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Esophageal function testing using multichannel intraluminal impedance

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Srinivasan, R., M. F. Vela, P. O. Katz, R. Tutuiian, J. A. Castell, and D. O. Castell. Esophageal function testing using multichannel intraluminal impedance. *Am J Physiol Gastrointest Liver Physiol* 280: G457–G462, 2001.—Multichannel intraluminal impedance (MII) is a new technique for evaluation of bolus transport. We evaluated esophageal function using bolus transport time (BTT) and contraction wave velocity (CWV) of liquid, semisolid, and solid boluses. Ten healthy subjects underwent MII swallow evaluation with various boluses of sterile water (pH 5), applesauce, three different sized marshmallows, and iced and 130°F water. The effect of bethanechol was also studied. There was no difference in BTT or CWV for all water volumes from 1 to 20 ml. There was significant linear increase of BTT with progressively larger volumes of applesauce, and BTT of applesauce was longer than for water. BTT was significantly longer with large marshmallows vs. small and medium and was longer than for water. BTT for iced water was similar to 130°F water. Applesauce showed a significant linear decrease of CWV with progressively larger volumes and was slower than water. Marshmallow showed significantly slower CWV with the large vs. small, and CWV for ice water was significantly slower than 130°F water. Therefore, BTT of liquid is constant, whereas BTT of semisolid and solid are volume dependent and longer than liquids. CWV of semisolids and solids are slower than liquids. CWV of cold liquids is slower than warm liquids. MII can be used as a discriminating test of esophageal function.

motility; manometry; esophageal contraction

ESOPHAGEAL FUNCTION HAS BEEN studied using various technologies. Currently, manometry is the gold standard in evaluating esophageal motility. However, it is limited to only the contractile patterns of the esophagus (18). Pressure waves of adequate amplitude and sequence of contractions ensure that the bolus is effectively swept through the esophagus. However, weaker contractions (<30 mmHg) are likely to be ineffective for bolus movement (4). Since bolus transport cannot be evaluated by esophageal manometry, other procedures are necessary to determine bolus movement through the esophagus. Scintigraphy and videofluoroscopy are both noninvasive procedures that have been used to compliment esophageal manometry by visualizing the transit of the bolus. However, these techniques are limited by access to specialized laboratories

and by radiation exposure. Ultrafast computerized tomography dynamically images the composition, distribution, and propulsion of esophageal contents during swallowing (14). This technology is limited by the economic and logistic factors of the equipment along with the complex nature of the methodology and interpretation of results.

Multichannel intraluminal impedance (MII) is a new technique that has been used to evaluate bolus transport and gastroesophageal reflux; however, its role in esophageal function testing has not been well studied. In this experiment, we aimed to evaluate esophageal function via bolus transport time (BTT) and contraction wave velocity (CWV) of various boluses having different characteristics: liquid, semisolid, and solid boluses, pH 2–8, temperature 35–130°F, volume 1–20 ml, and size 12–30 mm. Also, we challenged the esophagus with bethanechol to see if MII could be used as a discriminating esophageal function test.

METHODS

Subjects. Ten (5 males, 5 females) healthy subjects with a mean age of 34 yr (range 22–51 yr) had the impedance probe (Sandhill Technologies) placed transnasally, with the 2-cm recording segments located at 2, 4, 6, 8, 14, and 20 cm above the proximal border of lower esophageal sphincter, previously determined by manometry. Upper esophageal sphincter location was not determined, and therefore intersphincter length for the study subjects was not known. However, since the most proximal impedance electrode was placed 20 cm above the lower esophageal sphincter, we are confident that subjects accommodated all six recording sites on the basis of prior studies performed by our group showing that normal esophageal length is 22.9 ± 0.2 cm (23.6 ± 0.3 for males and 22.4 ± 0.3 for females) (10a).

All subjects were fasting for 6 h, were free of esophageal symptoms, and were not taking any medication. The study was approved and deemed ethical by the Graduate Hospital Internal Review Board, and written consent was obtained from all subjects.

MII. Recently, MII has been introduced as a new technique to study esophageal motility and bolus transport (16). Impedance is the average electrical resistance between two adjacent electrodes and is measured using a specialized catheter (Fig. 1) with a 2.1-mm diameter consisting of nine electrodes that make up six measuring segments, each 2 cm in length.

