



Archived at the Flinders Academic Commons:

<http://dspace.flinders.edu.au/dspace/>

This is a pre-copyedited, author-produced version of an article accepted for publication in *Diseases of the Esophagus* following peer review.

The version of record Omari TI, Szczesniak MM, Maclean J, Myers JC, Rommel N, Cock C and Cook IJ. Correlation of esophageal pressure-flow analysis findings with bolus transit patterns on videofluoroscopy. *Dis Esophagus*. 2016 Feb-Mar;29(2):166-73.

and is available online at:

<http://dx.doi.org/10.1111/dote.12300>

Copyright © 2017 The International Society for Diseases of the Esophagus

# Correlation of esophageal pressure-flow analysis findings with bolus transit patterns on videofluoroscopy

TI Omari<sup>1,2,3,4</sup>, MM Szczesniak<sup>5</sup>, J Maclean<sup>5</sup>, JC Myers<sup>6</sup>, N Rommel<sup>4,7</sup>, C Cock<sup>8</sup> and IJ Cook<sup>5</sup>

## Author Affiliations:

<sup>1</sup>Gastroenterology Unit, Women's and Children's Health Network, Adelaide, South Australia

<sup>2</sup>School of Paediatrics and Reproductive Health, University of Adelaide, South Australia

<sup>3</sup>School of Medicine, Flinders University, Bedford Park, South Australia

<sup>4</sup>Translational Research Center for Gastrointestinal Diseases, University of Leuven, Belgium

<sup>5</sup>Department of Gastroenterology, St George Hospital, Kogarah, Sydney, Australia

<sup>6</sup>Discipline of Surgery, University of Adelaide, Royal Adelaide Hospital, Adelaide, Australia

<sup>7</sup>Neurosciences, ExpORL, University of Leuven, Belgium

<sup>8</sup>Repatriation General Hospital, Daws Park, Adelaide, Australia.

## Author for correspondence:

A/Prof Taher Omari, PhD

NH&MRC Senior Research Fellow

Gastroenterology Unit, Women's and Children's Health Network

72 King William Rd, North Adelaide SA 5006 South Australia

Email: [taher.omari@adelaide.edu.au](mailto:taher.omari@adelaide.edu.au)

## Competing interests:

T Omari, Patent on pressure flow analysis methods.

T Omari, Sandhill Scientific Inc. Research Funding.

T Omari, Sandhill Scientific Inc. Consultancy.

**Abbreviations:**

AIM	automated impedance manometry
TNadImp	time of nadir impedance
PNadImp	pressure at nadir impedance
IBP	intrabolus pressure
PeakP	peak pressure
TNadImp to PeakP	time of nadir impedance to peak pressure
PFI	pressure flow index
Impedance Ratio (IR)	ratio of nadir impedance to impedance at peak pressure
Peristaltic breaks	length of break in peristalsis using 20mmHg isocontour
IRP4s	4 sec integrated relaxation pressure
EGJ	esophago-gastric junction

## Abstract

**INTRODUCTION:** Pressure-flow analysis quantifies the interactions between bolus transport and pressure generation. We undertook a pilot study to assess the inter-relationships between pressure-flow metrics and fluoroscopically determined bolus clearance and bolus transport across the EGJ. We hypothesised that findings of abnormal pressure-flow metrics would correlate with impaired bolus clearance and reduced flow across the EGJ. **METHODS:** Videofluoroscopic images, impedance and pressure were recorded simultaneously in 9 patients with dysphagia (62-82y, 7m) tested with liquid barium boluses. A 3.6mm diameter solid-state catheter with 25 x 1cm pressure/12 x 2cm impedance was utilised. Swallowed bolus clearance was assessed using a validated 7-point radiological bolus transport scale. The cumulative period of bolus flow across the EGJ was also fluoroscopically measured (EGJ flow time). Pressure only parameters included the length of breaks in the 20mmHg iso-contour and the 4 sec integrated EGJ relaxation pressure (IRP4s). Pressure-flow metrics were calculated for the distal esophagus, these were; time from nadir impedance to peak pressure (TNadImp to PeakP) to quantify bolus flow timing; Pressure Flow Index (PFI) to integrate bolus pressurisation and flow timing and Impedance Ratio (IR) assess bolus clearance.

