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Fourier Phase Analysis of Dynamic Antral Contraction Scintigraphy: New Software, Normal Values and Comparisons to Conventional Gastric Emptying

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Abstract (word count = 339/350)

Rationale: Dynamic antral contraction scintigraphy (DACS) has been used to evaluate for gastric dysmotility by measuring antral frequency and ejection fraction (EF). Fourier phase image analysis has the potential to assess gastric antral contractions for dyssynchrony as has been used for analyzing nuclear cardiology ventriculography(MUGA studies) for cardiac dyssynchrony. The aims of this study were to determine: 1) If Fourier phase analysis helps to characterize antral motility physiology; 2) If Fourier phase analysis correlates with conventional gastric emptying (GE); and 3) Which DACS parameters may aid in diagnosing gastric dysmotility, particularly delayed GE.

Methods: DACS and GE studies of normal volunteers(n=22) were compared to patients (n=99) with symptoms of gastroparesis. New DACS Fourier phase analysis software was developed.

Results: GE was delayed(n=53) and normal(n=46) in patients. There was a linear correlation of %Total of Proximal(P) and Distal(D) in-phase antral pixels @30 min(r = 0.37, p = 0.0001) and 60 min (r = 0.26, p = 0.007) with GE T1/2. In normals, the mean ratio P/D in-phase antral pixels increased from 1.67(30 min) to 2.65(120 min)(p = 0.035) and EF from 23%(30 min) to 32%(120 min)(p = 0.022). Multivariable regressions of %Total PD in-phase antral pixels (30 min) and EF(60 min) were best predictors of abnormal GE(adjusted odds ratio(95% CI):3.30(1.21, 9.00);2.97(1.08, 8.21)) respectively.

Conclusions: This study used Fourier phase analysis to analyze DACS in normal subjects and patients with symptoms of gastroparesis. In addition to establishing normal values, new physiologic information on antral motility was obtained. In normal subjects, there is an increasing ratio of Proximal/Distal in-phase antral pixels and antral EF over time following meal ingestion. The % Total Proximal and Distal in-phase antral pixels at both 30 and 60 minutes had good correlation with T1/2 GE values. For symptomatic patients, the % Total Proximal and Distal in-phase antral pixels at 30 min and the EF at 60 min post meal ingestion correlated with delayed conventional GE. Thus, Fourier phase analysis of DACS appears to have potential to further aid in diagnosing gastric dysmotility in GE scintigraphy studies.

Key Words: gastric emptying scintigraphy; antral contractility; antral dyssynchrony; Fourier analysis

Introduction

While in widespread clinical use, conventional gastric emptying scintigraphy(GES), which measures only the percentage of total gastric emptying(GE) of a standardized meal, does not always correlate well with symptoms of gastroparesis. In some studies, GES is able to detect abnormal GE in only up to 40% of patients where there is a high clinical suspicion of gastroparesis(*1*). Because conventional GES fails to detect gastric dysmotility as a cause of symptoms in some patients when there is a high clinical suspicion of impaired GE, efforts have been made to augment GES utilizing more advanced analysis of GES, particularly dynamic antral contraction scintigraphy(DACS) which permits assessment of antral contractility(*2-4*).

Antral hypomotility has been shown to be directly related to impaired GE using invasive manometric studies(*5*). In patients with dyspepsia and symptoms of gastroparesis, antroduodenal manometry has been associated with infrequent, low amplitude pressure waves in the antrum(*6*). However, other investigations, even in patients with severe dyspepsia, have failed to identify a strong positive correlation between symptoms, GE or postprandial manometric recordings of antral contractility (*7*).