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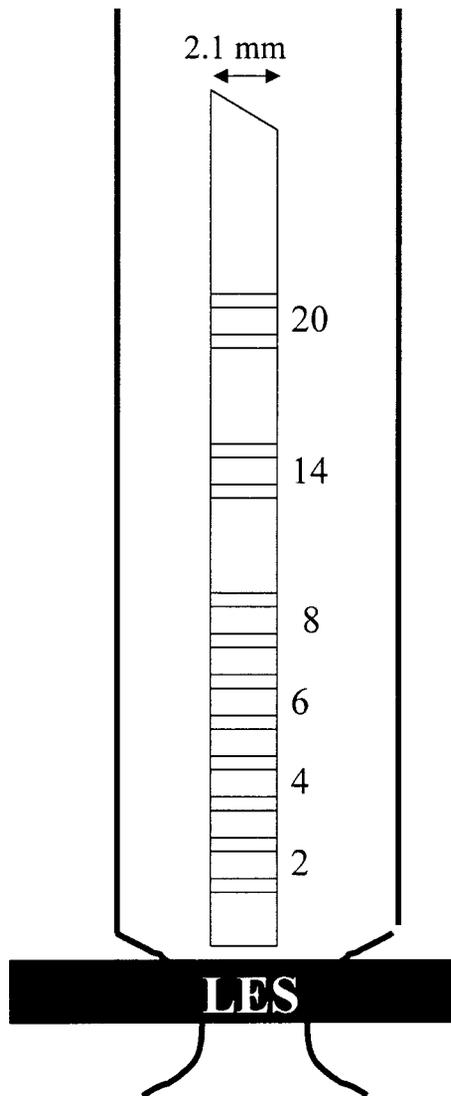


Fig. 1. This schematic representation shows the location of the 6 measuring segments [cm above the lower esophageal sphincter (LES)], which are 2 cm in length. The catheter consists of 9 stainless steel formulated rings, and impedance (the opposition to current flow) is calculated between 2 adjacent electrodes.

The intraluminal electrical impedance between the two electrodes is inversely proportional to the electrical conductivity of the luminal contents and the cross-sectional area. If a highly conductive bolus arrives at the measuring segment (i.e., saliva), impedance will decrease, and the opposite will occur with a resistive bolus (i.e., air). Also, increasing the luminal diameter (i.e., arrival of bolus into the measuring segment) results in an impedance drop, whereas a luminal narrowing (i.e., contraction wave) causes an impedance increase (16). Therefore, MII can evaluate esophageal motility along with assessing bolus transport throughout the entire esophagus in real time without the use of radiation.

With the principles of impedance in mind, one can understand the characteristic pattern produced by a bolus swallow (Fig. 2). The esophagus starts at a resting value (Fig. 2A) that represents the collapsed esophageal walls on the catheter. When a swallow is initiated, air is also swallowed. Air separates from the bolus and enters the measuring segment first, causing an increase in impedance (Fig. 2B). After the passage of air, the actual bolus causes a sharp decrease in impedance due to its conductivity and its effect on luminal dilatation. The bolus enters, traverses, and exits the measuring segment (C, D, and E, respectively). After the passage of the bolus, the lumen-occluding contraction (F) causes an increase in impedance. If the contraction wave completely clears the bolus from the segment, a return to the original impedance baseline is seen (G).

of air, the actual bolus causes a sharp decrease in impedance due to its conductivity and its effect on luminal dilatation. The bolus enters, traverses, and exits the measuring segment (Fig. 2, C, D, and E, respectively). After the passage of the bolus, the lumen-occluding contraction (Fig. 2F) causes an increase in impedance. If the contraction wave completely clears the bolus from the segment, a return to the original impedance baseline is seen (Fig. 2G). If a return is not seen, one can assume that the bolus has not been successfully propagated through that segment. Quantifying the intraluminal volume with impedance is currently under investigation.

The usefulness of MII in the study of esophageal motility has been successfully verified in comparative studies with volunteers with the use of manometry and fluoroscopy. The contraction wave as seen on impedance (Fig. 2F) is correlated with the maximal pressure produced during simultaneous manometry, and the bolus entry, transit, and exit (Fig. 2, C–E) with respect to the measuring segment have been correlated with simultaneous barium swallow (12, 17).

Study design. Different boluses with varying consistencies (liquid, semisolid, and solid) and characteristics (pH and temperature) were administered at different volumes (1–20 ml) and sizes (12–30 mm) while the subject was recumbent. Seven categories of bolus were tested: 1) sterile water, pH 5, room temperature, 2) sterile water, pH 2, room temperature, 3) sterile water, pH 8, room temperature, 4) sterile water, pH 5, iced, 5) sterile water, pH 5, 130°F, 6) applesauce (Mott's), and 7) marshmallow (Jet-Puffed). Solutions of pH 2 and pH 8 were made by adding 1 N HCl (Fisher Scientific) or 5 N NaOH (Titristar), respectively, to sterile water dropwise during titration with a calibrated pH meter (Corning 215). The pH of all solutions was verified before each subject study. Temperature of 130°F was maintained using a constant water bath (Precision 181). Iced solutions were prepared by placing two ice cubes made from sterile water in the 100-ml solution. The solution was allowed to cool for 15 min to gain appropriate temperature before use. Ice cubes were always present in the solution, keeping the temperature approximately in a range of 35–45°F.