**RESULTS:** When compared with controls, patients had longer peristaltic breaks, higher Impedance Ratios and higher residual EGJ relaxation pressures (break length of 8 [2, 13] vs. 2 [0, 2] cm,  $p = 0.027$ ; IR  $0.5 \pm 0.1$  vs.  $0.3 \pm 0.0$ ,  $p=0.019$ ; IRP4s  $11 \pm 2$  vs.  $6 \pm 1$  mmHg,  $p = 0.070$ ). There was a significant positive correlation between higher bolus transport scores and longer peristaltic breaks (Spearman correlation  $r = 0.895$ ,  $p<0.001$ ) and with higher Impedance Ratios ( $r = 0.661$ ,  $p<0.05$ ). Diminished EGJ flow times correlated with a shorter Time NadImp to PeakP ( $r = -0.733$ ,  $p<0.05$ ) and a higher IR ( $r = -0.750$ ,  $p<0.05$ ).

**CONCLUSION:** Longer peristaltic breaks and higher IR correlate with failed bolus clearance on videofluoroscopy. The metric TNadImp to PeakP appears to be a marker of the period of time over which the bolus flows across the EGJ.

## Introduction

Dysphagia is a common reason for referral for manometric investigation, yet standard measures of esophageal function relate poorly to patient perception of swallowed boluses and a proportion of patients with dysphagia demonstrate no apparent abnormality on barium radiography or endoscopy (1-3). Furthermore, despite a typical clinical history suggesting underlying dysmotility, manometry can be inconclusive and thereby dictates the need for further corroborative evidence such as radiography (4).

Automated impedance-manometry analysis (esophageal AIM analysis) reliably derives pressure-flow metrics that quantify the interactions between bolus transport and pressure generation (5-12). For the clinician, the potential advantages of this novel approach lie in complementing a conventional manometric diagnosis of disordered peristalsis and/or EGJ outflow obstruction. Objective measures can directly quantify the degree of pressure-flow abnormality; namely the degree and extent of bolus clearance failure and the forces being applied to the bolus as it is propelled from pharynx to esophagus, down to distal esophagus and then through into the stomach via the EGJ. Furthermore, in situations where a conventional diagnosis may be equivocal, pressure-flow analysis may help pin-point subtle variations of esophageal function. These may include structural impediments to flow or subtle motor disturbances to inhibitory pathways that are frequently not apparent on barium swallow or at endoscopy.

We undertook a pilot study in patients undergoing combined videofluoroscopy and high resolution impedance-pressure measurement to assess interrelationships between pressure-flow metrics and radiographically determined bolus clearance and bolus flow across the EGJ. We hypothesised that findings of abnormal pressure-flow metrics would correlate with abnormal esophageal bolus transport patterns, impaired bolus clearance and reduced flow across the EGJ.

## **Methods**

### *Patients*

This pilot study was undertaken in a population of patients with known head and neck cancer and post-radiotherapy related dysphagia in whom we have been evaluating, primarily, their pharyngeal and cricopharyngeal biomechanics using videofluoroscopy and pressure-flow analysis. A high proportion of these patients have peristaltic abnormalities of varying severity. In the absence of equivalent prospective data in a traditional esophageal dysphagia cohort we felt this cohort would nevertheless provide an excellent opportunity to evaluate the correlations among pressure-flow metrics and radiological bolus clearance across a broad spectrum of peristaltic dysfunction.

Nine patients (aged 62-82, 7 male) were included because they reported symptoms compatible with impaired esophageal clearance. These features included one or more of the following symptoms: post-swallow regurgitation; bolus holdup retrosternally or awareness of slow bolus transit through the esophagus. The study protocol was approved by the St George Hospital Research Ethics Committee and performed in the Department of Radiology, St George Hospital.

### *Age matched controls*

A dataset of equivalent control swallows matched for subject age and bolus volume was compiled from a master database of liquid swallows recorded in 68 asymptomatic subjects aged 20-91 years (studies acquired by author C.Cock). In order to remove any potential for bias, each patient was consecutively matched to the first control that was of the same age. When a precise age match was not available the next closest match was selected. Control swallows of identical number and volume to the patient swallows were then selected consecutively in order from first to last.