Although DACS was introduced over 20 years ago, the methodology and technical aspects of performing DACS have not been standardized. Furthermore, prior DACS studies utilized research software available only at the small number of institutions performing those studies, limiting the more widespread use of DACS. Two variables from Fourier analysis of DACS, antral frequency and amplitude, have typically been used to characterize antral contractility. The dominant antral frequency has been calculated as the frequency with the highest Fourier amplitude. Antral contraction amplitude has been measured using either the amplitude of the Fourier analysis(*4*) or ejection fraction(EF)(*2*) derived from the percent of radioactive content displaced by an average contraction from a region in the mid-antrum. These prior studies have shown the potential of DACS to characterize both normal and abnormal physiology of antral contractions. Urbain et al demonstrated in longstanding diabetes that the lag phase of GE was prolonged and was associated with a reduction in the amplitude of antral contractions(*4*). Knight et al showed that slower GE in women compared to men directly related to a mid-antral decrease in the EF which was correlated to antral manometry(*2*). Recently, we have demonstrated that DACS can be utilized to assist in partitioning the stomach into proximal and distal sections allowing measurement of fundic accommodation and to measure antro-pyloro-duodenal contractions in normal subjects(*3,8*).

Fourier analysis of nuclear cardiac ventriculography(MUGA studies) has been well established for analyzing cardiac dyssynchrony. Left ventricular(LV) dyssynchrony is present when there are temporal differences in the activation and contraction of various LV myocardial segments. Impairment of LV systolic function and reduced cardiac output can be the result of such LV dyssynchrony (*9*). Nuclear medicine DACS imaging of the stomach is performed in a similar manner to nuclear cardiac MUGA studies. The software needed to analyze either cardiac or antral contractions assigns a phase angle to each pixel of the Fourier phase image which is derived from the first Fourier harmonic. The phase angle reflects the similarity or difference in timing to the onset of contraction in each adjacent image pixel. Similar to its application in nuclear cardiology, this type of Fourier phase image analysis has the potential to assess gastric antral contractions for dyssynchrony.

The aims of this study were: 1) to investigate the potential of antral Fourier phase analysis(FPA) to add additional physiologic information on antral motility; 2) to investigate how FPA of DACS correlates with conventional gastric emptying(GE); and 3) and to study which DACS parameters may contribute to diagnosing delayed GE. To accomplish these aims, we developed and validated a new DACS processing software package allowing performance of Fourier phase analysis and established normal DACS results in normal subjects.

Methods and Patient Population

All normal volunteers included in this study were the same as those included in our prior study utilizing DACS to measure antro-pyloro-duodenal contractions(*3*). Our institutional review board (IRB) approved this study and all normal subjects signed a written informed consent. The retrospective symptomatic patient studies included 100 sequential patients referred for GES with DACS between 9/26/2018 to 3/24/2021 who had symptoms suggesting gastroparesis. An IRB waver was issued for review of the retrospective studies.

All normal volunteers were questioned to ensure they had no prior history of gastrointestinal disease, prior gastrointestinal surgery, and that they weren't taking medications that might affect gastrointestinal function. All normal volunteers and symptomatic patients came to Nuclear Medicine in the morning after an overnight fast. GES was performed using the currently recommended 4-hour, liquid egg white protocol described initially by Tougas et al (*10*) and recommended in the current Society of Nuclear Medicine and Molecular Imaging guideline(*11*) and the consensus report of the Society of Nuclear Medicine and Molecular Imaging and the American Neurogastroenterology and Motility Society(*12*). The meal consists of 120 g (4 oz. liquid egg white) radiolabeled with ^{99m}Tc sulfur colloid served with two pieces of white bread and jelly. In addition, patients were given 120 ml water immediately following ingestion of the solid portion of the meal. The dose of ^{99m}Tc sulfur colloid for GES with DACS was given in the normal subjects with a range of 74 MBq – 370 MBq(2mCi-10mCi) as previously described(*3*). All patient studies were performed with a minimal dose of 74MBq(2 mCi).

Following meal ingestion, conventional GE static imaging using a 128 x 128 matrix was performed at 0, 0.5, 1, 2, 3, and 4 hours with the subject upright in the anterior and then the posterior position each for 30 seconds. DACS was performed using continuous, list mode 1 sec images obtained for 10 minutes(total of 600 images) immediately following the static imaging 0, 0.5, 1, 2 hours as previously described (*2,8*).