Type of bolus administered was randomized by allowing the subject to blindly draw from a box that contained pieces of paper with all of the category numbers. According to the category selected, the methodology was different. After com-

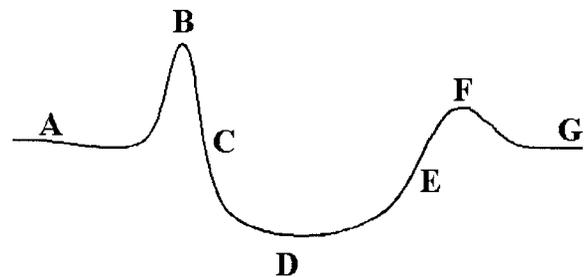


Fig. 2. Impedance changes due to bolus transit. The esophagus starts at a resting impedance value (A) that represents the collapsed esophageal walls on the catheter. When a swallow is initiated, air is also swallowed. Air separates from the bolus and enters the measuring segment first, causing an increase in impedance (B). After the passage of air, the actual bolus causes a sharp decrease in impedance due to its conductivity and its effect on luminal dilatation. The bolus enters, traverses, and exits the measuring segment (C, D, and E, respectively). After the passage of the bolus, the lumen-occluding contraction (F) causes an increase in impedance. If the contraction wave completely clears the bolus from the segment, a return to the original impedance baseline is seen (G).

pletion of the category, the subject then selected the next category using the same randomization method. The patient was laid recumbent for the study period and was instructed to swallow only when asked by the investigator. Wash out swallows are defined as 5-ml sterile water swallows at a temperature of 99°F used to clear the esophagus of any residual matter. A second constant water bath was used for this purpose.

Seven categories of study were performed, as defined below. The methodology for *categories 1* and *6* was as follows: sequential bolus volumes of 1, 2, 3, 4, and 5 ml were placed in the mouth via a 20-ml syringe, and then the subject was asked to swallow. Subsequently, the bolus volumes were tested in the reverse order (5, 4, 3, 2, and 1 ml) to test for reproducibility. Next, the volunteer was asked to swallow a 10-ml and a 20-ml bolus. After every applesauce swallow, one wash out swallow was administered and all swallows were separated after 30 s. Three wash out swallows were administered before proceeding to the next category.

The methodology for *categories 2–5* was as follows: sequential 1-, 5-, 10-, and 20-ml boluses administered via a 20-ml syringe were placed in the mouth, and the volunteer was asked to swallow. After completion of the swallows, three wash out swallows were administered before proceeding to the next category. All swallows were 30 s apart.

The methodology for *category 7* was as follows: 12-, 20-, and 30-mm marshmallows were sequentially placed in the mouth, and the volunteer was asked to swallow after each marshmallow. The same sequence of swallows was then repeated, thus giving two swallows of each size of marshmallow for each subject. After every marshmallow swallow, one wash out swallow was administered. The subjects were asked to swallow the marshmallow whole. After completion of the set of swallows, three wash out swallows were administered before proceeding to the next category. All swallows were 30 s apart.

Esophageal function was evaluated by calculating BTT and CWV for each swallow. BTT is defined as time (in s) from arrival of the bolus at the proximal segment to passage of the bolus from the most distal segment (18-cm distance). Bolus arrival was defined in the proximal segment when the impedance value dropped to a point 50% between baseline and nadir and did not rise above that point until after the nadir. Passage of the bolus in the most distal segment was identified when the impedance value returned after the nadir to a point 50% between baseline and nadir and remained above that point (Fig. 3, *segment AB*). CWV is defined as the speed (cm/s) of the contraction wave (highest impedance peak following passage of the bolus) from the most proximal to most distal segment (Fig. 3, *segment CD*). The end points used for identifying arrival and departure of the bolus as well as esophageal contraction wave were chosen on the basis of the initial reports of validation studies using impedance combined with manometry and fluoroscopy to evaluate water and curd swallows (13) as well as simultaneous impedance and manometry to evaluate liquid and semisolid (mashed potatoes) swallows (3). These studies demonstrate excellent correlation between impedance and both fluoroscopy and manometry for determination of bolus movement and esophageal contraction wave.