### *Measurement Protocol*

A 3.6mm diameter solid-state manometric and impedance catheter incorporating 25 1cm-spaced pressure sensors and 12 adjoining impedance segments, each of 2 cm (Unisensor USA Inc, Portsmouth, NH) was

used. Subjects were intubated after application of topical anaesthesia (lignocaine spray) to the nasopharynx and studied sitting upright. Pressure and impedance data were acquired at 50Hz (Solar GI acquisition system, MMS, The Netherlands). The catheter was positioned with sensors straddling the region proximal of the transition zone to stomach. Subjects were tested with 2-4 liquid barium boluses (3 patients received 5ml and 6 received 10ml bolus volumes). NaCl was added to bolus stock in order to achieve conductivity similar to normal saline.

### *Videofluoroscopy Analysis*

Pulse videofluoroscopy digital video sequences of all swallows were recorded at 12Hz and simultaneously acquired at 25 frames/sec. For each swallow, three assessments were performed:

Firstly, bolus transport was ranked according to the classification system of Fox and colleagues, which uses a seven-grade Likert-scale to score bolus transport (1 = successful bolus transport, 7 = complete failure of transport) (13, 14). Secondly, the video sequence was analysed in a frame by frame manner to identify periods where esophageal contents could be observed to flow into the stomach. The cumulative time of observed flow during each swallow was taken to represent to total period of trans-sphincteric flow during that swallow. Finally, the EGJ maximum diameter was assessed for each swallow. The width of the barium column was measured in pixels from the lateral projection at the narrowest point of the EGJ when it was maximally distended. Analysis of the still images was performed with *ImageJ* software (v1.46r, NIH, USA). To convert measurements from pixels to millimetres, a conversion factor was calculated for each image from the radiopaque solid-state manometric sensors of known size (3.65mm) visible on the radiographs.

### *Pressure-Flow Analysis*

Analysis was performed using a purpose designed analysis program written in MATLAB (version 7.9.0.529 R2009b, The MathWorks Inc, Natick, MA, USA). The analysis itself is framed around the spatio-temporal relationship between *Nadir Impedance*, which identifies when and where the lumen is most full, and Peak Pressure, when the esophageal muscle is maximally contracted (5, 9, 11, 12). As shown in Figure 1, during liquid bolus transport the nadir impedance is approximately located at the axial centre of the bolus and

follows the trajectory of the bolus as it is transported. Pharyngeal swallow propels the bolus to the distal esophagus, where the bolus remains static until pressurised by advance of the peristaltic wave front that drives bolus transit through the relaxed EGJ (9). Pressure-flow variables were derived for the distal esophagus (transition zone to EGJ). The analysis approaches used to derive variables have been described previously (5-12) and these metrics are summarised below:

- i. *Pressure at nadir impedance* (PNadImp, mmHg) and *median Intrabolus pressure* (IBP, mmHg) measuring of bolus distension pressures.
- ii. *Intrabolus pressure slope* (IBP slope, mmHg/sec) measuring the rate of pressure change during luminal closure/propulsion of luminal content.
- iii. *Peak pressure* (PeakP, mmHg) measuring maximum contractile pressure following luminal emptying.
- iv. *Time interval between nadir impedance and peak esophageal pressure* (TNadImp to PeakP, sec) measuring the latency from bolus distension to the contractile peak.
- v. The *pressure flow index* (PFI), calculated using the formula below, which is a global measure of pressure-flow abnormality elevated in circumstances of high flow resistance (6-8, 10):  
$$\text{PFI} = (\text{IBP} * \text{IBP slope}) / (\text{TNadImp} - \text{PeakP}).$$
- vi. The *ratio of nadir impedance to impedance at peak pressure* (Impedance Ratio) as measure of bolus clearance during transport (high ratio = less complete clearance, 5 and 6).

Peristaltic break size was measured as previously described (14-16). Maximum pressures within a 10sec region of interest encompassing the extent and relaxation period of the EGJ were used to determine the EGJ 4sec integrated relaxation pressure (IRP4s) (14-17). In addition the EGJ nadir pressure and EGJ nadir impedance were defined as the lowest level of pressure and impedance measured within the EGJ during swallow related relaxation.

