile. These shifts, in conjunction with the computer algorithm used to generate the HRM color isobaric contour plots, change the location of the LES border on the HRM color isobaric contour plot. 2) Each transducer itself is 4mm long and if the HPZ encompasses only a part of the length vs the entire length of the transducer it may record different pressure thus allowing for some changes in pressure even when the HPZ movement is less than one cm. Irrespective of the explanation, actual measurements using sensitive piezocrystal technique proves our claim. One can observe oral and aboral LES movement of 2–3mm with tidal respiration (see, figure 2) and greater with forced inspiration on HRM recording, proving that the latter can indeed record axial LES movements using HRM.

Cranial movement of the LES with swallows has been observed by radiologists for more than 50 years. Dodds implanted radio-opaque markers along the esophagus and LES, and clearly demonstrated that with swallows and secondary peristalsis, the LES moves orally and results in a relative movement between the side hole of the manometry catheter and LES^{13, 14}. The latter results in a possible artifact of LES pressure recording during LES relaxation if the LES pressure were to be monitored by a side-hole sensor. To avoid the above artifact, Dent devised the sleeve sensor¹⁵. Mucosal clips implanted endoscopically in

the distal esophagus also show oral movement of the LES with both swallow and peristalsis^{16, 17}. Oral movement of the LES with swallows is observed consistently by HRM, albeit the magnitude of this movement is relatively small as compared to the one observed by fluoroscopy imaging studies. The reason may be that we studied spontaneous swallows in which LES relaxation is small as compared to the wet swallows (water or barium) in which the LES relaxation is more complete. The reason for studying spontaneous swallows in our study was that if the LES is fully relaxed, LES lift can't be measured by the HRM technique. The other reason may be that the HRM technique is relatively less accurate when the LES lift is less than 5mm. Using water infusion manometry, Bredenoord et al performed high resolution manometry for 1–2 hours in stationary subjects. They observed separation of the LES and crural diaphragm, intermittently during these recording periods¹⁸, which proves the feasibility of recording axial movements of the high pressure zone with HRM. Interestingly, those periods when LES and crural diaphragm were separated were more likely to be associated with reflux than when they were not.

Pandolfino et al used endoscopically placed mucosal clips to study esophageal shortening during TLESR and found significant and sustained shortening of the esophagus during the entire period of TLESR¹⁹. Babei et al found a unique pattern of longitudinal muscle contraction of the esophagus in association with TLESR, which is different from the one associated with swallow-induced peristalsis¹². The longitudinal muscle contraction starts just above the LES and proceeds in an antiperistaltic fashion towards the mouth. On the other hand, swallow-induced peristalsis is associated with simultaneous contraction of the circular and longitudinal muscle that traverses from the oral to the aboral direction in a peristaltic fashion^{7, 20}. Another study by Pandolfino also revealed a greater segmental shortening of the distal as compared to mid esophagus in association with TLESR¹⁹. Once the LES is fully relaxed during complete TLESRs it can't be recognized on the HRM color isobaric contour plot. Therefore, the LES lift can't be measured during complete TLESRs. However, with incomplete TLESRs we observed LES lift during the entire period of TLESR. Usually the LES lift starts before the onset of LES relaxation and lasts throughout the TLESR. Ultrasound images during the period of incomplete TLESR show the presence of longitudinal muscle contraction, similar to what we observed in an earlier study.

A mechanical axial stretch on the LES in the cranial direction induces LES relaxation that is blocked by L NAME (blocker of nitric oxide)². Axial stretch-induced LES relaxation is caused by activation of inhibitory motor neurons because it is not blocked by any of the neuronal synaptic blockers³. Fundoplication restricts axial stretch on the LES and prevents LES relaxation²¹. Based on the above studies, we expected a linear relationship between the LES lift and percent LES relaxation, which was not observed in our study. It is possible that the movement of LES was influenced by respiration. Similar to *in-vivo* studies, it is not possible to separate respiration-induced LES movements from those caused by longitudinal muscle contraction.