Total stomach, conventional GE was analyzed from the static images as the percentage of radioactivity retained in the whole stomach using the geometric mean of the decay-corrected anterior and posterior counts for each time point. As Fourier analysis of the DACS images does not require geometric mean depth correction of counts, the DACS images were acquired and processed using anterior images only. Gastric retention of the ^{99m}Tc labeled solid meal of greater than 60% at 2 hours and/or greater than 10% at 4 hours or a T1/2 emptying time(time for stomach to empty 50% of the meal) computed by a power exponential curve fit > 132 minutes was considered delayed GE(*10,12*).

All DACS images were analyzed using a beta version MIM Software(Cleveland, OH) workflow developed for this study. Before processing of the DACS images, the serial continuous dynamic images consisting of a total of 600 images of 1 second each were first reviewed and motion-corrected to help eliminate patient movement artifacts using standard motion correction software. A 2 cm region of interest(ROI) was then placed over the mid antrum to record a time activity curve(TAC) of antral contractions from the serial DACS image set. To further minimize patient movement artifacts and to ensure analysis of consistent peristaltic contractions, the TAC from the continuous dynamic set was visually reviewed and a minimum set of 4 consecutive antral peristaltic waves which demonstrated consistent frequency and amplitude of contractions was selected for analysis(Figure 1).

During visual review of the serial images used to create the final DACS composite image sequence we observed, as others have reported(*13*), short intermittent periods of irregular antral contractions. Any such periods of antral dysrhythmia were excluded for final DACS analysis. To establish how often these occurred in the normal volunteers both readers measured the percentage of time these were observed during the 10 minute DACS recordings. An average percentage of the time these episodes of antral dysthymias were observed in normal subjects was calculated for the two readers.

The software workflow calculates a mean frequency of antral contractions by measuring the peak to peak time intervals from the TAC. A mean EF is then calculated from the TAC where the EF_i(%) for each individual contraction(i) is given by:

$$EF_i(\%) = 100 \text{ X } (Max_i - Min_i) / Max_i$$

where Max is the maximum and Min is the minimum counts derived from the antral TAC for each time interval i.

The software reformats a grouped image series using the set of selected antral contractions for Fourier analysis. This final composite cinematic image series provides a movie display of the temporal movement of the antral peristaltic wave which typically starts in the area of the incisura and propagates distally towards the pylorus. The results of the Fourier analysis for all antral pixels are color coded in a final display of the Fourier derived phase angles and amplitude(Figure 2).

After visual display and review of the phase and amplitude maps, the software permits the operator to manually define regions of interest for the proximal, distal and total area of the antrum. The software then applies an automated threshold (40% threshold of the antral derived phase angles) to calculate the number of pixels in the proximal and distal antral areas which, as a group, are in-phase and have similar timing in their onset of contraction where:

%Total = (# proximal antral in-phase pixels + # distal antral in-phase pixels) / total # antral pixels

A ratio of the # in-phase proximal/# distal pixels(Prox/Dist) is also calculated to characterize the relative contribution of proximal vs distal antral pixels with in-phase contractions.

The DACS and conventional GE study results of the patients with suspected gastroparesis were compared to the results of the normal volunteers and correlated with results of conventional GE including the percentage of total GE at 2 and 4 hours and measurement of a power exponential fit to calculate the T1/2 of GE. For classification of the results of the conventional GE, a patient study was considered to have delayed GE if any one of the following criteria were met: 2 hour retention was abnormal (> 60% retained), or 4 hour retention was abnormal (> 10% retained) or the T1/2 emptying was > 132 minutes.(*10*)