### *Statistics*

The individual swallow data determined for each subject, patient and their age-matched control, were pooled within each group and averaged for the purposes of statistical comparisons between the groups.



Data are expressed as means  $\pm$  standard error (SE) or median [inter-quartile range, IQR]. Grouped measures were compared using t test or sign rank test and one-way ANOVA or ANOVA on Ranks. Relationships between continuous variables were assessed using Spearman Rank Order Correlation. Statistical tests were performed using SigmaPlot ver11.0 (Systat Software Inc., Chicago,IL, USA).

## Results

Twenty six patient swallows (10 x 5ml and 16 x 10ml in the upright position) were simultaneously recorded and analysed. These were compared with age and volume matched control swallows. Patients, when compared to controls, had larger peristaltic breaks (break size 8 [2, 13] vs. 2 [0, 2] cm,  $p = 0.027$ ) and less complete EGJ relaxation (IRP4s  $11 \pm 2$  vs.  $6 \pm 1$  mmHg,  $p = 0.070$ , EGJ nadir pressure  $4 \pm 1$  vs.  $0 \pm 1$  mmHg,  $p = 0.032$ , EGJ nadir impedance 134 [113, 188] vs. 91 [86, 149] ohms,  $p=0.064$ ). Three patients had abnormal IRP4s (>15mmHg) hence meeting the criteria for EGJ outflow obstruction. Of six remaining patients with normal IRP4s, four had weak peristalsis and two had normal peristalsis.

The median Pressure Flow Index was not statistically different between patients vs. controls (7 [1, 117] vs. 8 [3, 10],  $p = 0.860$ ). The Impedance Ratio was higher in patients ( $0.5 \pm 0.1$  vs.  $0.3 \pm 0.0$ ,  $p=0.019$ ). Two patients had a PFI exceeding the control 90<sup>th</sup> percentile (PFI 89) suggesting abnormal bolus flow resistance. Three separate patients an Impedance Ratio exceeding the control 90<sup>th</sup> percentile (0.44) suggesting ineffective bolus clearance.

PFI and Impedance Ratio were then used in combination to distinguish patients on the grounds of abnormal flow resistance and/or clearance. Figure 3A demonstrates how patients could be separated into three of four possible groups based on whether the PFI/Impedance Ratio were abnormal i.e. Group 1 normal PFI/normal IR (n=4), Group 2 abnormal PFI /normal IR (n=2), Group 3 normal PFI/ abnormal IR (n=3) and Group 4 abnormal PFI /abnormal IR (not seen). All of Group 3 patients were characterised by the existence of large peristaltic breaks. However patients in Groups 1 and 2, who have a different pressure-flow signature and normal bolus clearance, could not be distinguished based on peristaltic break size (Group 1 vs. 2 were  $3 \pm 1$ cm vs.  $3 \pm 2$ cm respectively) or IRP4s (Group 1 vs. 2 were  $12 \pm 5$ mmHg vs.  $12 \pm 5$ mmHg respectively).

### *Correlations with Videofluoroscopy*

Patient bolus transit scores ranged from 1-6 and three patients had abnormal bolus transport (score of  $\geq 3$ ). A higher transit score (more severe failure), correlated with larger peristaltic breaks, lower peak pressures, higher Impedance Ratio's and a briefer period of trans-EGJ flow (Table 1, Figure 2). In patients with normal vs. failed bolus transport respectively, peristaltic break size was  $5 \pm 2$  vs.  $12 \pm 2$  cm ( $p=0.074$ ), peak pressure

was  $62 \pm 16$  vs.  $16 \pm 2$  mmHg ( $p=0.083$ ), Impedance Ratio was  $0.3 [0.2, 0.4]$  vs.  $0.8 [0.6, 1.0]$  ( $p=0.024$ ), and the trans-EGJ flow period was  $4.1 [3.4, 5.9]$  vs.  $2.1 [1.7, 2.3]$  sec ( $p=0.024$ ).