Bethanechol stimulation. Five of the normal volunteers (4 male, 1 female) with a mean age of 34 yr (range 24–35 yr) were recruited for the bethanechol challenge. The impedance probe was placed transnasally on a separate day as per the methodology described above. Five swallows each of 5 ml water, 5 ml applesauce, and 15-mm spherical ionic marshmallows (Sandhill Scientific) were administered (15 swallows

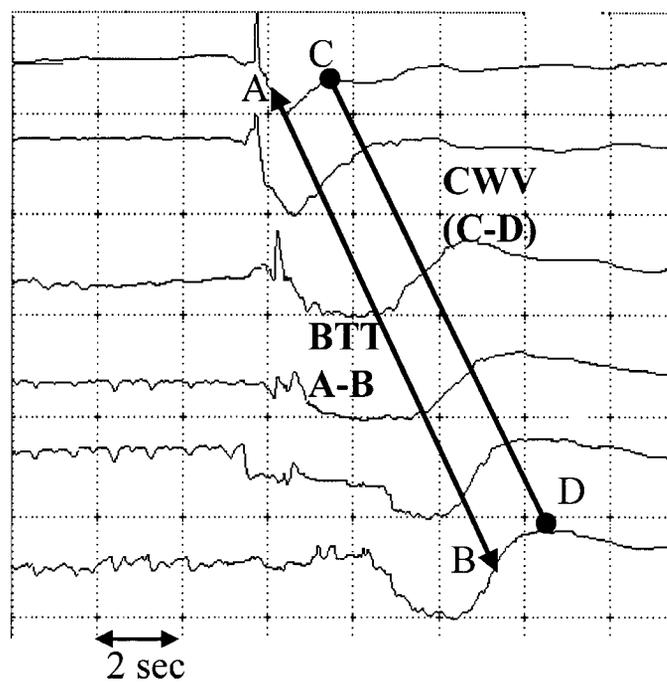


Fig. 3. *A*: arrival of a bolus in the most proximal measuring segment (50% of baseline to nadir). *B*: passage of a bolus from the most distal measuring segment (50% of nadir to baseline). *Segment AB* represents bolus transport time (BTT), the time (in s) from arrival of bolus at proximal measuring segment (*A*) to clearance of bolus from most distal segment (*B*) (18-cm distance) *C*: contraction wave in the most proximal measuring segment (highest impedance value after nadir) *D*: contraction wave in the distal measuring segment (highest impedance value after nadir) *Segment CD*: contraction wave velocity (CWV), the speed (in cm/s) of contraction wave from most proximal (*C*) to the most distal segment (*D*)

total), waiting 30 s between swallows. A wash out swallow was given after every applesauce and marshmallow swallow. After a baseline study, bethanechol (80 μ g/kg, not to exceed 5 ng) was administered subcutaneously in the abdomen. The swallows were then repeated in the same sequence after 15 min.

Analysis. All tracings were read manually by two separate investigators who were blinded to the study conditions. The investigators analyzed the impedance tracings for BTT and CWV for each swallow. A one-way ANOVA with a Newman-Keuls post hoc test using GraphPad 3.0 was applied. For the bethanechol challenge, tracings were also analyzed for BTT and CWV for each swallow. A paired *t*-test using GraphPad 3.0 was applied. Swallows were disqualified from analysis if a second swallow occurred or a reflux event occurred within 10 s of the solicited swallow.

RESULTS

Reproducibility. Volumes (1–5 ml) of pH 5 solution and applesauce, along with the three sizes of marshmallows, were tested twice according to the methodology to test for reproducibility. No differences ($P > 0.05$) were found between the two sets of the same volume for BTT and CWV by paired *t*-test. Means \pm SE of the first and second swallows for each of the 10 subjects for these volumes or sizes are shown in Table 1. These results confirm that the MII technique is highly reproducible in determining esophageal function.

Table 1. Values for BTT and CWV for 1st and 2nd set of swallows of varying size and composition in 10 normal volunteers

	BTT, s		CWV, cm/s	
	1st Swallow	2nd Swallow	1st Swallow	2nd Swallow
Water				
1 ml	5.48 ± 0.34	6.14 ± 0.27	3.16 ± 0.18	3.24 ± 0.19
2 ml	5.66 ± 0.29	6.09 ± 0.31	3.10 ± 0.17	3.32 ± 0.18
3 ml	5.92 ± 0.35	5.90 ± 0.36	3.15 ± 0.14	3.22 ± 0.18
4 ml	6.00 ± 0.36	5.86 ± 0.31	3.28 ± 0.31	3.47 ± 0.25
5 ml	6.05 ± 0.34	6.23 ± 0.26	3.09 ± 0.13	2.81 ± 0.21
Applesauce				
1 ml	5.66 ± 0.36	6.23 ± 0.28	3.71 ± 0.21	3.14 ± 0.26
2 ml	6.05 ± 0.32	6.44 ± 0.19	3.13 ± 0.09	3.07 ± 0.17
3 ml	6.38 ± 0.44	6.72 ± 0.45	2.76 ± 0.16	2.79 ± 0.19
4 ml	6.86 ± 0.26	7.75 ± 0.59	2.89 ± 0.17	2.53 ± 0.21
5 ml	7.42 ± 0.50	6.89 ± 0.63	2.69 ± 0.23	2.89 ± 0.25
Marshmallow				
12 mm	6.12 ± 0.48	6.38 ± 0.57	3.56 ± 0.24	2.88 ± 0.22
20 mm	6.30 ± 0.41	6.58 ± 0.57	3.31 ± 0.14	2.95 ± 0.15
30 mm	7.74 ± 0.52	7.53 ± 0.38	2.58 ± 0.15	2.60 ± 0.09

Values are means ± SE. BTT, bolus transport time; CWV, contraction wave velocity.