Statistical Analysis

The DACS data on healthy volunteers for % Total, ratio Prox/Dist, EF, and Frequency were tested for normality using the Kolmogorov-Smirnov normality test and found to depart from being normally distributed at almost all the time points (30, 60, and 120 minutes). The normal results by DACS therefore were expressed using median values and 90% percentile intervals for all time points for these four parameters based on healthy volunteers' data. Linear (mixed-effects) regression analysis was utilized to correlate the DACS data to those of the conventional GE on T1/2 and percentages of gastric retention at 2,3,4 hours as well as for time trend analyses for the four DACS parameters among patients and/or healthy volunteers. The 90% DACS percentile intervals based on the healthy volunteers were used to define abnormality by DACS and associated with or used to predict conventional GE diagnosis results. Group comparisons of DACS abnormality between normal (including healthy volunteers) and abnormal patients by conventional GE diagnosis were performed using the Fisher's Exact test. Univariable and multivariable logistic regression analyses were performed to determine which DACS parameters could be used to help predict abnormal GE diagnosis results, and raw and adjusted Odds Ratio (95% Confidence Intervals) were reported from such logistic regression models with the multiple regression model selected using the stepwise variable selection method. P-values less than 0.05 were considered statistically significant. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for all the data analyses. There was no adjustment for multiple comparisons as this was an exploratory observational study not confirming any *a prior* hypothesis or intent to make a statement regarding 2 or more parameters combined together at the same time.

Results

Study Subjects

Conventional GES results were normal for all the 22 normal control volunteers (13/22 (59.1%) male; median (range) age 34.5 (23.0, 69.0) years). Of the 100 patients studied, 99 patient had studies suitable for analysis. One patient's DACS study could not be analyzed due to marked motion artifact at all time points and was therefore excluded. Of the 99 patients, 53 had delayed GE (12/53 (22.6%) male; median (range) age 42.0 (19.0, 82.0) years) and 46 (6/46 (13.0%) male; median (range) age 40.0 (19.0, 78.0) years) had normal GE.

DACS in Normal Subjects

An example of a normal subject's DACS software analysis output is shown in Figure 2. The normal volunteers' DACS results consistently demonstrated two well defined areas of in-phase, color-coded pixels which localized in the proximal and distal antrum. The pixels with similar phase angles were separated by a band of pixels with no in-phase pixels which correlated with a mid antral area showing the highest Fourier derived amplitude. This mid antral region corresponded on the cine images visually to the peaks of bolus food antegrade and retrograde movements through the mid antrum (Figure 2B).

A summary of the normal volunteers(n=22) DACS results for %Total in-phase antral pixels, ratio Prox/Distal, EF and frequency for all time points are shown in Table 1. The ratio Prox/Distal significantly increased over time from a median of 1.67 at 30 min to 2.65 at 120 min (p = 0.035). Figure 3 shows an example of how the Fourier phase images demonstrate this normal increase in the ratio Prox/Distal in-phase pixels from 30 min to 120 min. Similarly, the EF significantly increased with time from a median of 23% at 30 min to 32% at 120 min (p = 0.022). In normal subjects, the %Total in-phase antral pixels did not change significantly over time from a median of 45% at 30 min to 51% at 120 min (p = 0.11). The frequency of antral contractions also did not significantly change over time, ranging from a median of 3.08 cycle/min at 30 min to 2.91 cycle/min at 120 min (p = 0.11).

The mean % irregular contractions recorded by the two readers were: 9.9% with range (0-34.7%) @30 min; 11.7% with range (0-35.4%)@60 min and 11.3%% with range (0-23.1%)@120min).

DACS in Normal Subjects and Patients

Linear regression of the %Total versus the T ½ of GE using the normal volunteers and all patients (n=121) revealed that they were significantly linearly correlated at the 30 and 60 minute time points (Figure 4): 30 min (%Total 30min = 0.4630 - 0.0008*T1/2, r=0.37, p-value=0.0001) and 60 min(%Total 60min = 0.4415 + -0.0005*T1/2, (R=0.2559, p-value=0.0065). A similar linear trend seemed to exist for %Total at 120 minutes but did not achieve statistical significance (%Total 120min = 0.4024 + -0.0003*T1/2, (R=0.1456, p-value=0.1680).