Average trans-EGJ flow period ranged from 1.6 to 8.6 sec. A shorter period of EGJ flow correlated with a shorter TNadImp to PeakP, a higher distal Impedance Ratio and narrower EGJ opening diameter (Table 1, Figure 2). Metrics indicative of EGJ function did not correlate with any of the fluoroscopic measures (Table 1). Comparisons of fluoroscopic measures amongst patients dichotomously defined based on PFI and Impedance Ratio (Figure 3) showed bolus transport abnormalities in Group 3 (Figure 3B) and EGJ flow time was longest in Group 1 and shortest in Group 3 (Figure 3C).

## Discussion

In this pilot study we explored how pressure-flow analysis of swallowing relates to bolus transit patterns determined by videofluoroscopy. Disordered esophageal motility was prevalent in our patients and, as has been previously reported, associated with bolus transport failure on radiology (13-19). Novel pressure-flow metrics also correlated with failed bolus transport and diminished bolus flow time across the EGJ.

Esophageal pressure-flow analysis objectively derives new metrics based on the integration of impedance and pressure using automated software algorithms. Quantifying pressure-flow disturbances may distinguish potential causes of symptoms in dysphagia patients (5-8, 10-12). Amongst the pressure-flow metrics assessed, the latency from bolus accumulation to contractile peak (TNadImp to PeakP) appeared to correlate best with the period of bolus flow across the EGJ during swallow induced EGJ relaxation. ~~The timing of nadir impedance in the most distal esophagus appeared to approximate the time of onset of flow across the EGJ (as illustrated in Figure 1).~~ Several factors may explain this relationship. Flow of a bolus into the stomach requires the presence of a favourable pressure gradient across the EGJ (20, 21) and this depends upon the integrity of the esophageal contractile front (to prevent retrograde de-pressurisation of the bolus domain) as well as the ability of the EGJ to relax and open (to allow the bolus to pass through). During optimisation of these driving and resistive pressures, the lumen proximal to the EGJ steadily distends until flow permissive conditions are achieved. With onset of flow through the EGJ, the lumen proximal to the EGJ will passively recoil, then narrow and close due to muscle contraction. The measured intraluminal impedance may be lowest at the time of EGJ flow onset because this corresponds to when the esophageal lumen is most dilated by the accumulated swallowed bolus (wider diameter = lower impedance). A short period of EGJ flow also correlated with the existence of large peristaltic breaks and high Impedance Ratio. Hence if there is a break in the contractile wave front, bolus pressurisation that drives flow across the EGJ does not occur until later in the swallow sequence. That is, when any remnant contraction front reaches the EGJ. The distal esophagus is an anatomically and mechanically less complex region than the EGJ and our data suggest that the TNadImp to PeakP metric may be a useful, indirect and pressure independent, marker of diminished bolus flow.

Interestingly, our study did not demonstrate any relationship between high IRP4s and diminished flow across the EGJ. The measurement of EGJ relaxation based upon the IRP4s is fundamental to the diagnostic categorisation of EGJ outflow obstruction based on the Chicago Classification (22). The EGJ is a complex region demonstrating radial pressure asymmetries due to extrinsic structures (23, 24) and our use of unidirectional sensors and an upright posture may have increased variability of pressure readings across the EGJ (25). However, we note that high IRP4s readings despite evidence of flow can also be seen even when optimal circumferential sensors are used (20). Conditions allowing bolus flow through the EGJ can be accurately predicted based on the *flow permissive time* (20) with further improvement in the technique using 3D HRM (21).

We have proposed the Pressure Flow Index as an empirical composite index to quantifying the overall degree of pressure-flow disturbance (5-8, 10) and the Impedance Ratio (IR) to separately quantify the extent of bolus transport failure (5, 6, 11). When patients were categorised based on whether PFI and IR results were normal/abnormal, they could be separated into one of four possible groups (Figure 3). Comparisons among the groups in relation to fluoroscopic measures showed that Group 3 patients (normal PFI/High IR) had bolus transport scores consistent with poor clearance and a reduced period of EGJ flow. In contrast, Group 2 patients (high PFI/normal IR) had normal bolus transport scores and intermediate periods of EGJ flow that were between those of Group 1 (normal PFI and IR) and Group 3.