The increase in intraesophageal pressure during complete TLESRs, referred to as common cavity pressure, is thought to represent reflux of gastric contents into the esophagus^{22–24}. However, Tipnis et al reported that even though pressure increases simultaneously throughout the length of the esophagus, the reflux of gastric contents into the esophagus occurs sequentially, i.e., reflux occurs first in the distal esophagus and traverses to the proximal esophagus²⁵. They found that contractions of the longitudinal muscle of the esophagus occur in association with increases in esophageal pressure and the proposed shortening of the esophagus, in accordance with Boyle's law of physics, is the reason for increase in esophageal pressure. Since gastroesophageal reflux does not occur during incomplete TLESRs^{26–28}, the increase in esophageal pressure during incomplete TLESRs is most likely related to the contraction of longitudinal muscles and esophageal shortening. We

recently reported that the simultaneous pressure waves in the achalasic esophagus are also related to longitudinal muscle contraction and esophageal shortening²⁹. We propose that increases in esophageal pressure could be an important marker of longitudinal muscle contraction of the esophagus.

Ultrasound imaging clearly show longitudinal muscle contraction of the distal esophagus during incomplete TLESR. It has been suggested that the LES relaxation during TLESR may begin from the lower edge of LES; such relaxation would appear as a LES lift in the HRM color isobaric contour plot and is an important limitation of the technique. The use of LES lift as a marker of longitudinal muscle contraction has significant clinical implications for the diagnostic evaluation of esophageal symptoms. Sustained contraction of longitudinal muscles of the esophagus may be the cause of heartburn⁵ and “angina like” esophageal pain⁴. Longitudinal muscle contraction was measured using HFIUS imaging in those studies, which is time consuming and not practical. Furthermore, esophageal symptoms occur infrequently and at unpredictable times and in order to make a temporal association between symptoms and abnormal motor events long term monitoring is actually required. Using ambulatory HRM and LES lift as a marker of longitudinal muscle contraction, future studies may be able to determine the true correlation between esophageal symptoms and longitudinal muscle spasm.

Acknowledgments

Grant Support: NIH-RO1-DK060733

BIBLIOGRAPHY

1. Mittal RK, Liu J, Puckett JL, Bhalla V, Bhargava V, Tipnis N, Kassab G. Sensory and motor function of the esophagus: lessons from ultrasound imaging. *Gastroenterology*. 2005; 128:487–97. [PubMed: 15685559]
2. Dogan I, Bhargava V, Liu J, Mittal RK. Axial stretch: A novel mechanism of the lower esophageal sphincter relaxation. *Am J Physiol Gastrointest Liver Physiol*. 2007; 292:G329–34. [PubMed: 17023549]
3. Jiang Y, Bhargava V, Mittal RK. Mechanism of stretch-activated excitatory and inhibitory responses in the lower esophageal sphincter. *Am J Physiol Gastrointest Liver Physiol*. 2009; 297:G397–405. [PubMed: 19520741]
4. Balaban DH, Yamamoto Y, Liu J, Pehlivanov N, Wisniewski R, DeSilvey D, Mittal RK. Sustained esophageal contraction: a marker of esophageal chest pain identified by intraluminal ultrasonography. *Gastroenterology*. 1999; 116:29–37. [PubMed: 9869599]
5. Pehlivanov N, Liu J, Mittal RK. Sustained esophageal contraction: a motor correlate of heartburn symptom. *Am J Physiol Gastrointest Liver Physiol*. 2001; 281:G743–51. [PubMed: 11518687]
6. Miller L, Dai Q, Korimilli A, Levitt B, Ramzan Z, Brasseur J. Use of endoluminal ultrasound to evaluate gastrointestinal motility. *Dig Dis*. 2006; 24:319–41. [PubMed: 16849860]
7. Nicosia MA, Brasseur JG, Liu JB, Miller LS. Local longitudinal muscle shortening of the human esophagus from high-frequency ultrasonography. *Am J Physiol Gastrointest Liver Physiol*. 2001; 281:G1022–33. [PubMed: 11557523]
8. Boesmans W, Vanden Berghe P, Farre R, Sifrim D. Oesophageal shortening: in vivo validation of high-frequency ultrasound measurements of oesophageal muscle wall thickness. *Gut*. 2010; 59:433–40. [PubMed: 20332517]
9. Yamamoto Y, Liu J, Smith TK, Mittal RK. Distension-related responses in circular and longitudinal muscle of the human esophagus: an ultrasonographic study. *Am J Physiol*. 1998; 275:G805–11. [PubMed: 9756512]
10. Tutuian R, Pohl D, Castell DO, Fried M. Clearance mechanisms of the aperistaltic oesophagus: the “pump gun” hypothesis. *Gut*. 2006; 55:584–5. [PubMed: 16354796]

11. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. *Gastroenterology*. 2008; 135:1526–33. [PubMed: 18722376]
12. Babaei A, Bhargava V, Korsapati H, Zheng WH, Mittal RK. A unique longitudinal muscle contraction pattern associated with transient lower esophageal sphincter relaxation. *Gastroenterology*. 2008; 134:1322–31. [PubMed: 18384786]
13. Dodds WJ, Stewart ET, Hodges D, Zboralske FF. Movement of the feline esophagus associated with respiration and peristalsis. An evaluation using tantalum markers. *J Clin Invest*. 1973; 52:1–13. [PubMed: 4682383]
14. Dodds WJ. 1976 Walter B Cannon Lecture: current concepts of esophageal motor function: clinical implications for radiology. *AJR Am J Roentgenol*. 1977; 128:549–61. [PubMed: 403780]
15. Dent J. A new technique for continuous sphincter pressure measurement. *Gastroenterology*. 1976; 71:263–7. [PubMed: 939387]
16. Edmundowicz SA, Clouse RE. Shortening of the esophagus in response to swallowing. *Am J Physiol*. 1991; 260:G512–6. [PubMed: 2003613]
17. Poudroux P, Lin S, Kahrilas PJ. Timing, propagation, coordination, and effect of esophageal shortening during peristalsis. *Gastroenterology*. 1997; 112:1147–54. [PubMed: 9097997]
18. Bredenoord AJ, Weusten BL, Timmer R, Smout AJ. Intermittent spatial separation of diaphragm and lower esophageal sphincter favors acidic and weakly acidic reflux. *Gastroenterology*. 2006; 130:334–40. [PubMed: 16472589]
19. Pandolfino JE, Zhang QG, Ghosh SK, Han A, Boniquit C, Kahrilas PJ. Transient lower esophageal sphincter relaxations and reflux: mechanistic analysis using concurrent fluoroscopy and high-resolution manometry. *Gastroenterology*. 2006; 131:1725–33. [PubMed: 17087957]
20. Mittal RK, Padda B, Bhalla V, Bhargava V, Liu J. Synchrony between circular and longitudinal muscle contractions during peristalsis in normal subjects. *Am J Physiol Gastrointest Liver Physiol*. 2006; 290:G431–8. [PubMed: 16210472]
21. Jiang Y, Sandler B, Bhargava V, Mitta RK. Antireflux Action of Nissen Fundoplication and Stretch-Sensitive Mechanism of Lower Esophageal Sphincter Relaxation. *Gastroenterology*. 2011; 140:442–449. [PubMed: 20955702]
22. Aanen MC, Bredenoord AJ, Samsom M, Smout AJ. The gastro-oesophageal common cavity revisited. *Neurogastroenterol Motil*. 2006; 18:1056–61. [PubMed: 17109688]
23. Kahrilas PJ, Dodds WJ, Dent J, Wyman JB, Hogan WJ, Arndorfer RC. Upper esophageal sphincter function during belching. *Gastroenterology*. 1986; 91:133–40. [PubMed: 3710062]
24. Dent J, Dodds WJ, Friedman RH, Sekiguchi T, Hogan WJ, Arndorfer RC, Petrie DJ. Mechanism of gastroesophageal reflux in recumbent asymptomatic human subjects. *J Clin Invest*. 1980; 65:256–67. [PubMed: 7356677]
25. Tipnis NA, Liu J, Puckett JL, Mittal RK. Common cavity pressure during gastroesophageal reflux: reassessment using simultaneous pressure, impedance, and ultrasound imaging. *Am J Physiol Gastrointest Liver Physiol*. 2006; 290:G1149–56. [PubMed: 16439471]
26. Mittal RK, Holloway RH, Penagini R, Blackshaw LA, Dent J. Transient lower esophageal sphincter relaxation. *Gastroenterology*. 1995; 109:601–10. [PubMed: 7615211]
27. Ireland AC, Holloway RH, Toouli J, Dent J. Mechanisms underlying the antireflux action of fundoplication. *Gut*. 1993; 34:303–8. [PubMed: 8472975]
28. Bredenoord AJ, Draaisma WA, Weusten BL, Gooszen HG, Smout AJ. Mechanisms of acid, weakly acidic and gas reflux after anti-reflux surgery. *Gut*. 2008; 57:161–6. [PubMed: 17895353]
29. Hong SJ, Bhargava V, Jiang Y, Denboer D, Mittal RK. A unique esophageal motor pattern that involves longitudinal muscles is responsible for emptying in achalasia esophagus. *Gastroenterology*. 2011; 139:102–11. [PubMed: 20381493]