BTT. Results for BTT of the various substances tested at different volumes are summarized in Table 2. We found that the mean BTT of all volumes (1–20 ml) of sterile water at pH 5 and at pH 8 were not significantly ($P > 0.05$) different from each other. However, 10 ml of pH 2 solution had a significantly ($P < 0.05$) longer BTT (8.60 ± 0.80 s) than 1 (5.52 ± 0.36 s), 5 (6.02 ± 0.41 s), or 20 (6.31 ± 0.95 s) ml. The BTT of all volumes (1–20 ml) of iced water were not significantly ($P > 0.05$) different from each other. The BTT of all volumes (1–20 ml) of 130°F water were not significantly ($P > 0.05$) different from each other.

Applesauce showed a significant ($r = +0.93$, $P < 0.002$) linear increase of BTT with progressively larger volumes and a longer BTT than pH 5 water (e.g., 10 ml: 7.81 ± 0.51 vs. 5.69 ± 0.27 s; $P < 0.05$). Marshmallow also showed increased BTT with the large bolus (7.64 ± 0.31 s), being significantly ($P < 0.05$) longer than small (6.26 ± 0.37 s) and medium (6.46 ± 0.36 s) boluses.

When water at pH 2, pH 5, pH 8, iced, and 130°F and applesauce were all compared at 1 ml, there was no

Table 2. BTT summary

	1 ml	5 ml	10 ml	20 ml
Water				
pH 5	5.81 ± 0.23	6.12 ± 0.23	5.69 ± 0.27	6.29 ± 0.79
pH 2	5.52 ± 0.36	6.02 ± 0.41	8.60 ± 0.79	6.31 ± 0.95
pH 8	5.57 ± 0.18	5.92 ± 0.48	6.22 ± 0.40	6.56 ± 0.44
Iced	5.71 ± 0.43	5.31 ± 0.32	6.22 ± 0.41	6.93 ± 0.59
130°F	5.76 ± 0.16	5.54 ± 0.28	5.12 ± 0.34	5.32 ± 0.42
Applesauce	5.93 ± 0.24	7.22 ± 0.38	7.81 ± 0.51	8.89 ± 0.66
Marshmallow				
12 mm	6.25 ± 0.37	6.46 ± 0.36	7.64 ± 0.31	

Values are means ± SE given in seconds.

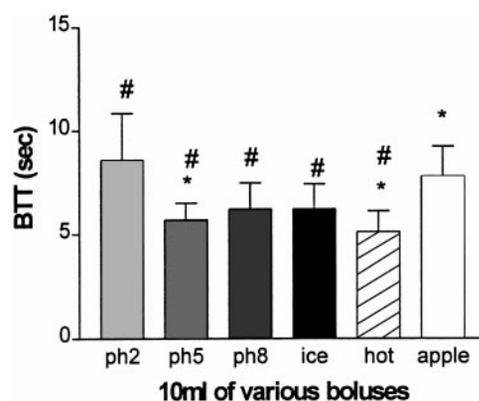


Fig. 4. Mean ± SE BTT of various boluses at 10 ml. * $P < 0.05$ with applesauce; # $P < 0.01$ with pH 2 solution.

significant ($P > 0.05$) difference in BTT values. When volumes were compared at 5 ml, applesauce had a BTT (7.22 ± 0.38 s) that was significantly ($P < 0.05$) longer than pH 8 (5.92 ± 0.48 s), iced (5.31 ± 0.32 s), and 130°F (5.54 ± 0.28 s) solutions. When volumes were compared at 10 ml, the pH 2 solution had a BTT (8.60 ± 0.79 s) that was significantly ($P < 0.01$) longer than pH 5 (5.69 ± 0.27 s), pH 8 (6.22 ± 0.40 s), iced (6.22 ± 0.41 s), and 130°F (5.12 ± 0.34 s) solutions. Also at 10 ml, applesauce had a BTT that was significantly ($P < 0.05$) longer than pH 5 and 130°F solutions (Fig. 4). When volumes were compared at 20 ml, applesauce had a BTT (8.89 ± 0.66 s) that was significantly longer than pH 5 (6.29 ± 0.79 s) or 130°F (5.32 ± 0.42 s) solutions.