We have previously found that a pattern of high PFI correlates with heightened perception of bolus transport (5, 6). In the current study, patients with a high PFI pattern had radiologically normal bolus transport. Together, these findings may suggest that some patients may experience symptoms of dysphagia due to bolus over pressurization/flow resistance during what appears to be normal bolus transport. This may potentially account for the high proportion of normal manometric studies in patients who experience the subjective sensation of esophageal dysphagia. Our study is however limited due to the lack of perception scores and the absence of data with more challenging viscous and solid bolus consistencies, further studies are therefore needed.

A weakness of our study is that our data are based on a small atypical patient cohort. Our patients were however investigated with esophageal HRM because their symptoms were considered compatible with impaired esophageal clearance. Furthermore our patients were studied upright where the effects of gravity would have changed bolus flow even though standardised across patients and controls. Nevertheless, the strengths of our study lie in the use of objective measures which, despite low numbers, show intuitively relevant differences between patients and controls and correlated well with independent measures of dysfunction based on the gold standard of radiology.

In conclusion, we demonstrate that novel pressure-flow metrics can be used to detect disturbed esophageal function, which leads to failed bolus clearance and/or reduced flow time across the EGJ. Furthermore, Impedance Ratio and Pressure Flow Index may be used in combination to discriminate the extent of clearance failure and the degree of bolus pressure-flow abnormality. These additional functional measures may complement routine clinical HRM findings of normal or disordered esophageal motility. The pressure-flow metric TNadImp to PeakP appears to be a specific marker of EGJ flow time even though measured proximal to the EGJ high pressure zone itself. Further studies combining HRIM with fluoroscopy, evaluating viscous and solid bolus consistencies and relating pressure-flow metrics to the perception of bolus transit in patients specifically referred for esophageal dysphagia are indicated.

## References

1. Chen CL, Yi CH. Clinical correlates of dysphagia to oesophageal dysmotility: studies using combined manometry and impedance. *Neurogastroenterol Motil* 2008;20:611-7. Lazarescu et al., *NGM* 2010
2. Conchillo JM, Nguyen NQ, Samsom M, Holloway RH, Smout AJ. 2005 Multichannel intraluminal impedance monitoring in the evaluation of patients with non-obstructive. *Dysphagia*. *Am J Gastroenterol* 2005;100:2624-2632.
3. Lazarescu A, Karamanolis G, Aprile L, De Oliveira RB, Dantas R, Sifrim D. 2010 Perception of dysphagia: lack of correlation with objective measurements of esophageal function. *Neurogastroenterol Motil* 2010;22:1292-1297, e1336-1297
4. Hirano I, Tatum RP, Shi G, Sang Q, Joehl RJ, Kahrilas PJ. Manometric heterogeneity in patients with idiopathic achalasia. *Gastroenterology*. 2001;120:789-98
5. Omari TI, Wauters L, Rommel N, Kritas S and Myers JC. Esophageal pressure-flow metrics in relation to bolus volume, bolus consistency and bolus perception. *UEG Journal* (In Press Accepted May 2013).
6. Chen CL, Yi CH, Lui TT, Hsu TT and Omari TI. Characterisation of Esophageal Pressure-Flow Abnormalities in Patients with Non-Obstructive Dysphagia and Normal Manometry Findings. *J Gastroenterol Hepatol*. 2013; Accepted 21 January, 2013.
7. Nguyen NQ, Holloway RH, Smout AJ, and Omari TI. Automated impedance-manometry analysis detects esophageal motor dysfunction in patients who have non-obstructive dysphagia with normal manometry. *Neurogastroenterol Motil*. Accepted 8/10/2012
8. Loots CM, Van Herwaarden MY, Benninga MA, VanderZee DC, Van Wijk MP, Omari TI. Gastroesophageal reflux, esophageal function and gastric emptying in relation to dysphagia before and after anti-reflux surgery in children. *J Pediatrics* Accepted 30/08/2012.
9. Omari T, Kritas S, Cock C. New Insights into Pharyngo-Esophageal Bolus Transport Revealed by Pressure-Impedance Measurement. *Neurogastroenterol Motil*. Accepted Jul 2012.