Figure 1. A, B and C. High Resolution Manometry and Axial Movements of a High Pressure Zone: In-Vitro Validation

Figure 1A shows the schematic of the high resolution manometry catheter and agar cylinder wrapped in a pressure cuff. Two piezoelectric crystals were used to measure the axial movements between the HPZ and the HRM catheter. One piezo-electric crystal was embedded in the agar cylinder and the other was glued to the HRM catheter. Figure 1B shows the actual sonographic HPZ movement as recorded by piezo-electric crystals (red line) and HRM color isobaric contour plot. Note, the congruity of the movements recorded by the two techniques. Figure 1C shows the relationship between HPZ movement recorded by the two techniques; note, a strong linear correlation between the two values.

Figure 2. LES Lift During Swallow Induced LES Relaxations

Two spontaneous, dry swallow-induced LES relaxations are shown in this figure. LES relaxations are incomplete. Note, the LES lift of 4 and 2 mm with these LES relaxations.

Figure 3. Correlation Between LES Lift and LES Relaxation

panels A and B show the correlation between change in delta LES pressure and percent LES relaxation with the LES lift during incomplete transient LES relaxations. Panels C and D show the correlation between LES lift and LES relaxation during spontaneous or dry swallow induced LES relaxations. Note that the LES lift is greater with incomplete TLESR as compared to swallow-induced LES relaxations. With both incomplete TLESR and swallow-induced LES relaxation, there is poor correlation between the LES relaxation and LES lift.

Figure 4. LES Lift During Complete and Incomplete Transient LES Relaxation

This figure shows examples of two complete (A) and two incomplete (B) transient LES relaxations. In the left panel of A, the LES relaxes completely and quickly and no LES lift can be seen with the complete TLESR. On the other hand, on the right panel of A, the LES relaxes somewhat slowly during complete TLESR. Note, LES lift and LES relaxation during the early period (follow red dotted line). In panel B, two examples of incomplete TLESR are shown. Note LES lifts of 7 and 17 mm during these two incomplete TLESRs. Also note the increase in esophageal pressure during complete as well as incomplete TLESRs.

Figure 5. Increase in Esophageal Pressure during Complete and Incomplete TLESRs
 Changes in esophageal pressure during complete and incomplete TLESRs is plotted in this graph. Esophageal pressure was measured as the minimum, maximum and mean pressure over a 10 s interval before and during the TLESR. These pressures were measured with reference to atmospheric pressure. Note that the esophageal pressure increases during both types of TLESRs and there is no difference in the increase in esophageal pressure during the two types of TLESRs.

Figure 6. A & B. Longitudinal Muscle Contraction, Detected by Ultrasound Imaging During Complete and Incomplete Transient LES Relaxations

Longitudinal muscle contraction was determined by ultrasound imaging of the esophagus using a catheter based high frequency ultrasound imaging system. The ultrasound transducer was positioned 2 cm above the LES. Tomographic ultrasound images were converted into m-mode images (see methods) and shown at the bottom of the HRM color isobaric contour plot. Changes in muscle thickness were measured from ultrasound images and superimposed on the HRM color isobaric contour plot. Note the increase in esophageal muscle thickness during each of the two transient LES relaxation periods. Increases in esophageal muscle thickness are a marker of longitudinal muscle contraction of the esophagus⁷.