Using a displacement technique, it was found that the 12-mm marshmallow displaces 3 ml of water, the 20-mm marshmallow displaces 5 ml of water, and the 30-mm marshmallow displaces 8 ml of water. When comparing liquid (pH 5), semisolid (applesauce), and solid (marshmallow) at 3- and 5-ml volumes, there were no significant ($P > 0.05$) differences in BTTs.

CWV. Results for CWV of the various substances tested at different volumes are shown in Table 3. The CWV of all volumes (1–20 ml) of pH 5, pH 2, iced, and 130°F water were not significantly ($P > 0.05$) different from each other. One milliliter of pH 8 had a significantly ($P < 0.05$) faster CWV (3.45 ± 0.16 cm/s) than 20 ml (2.83 ± 0.17 cm/s).

Table 3. CWV summary

	1 ml	5 ml	10 ml	20 ml
Water				
pH 5	3.20 ± 0.13	2.99 ± 0.12	3.12 ± 0.12	2.69 ± 0.14
pH 2	3.20 ± 0.24	3.04 ± 0.15	2.57 ± 0.19	3.55 ± 0.86
pH 8	3.45 ± 0.16	3.22 ± 0.15	3.08 ± 0.12	2.83 ± 0.17
Iced	3.18 ± 0.28	2.84 ± 0.11	2.73 ± 0.14	2.98 ± 0.49
130°F	3.58 ± 0.22	3.58 ± 0.23	3.82 ± 0.26	3.85 ± 0.26
Applesauce	3.41 ± 0.18	2.78 ± 0.17	2.61 ± 0.11	2.36 ± 0.15
Marshmallow				
12 mm	3.17 ± 0.18	3.12 ± 0.11	2.59 ± 0.08	

Values are means ± SE (cm/s).

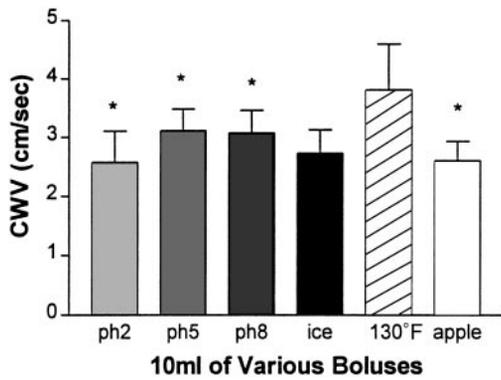


Fig. 5. Mean \pm SE CWV of various boluses at 10 ml. * $P < 0.01$ with 130°F solution.

Applesauce showed a significant ($r = -0.80$, $P < 0.03$) linear decrease of CWV with progressively larger volumes and was slower vs. water (e.g., 10 ml: 2.61 ± 0.11 vs. 3.12 ± 0.12 cm/s). Marshmallow showed a decreasing CWV with the large bolus (2.59 ± 0.08 cm/s) that was significantly ($P < 0.01$) slower than small (3.17 ± 0.18 cm/s) and medium (3.12 ± 0.11 cm/s) boluses.

When pH 2, pH 5, pH 8, iced, and 130°F water and applesauce were all compared at 1 ml, there was no significant ($P > 0.05$) difference in CWV values. When volumes were compared at 5 ml, the CWV of iced solution (2.84 ± 0.11 cm/s) was significantly ($P < 0.05$) slower than 130°F solution (3.58 ± 0.23 cm/s). Also at this volume, applesauce (2.78 ± 0.17 cm/s) was significantly ($P < 0.05$) slower than 130°F solution. When liquid volumes were compared at 10 ml, the CWV of 130°F (3.82 ± 0.26 cm/s) solution was significantly ($P < 0.01$) faster than pH 2 (2.57 ± 0.19 cm/s), pH 5 (3.12 ± 0.12 cm/s), pH 8 (3.08 ± 0.12 cm/s), and iced water (2.73 ± 0.14 cm/s) and applesauce (2.61 ± 0.11 cm/s) (Fig. 5). When volumes were compared at 20 ml, the CWV of 130°F solution (3.85 ± 0.26 cm/s) was significantly faster ($P < 0.05$) than pH 5 (2.69 ± 0.14 cm/s), pH 8 (2.83 ± 0.17 cm/s), and applesauce (2.36 ± 0.15 cm/s). When comparing liquid (pH 5), semisolid (applesauce), and solid (marshmallow) at 3- and 5-ml volumes, it was found that no significant ($P > 0.05$) differences in CWVs existed.

Bethanechol stimulation. The effects of bethanechol on BTT and CWV are shown in Table 4. Compared with baseline, all BTTs of liquid, semisolid, and solid boluses significantly ($P < 0.0001$) increased with bethanechol and all CWVs significantly ($P < 0.0001$) decreased.