10. Myers JC, Nguyen NQ, Jamieson GG, Van't Hek JE, Ching K, Holloway RH, Dent J, Omari TI. Susceptibility to dysphagia after fundoplication revealed by novel automated impedance manometry analysis. *Neurogastroenterol Motil.* 2012;24:812-820, e392-e393.
11. Rohof WO, Myers JC, Estremera FA, Ferris LS, van de Pol J, Boeckstaens GE, Omari TI. Inter- and Intra-Rater Reproducibility of Automated and Integrated Pressure-Flow Analysis of Esophageal Pressure-Impedance Recordings. *Neurogastroenterol Motil.* Accepted Aug 2013.
12. Rommel N, Van Oudenhove L, Tack J, Omari TI. Automated Impedance Manometry Analysis as a Method to Assess Esophageal Function. *Neurogastroenterol Motil.* 2014 In Press.
13. Fox M, Hebbard G, Janiak P, Brasseur JG, Ghosh S, Thumshirn M, Fried M, Schwizer W. High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry. *Neurogastroenterol Motil.* 2004 Oct;16(5):533-42.
14. Bogte A, Bredenoord AJ, Oors J, Siersema PD, Smout AJ. Relationship between esophageal contraction patterns and clearance of swallowed liquid and solid boluses in healthy controls and patients with dysphagia. *Neurogastroenterol Motil.* 2012 Aug;24(8):e364-72.
15. Bulsiewicz WJ, Kahrilas PJ, Kwiatek MA, et al. Esophageal pressure topography criteria indicative of incomplete bolus clearance: a study using high-resolution impedance manometry. *Am J Gastroenterol.* 2009;104:2721-8.
16. Roman S, Lin Z, Kwiatek MA, Pandolfino JE, Kahrilas PJ. Weak peristalsis in esophageal pressure topography: classification and association with Dysphagia. *Am J Gastroenterol.* 2011 Feb;106(2):349-56.
17. Ghosh SK, Pandolfino JE, Rice J, Clarke JO, Kwiatek M, Kahrilas PJ. Impaired deglutitive EGJ relaxation in clinical esophageal manometry: a quantitative analysis of 400 patients and 75 controls. *Am J Physiol Gastrointest Liver Physiol.* 2007 Oct;293(4):G878-85.
18. Kahrilas PJ, Dodds WJ, Hogan WJ. Effect of peristaltic dysfunction on esophageal volume clearance. *Gastroenterology.* 1988 Jan;94(1):73-80.



19. Ren J, Massey BT, Dodds WJ, Kern MK, Brasseur JG, Shaker R, Harrington SS, Hogan WJ, Arndorfer RC. Determinants of intrabolus pressure during esophageal peristaltic bolus transport. *Am J Physiol.* 1993 Mar;264(3 Pt 1):G407-13.
20. Pandolfino JE, Ghosh SK, Lodhia N, Kahrilas PJ. Utilizing intraluminal pressure gradients to predict esophageal clearance: a validation study. *Am J Gastroenterol.* 2008 Aug;103(8):1898-905.
21. Nicodème F, Pandolfino JE, Lin Z, Xiao Y, Escobar G, Kahrilas PJ. Adding a radial dimension to the assessment of esophagogastric junction relaxation: validation studies of the 3D-eSleeve. *Am J Physiol Gastrointest Liver Physiol.* 2012 Aug 1;303(3):G275-80.
22. Bredenoord AJ, Fox M, Kahrilas PJ, Pandolfino JE, Schwizer W, Smout AJPM, International High Resolution Manometry Working Group. Chicago Classification Criteria of Esophageal Motility Disorders Defined in High Resolution Esophageal Pressure Topography (EPT). *Neurogastroenterol Motil.* 2012 March; 24(Suppl 1): 57–65.
23. Kwiatek MA, Nicodeme F, Pandolfino JE, Kahrilas PJ. Pressure morphology of the relaxed lower esophageal sphincter: the formation and collapse of the phrenic ampulla. *Am J Physiol Gastrointest Liver Physiol* 302: G389–G396, 2012.
24. Kwiatek MA, Pandolfino JE, Kahrilas PJ. 3D-high resolution manometry of the esophagogastric junction. *Neurogastroenterol Motil* 2011; 23: e461–e469.
25. Bogte A, Bredenoord AJ, Oors J, Siersema PD, Smout AJ. Normal values for esophageal high-resolution manometry. *Neurogastroenterol Motil.* 2013 Sep;25(9):762-e579.
26. Omari TI, Ferris L, Dejaeger E, Tack J, Vanbeckevoort D, Rommel N. Upper esophageal sphincter impedance as a marker of sphincter opening diameter. *Am J Physiol Gastrointest Liver Physiol.* 2012;302(9):G909-13.

## Figure Legends

**Figure 1. Radiological correlation of bolus trajectory and the timing of nadir impedance during swallowing of a 10ml liquid bolus.** Pressure-flow landmarks based upon the AIM analysis plot below are transposed onto corresponding radiological images above (Top image: NadImp or Z = nadir impedance, 20 = 20mmHg iso-contour and P = peak pressure; serial images captured at 0.5sec intervals). Insets (middle of figure) show magnified radiological images of the EGJ at the start and stop of flow.

Note that the position of nadir impedance, Z, is approximately at the axial centre of the radiological image of the liquid bolus. Liquid flow stasis is associated with the bolus pooling above the EGJ. Further pressurisation of the bolus leads to aboral movement of the position of nadir impedance, Z, within the distal 50% of the esophagus and coincides with the onset of trans-sphincteric flow.

**Figure 2. Key metrics showing statistically significant correlations with bolus transport score (A and B) and EGJ flow period (C and D) in patients with dysphagia.**

**Figure 3. Dichotomous classification of patients in relation to bolus flow resistance and bolus clearance using the Pressure-Flow Index and Impedance Ratio. A.** Patients could be separated into three of a possible 4 groups. Dotted lines indicate the 90<sup>th</sup> percentile reference range based on aged matched control swallows. **B-D** comparisons of fluoroscopic measures amongst individuals in each group. P-values are for Kruskal-Wallis One Way Analysis of Variance on Ranks.

	r vs. Bolus Transport Score	r vs. EGJ Flow Time	r vs. EGJ Max Diameter
<b>Fluoroscopic Measures</b>			
<i>Bolus Transport Score</i>	-	-0.703*	-0.402
<i>EGJ Flow Time</i>	-	-	0.683*
<i>EGJ Max Diameter</i>	-	-	-
<b>Esophageal Metrics</b>			
<b>100% of Distal Esophagus</b>			
<i>Peristaltic Break Size</i>	<b>0.895***</b>	-0.383	-0.033
<i>Peak P</i>	<b>-0.929***</b>	0.450	0.167
<i>PNadImp</i>	-0.326	0.500	0.817**
<i>IBP</i>	-0.050	0.017	0.350
<i>IBP slope</i>	-0.126	-0.217	0.000
<i>TNadImp-PeakP</i>	-0.377	0.767*	0.367
<i>Pressure Flow Index</i>	-0.126	-0.217	0.000
<i>Impedance Ratio</i>	0.577(0.09)	-0.650(0.050)	-0.217
<b>Lower 50% of Distal Esophagus</b>			
<i>Peak P</i>	<b>-0.887***</b>	0.450	0.083
<i>PNadImp</i>	-0.226	0.150	0.350
<i>IBP</i>	-0.050	0.016	0.350
<i>IBP slope</i>	0.008	-0.233	-0.033
<i>TNadImp-PeakP</i>	-0.402	<b>0.733*</b>	0.500
<i>Pressure Flow Index</i>	0.059	-0.283	-0.083
<i>Impedance Ratio</i>	<b>0.661*</b>	<b>-0.750*</b>	-0.400
<b>EGJ</b>			
<i>IRP4s</i>	0.197	0.034	0.067
<i>Nadir P</i>	0.494	-0.267	-0.117
<i>PNadImp</i>	0.435	-0.016	0.217
<i>Nadir Impedance</i>	0.184	-0.450	-0.200

**Table 1.** Correlations amongst patient averages for videofluoroscopic measures and pressure-impedance metrics. Data are Spearman Rank Order correlation coefficients (r) (\*p<0.05, \*\*p<0.01, \*\*\*p<0.001; p values 0.05-0.1 shown in parentheses). Significant correlations in bold are also shown as scatter plots in Figure 2.