DISCUSSION

This report summarizes studies using the new and evolving technique of MII recording to evaluate esophageal function in response to varying swallowed boluses. Esophageal function was analyzed using BTT, defined as time (in s) from arrival of the bolus at the proximal segment to passage of the bolus from the most distal segment, and CWV, defined as the speed (cm/s) of the contraction wave (highest impedance peak

following passage of the bolus) from the most proximal to most distal segment.

Our study shows that BTT stays constant for liquid boluses at varying volumes of 1–20 ml. This phenomenon held true when pH 2, pH 8, iced, and 130°F solutions were also tested at varying volumes. However, 10 ml of pH 2 solution had a significantly longer BTT than 1, 5, or 20 ml. This quite likely represents a type 1 error resulting from multiple statistical tests rather than a truly meaningful finding.

When semisolid (applesauce) and solid (marshmallow) boluses were tested, there was a linear increase of BTT with progressively larger volumes. Thus our results indicate that, in the recumbent position, BTT of liquid is constant and BTT of semisolid and solid are volume dependent. In addition, we found that semisolid (applesauce) boluses take longer to clear from the esophagus. Our results are consistent with those of Nguyen et al. (11), with MII showing that a viscous bolus tends to remain compact during its propulsion and that an increase of bolus viscosity will result in an increase of intraluminal resistance and thereby slow its transport.

When volume was held constant (3 and 5 ml) and consistencies were changed (liquid, semisolid, solid), our results indicated that BTT was not significantly different among the different consistencies. These data are not consistent with Kim et al. (10), who performed scintigraphy studies of esophageal emptying with five different semisolid viscosities. Their studies showed that esophageal emptying was inversely related to bolus viscosity.

Consistent results were obtained when CWV was measured. Our studies show that for liquid boluses at varying volumes of 1–20 ml, CWV stays constant. To our knowledge, CWV of differing liquid volumes has not been assessed; however, the results are in agreement with those of Hollis and Castell (5) that stated that the amplitude of the contraction wave following swallows ranging from 2 to 20 ml was consistent. The CWV results held true when pH 2, pH 8, iced, and 130°F solutions were also tested at varying volumes. However, 1 ml of pH 8 solution had a significantly ($P < 0.05$) quicker CWV than 20 ml. Again, we believe this may be due to a type 1 statistical error.

When semisolid (applesauce) and solid (marshmallow) boluses were tested, there was a linear decrease of CWV with progressively larger volumes. Thus

Table 4. BTT and CWV before and after bethanechol stimulation

	Baseline	Bethanechol
BTT Water	5.57 ± 0.24	8.18 ± 0.33
BTT Applesauce	7.28 ± 0.29	9.43 ± 0.32
BTT Marshmallow	7.01 ± 0.57	9.78 ± 0.34
CWV Water	3.87 ± 0.21	2.30 ± 0.14
CWV Applesauce	2.73 ± 0.09	1.94 ± 0.09
CWV Marshmallow	2.91 ± 0.17	1.98 ± 0.09

Values (in s for BTT and cm/s for CWV) are means \pm SE. $P < 0.0001$ vs. baseline for all bethanechol measurements.

CWV of liquid was constant, whereas CWV of semisolid and solid were volume dependent and longer than those of liquids.

At 5 and 10 ml, the CWV of iced water was significantly slower than that of 130°F water. It has been suggested by Dooley et al. (1) that bolus temperature does not have a significant role in the modulation of human esophageal peristalsis except under conditions that cause a change in esophageal wall temperature. In an earlier motility study by Kaye et al. (9), iced water caused reduced strength, increased duration, and reduced velocity of distal esophageal contraction. Careful review of the methodology of Kaye et al. and other similar studies (13, 19) shows that all used some mechanism to alter the ambient temperature of the esophageal wall. These mechanisms included the cooling or warming of the esophageal muscle with very large (100–200 ml) volumes. We believe that the differences found in our study because of changes in temperature were due to the effect of repetitive cold swallows and the change in esophageal wall temperature.

When volume was held constant and consistencies were changed (liquid, semisolid, solid), CWV was not significantly different among the different consistencies. This is supported by a study by Nguyen et al. (11) in which 10 healthy volunteers were tested with liquid and semisolid boluses. They found that the propagation velocity was not significantly influenced by increased bolus viscosity. Also, Frieling et al. (3) showed that esophageal wall contraction velocities as measured by manometry and by impedancometry were not significantly different for both liquid and semisolid swallows. Our study, along with the previous impedancometry studies, differ with previously reported data using intraluminal manometry (7, 8). These studies, however, use bread swallows, use different positions (erect, semierect), and the patients are allowed to chew the bread to break it up for easier swallowing. A study by Dooley et al. (2) showed that medium- and high-viscosity fluids slowed the esophageal peristaltic waves, whereas low-viscosity fluid and water were similar.

Previous manometric studies (6, 15) have shown that cholinergic stimulation significantly increases peristaltic amplitude and significantly reduces CWV of esophageal peristalsis. In our study using MII, we found similar results. All BTTs of liquid, semisolid, and solid boluses significantly increased with bethanechol, and all CWVs significantly decreased.

In conclusion, we believe that these studies using standardized volumes and consistencies of swallowed boluses indicate that MII can be used as a discriminating test of esophageal function evaluating bolus transport. In addition, it is our hope that further development of this technique will provide a means to study esophageal function without the use of radiation.

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REFERENCES

1. Dooley CP, Lorenzo CD, and Valenzuela JE. Esophageal function in humans: effects of bolus consistency and temperature. *Dig Dis Sci* 35: 167–172, 1990.
2. Dooley CP, Schollossmacher B, and Valenzuela JE. Effects of alterations in bolus viscosity on esophageal peristalsis. *Am J Physiol Gastrointest Liver Physiol* 254: G8–G18, 1988.
3. Frieling T, Hermann S, Kuhlbusch R, Enck P, Silny J, Lubke HJ, Strohmeier G, and Haeussinger D. Comparison between intraluminal multiple electric impedance measurement and manometry in the human oesophagus. *Neurogastroenterol Motil* 8: 45–50, 1996.
4. Goyal R and Sivarao DV. Functional anatomy and physiology of swallowing and esophageal motility In: *Esophagus* (3rd ed.), edited by Castell DO and Richter J. Philadelphia: Lippincott Williams & Wilkins, 1999, p. 1–32.
5. Hollis JB and Castell DO. Effect of dry swallows and wet swallows of different volumes on esophageal peristalsis. *J Appl Physiol* 38: 1161–1164, 1975.
6. Hollis JB and Castell DO. Effects of cholinergic stimulation on human esophageal peristalsis. *J Appl Physiol* 40: 40–43, 1976.
7. Howard PJ, Maher L, Pryde A, and Heading RC. Systematic comparison of conventional oesophageal manometry with oesophageal motility while eating bread. *Gut* 32: 1264–1269, 1991.
8. Johnston BT, Collings JSA, McFarland RJ, Blackwell JN, and Love AHG. A comparison of esophageal motility response to bread swallows and water swallows. *Am J Gastroenterol* 88: 351–355, 1993.
9. Kaye MD, Kilby AE, and Harper PC. Changes in distal esophageal function in response to cooling. *Dig Dis Sci* 32: 22–27, 1987.
10. Kim CH, Hsu JJ, O'Connor MK, Weaver AL, Brown M, and Zinsmeister AR. Effect of viscosity on oropharyngeal and esophageal emptying in man. *Dig Dis Sci* 39: 189–192, 1994.
- 10a. Li Q, Castell JA, and Castell DO. Manometric determination of esophageal length. *Am J Gastroenterol* 89: 722–725, 1994.
11. Nguyen HN, Silny J, Albers D, Roeb E, Gartung C, Rau G, and Matern S. Dynamics of esophageal bolus transport in healthy subjects studied using multiple intraluminal impedancometry. *Am J Physiol Gastrointest Liver Physiol* 273: G958–G964, 1997.
12. Nguyen HN, Silny J, and Matern S. Multiple intraluminal electrical impedancometry for recording of upper gastrointestinal motility: current results and further implications. *Am J Gastroenterol* 94: 306–317, 1999.
13. Ott DJ, Kelly RJ, and Gelfand DW. Radiographic effects of cold barium suspensions on esophageal motility. *Radiology* 140: 830–833, 1981.
14. Poudroux P, Gulchin EA, Lin S, and Kahrilas J. Esophageal bolus transit imaged by ultrafast computerized tomography. *Gastroenterology* 110:1422–1428, 1996.
15. Richter JE, Hackshaw BT, Wu WC, and Castell DO. Edrophonium: a useful provocative test for esophageal chest pain. *Ann Intern Med* 103: 14–21, 1985.
16. Silny J. Intraluminal multiple electric impedance procedure for measurement of gastrointestinal motility. *J Gastrointest Motil* 3: 151–162, 1991.
17. Silny J, Knigge KP, Fass J, Rau G, Matern S, and Schumpelick V. Verification of the intraluminal multiple electrical impedance measurement for the recording of gastrointestinal motility. *Neurogastroenterol Motil* 5: 107–122, 1993.
18. Silny J and Rau G. A novel procedure to study bolus movement by intraluminal electrical impedance measurements. In: *Progress in Understanding and Management of Gastro-intestinal Motility Disorders*, edited by Jannens J. Leuven, Belgium: Katholik Univ. Leuven, 1993, p. 197–208.
19. Winship DH, Viegas De Andrade SE, and Zboralske FF. Influence of bolus temperature on human esophageal motor function. *J Clin Invest* 49: 243–250, 1970.