The Prox/Distal ratios at 30 and 120 min did not significantly correlate linearly with T ½. There was, however, a fair linear correlation for Proximal/Distal at 60 min (Proximal/Distal 60min = 1.3361 + 0.0072*T1/2, r=0.19, p-value=0.049)). Frequency at 30 min had a good linear correlation to T½ emptying (Freq30min = 2.8237 + 0.0017*T1/2, r=0.30, p=0.003). EF showed no significant linear relationship T1/2.

DACS in Patients with Delayed Gastric Emptying

Table 2 summarizes the performance using the DACS parameters one at a time for detection of abnormal conventional GE diagnosis (CGE). The measurement of the %Total at all times (30, 60, and 120 minutes) appeared to be correlated with the abnormal conventional GE, with the strength of this correlation decreasing over time and achieving a statistical significance only at 30 minutes. The %Total 30min(p=0.001), Prox/Distal 60min(p=0.017), and EF 60min(p=0.011) were the only three variables among all the DACS parameters that had a statistically significant predictive capability for the abnormality compared to conventional GE with a sensitivity of at least 35% and a specificity of at least 75% predicting the CGE abnormal cases. The raw odd ratios(ORs)(95% CIs) of having abnormal conventional GE were 4.49 (1.81, 11.15), 2.72 (1.23, 5.99), and 3.47 (1.33, 9.06), respectively, when comparing the corresponding DACS abnormal to its normal group for these three DACS parameters. Figure 5 shows an example of how the Fourier phase images demonstrate the lack of a consistent increase in the ratio Prox/Distal in-phase pixels from 30 min to 120 min.

Based on multivariable logistic regression results, two abnormal values, the % total antral pixels at 30 minutes and the EF at 60 minutes, as defined using the normal volunteers' DACS data, were the best subset of all DACS values for predicting abnormal conventional GE (Table 3; adjusted odds ratio (95% CI): 3.30 (1.21, 9.00), 2.97 (1.08, 8.21), respectively).

Discussion

There is increasing interest to utilize advanced imaging to more completely characterize the complex coordination of gastric motility within different functional areas of the stomach and how each contributes to overall gastric emptying and potential treatment of gastroparesis(*14,15*). Up to now, DACS studies have primarily focused on measuring the frequency and amplitude of antral contractions. We have previously shown that DACS can significantly enhance the information provided by GES not only for measuring antral contraction amplitude and frequency (*8*) but can also permit assessment of antropyloric contractions that produce coordinated, antropyloduodenal bolus propagation(*3*). Analogous to cardiac MUGA studies assessing for ventricular dyssynchrony, DACS may provide information on the in-phase relationship of the timing to onset of antral contractions. In this study, we have investigated the use of Fourier phase analysis to augment DACS analysis of the contractility of the proximal and distal antrum. We have also correlated how DACS measurements of frequency, EF and proximal and distal antral phase analysis correlate with conventional measurement of overall T1/2 gastric emptying. This study shows that DACS % total in-phase antral pixels at 30 minutes and the EF at 60 minutes are potential new measures of antral contractility which may have added value for predicting abnormal gastric emptying. Importantly, this study has led to development of a software package and associated normal values which can now be available to others and offers the potential for more widespread clinical use.

Other imaging techniques have been used to assess for antral contractility, particularly most recently magnetic resonance imaging(MRI), which can be used to measure gastric volumes and the phasic and amplitude components of the gastric contractions(*16*). Although MRI has greater spatial and temporal resolution than scintigraphy, MRI imaging for gastric motility currently has limitations including: use of non physiologic meals, limited scanner time for prolonged imaging, high costs and current availability limited only to research centers.

This study shows: 1) DACS imaging in normal subjects demonstrates a consistent pattern of two in-phase areas of the antrum which show coordinated contractions. The first area is the proximal antrum where antral contractions originate. This is separated from the distal antrum by a mid antral segment where the peristaltic wave propagates bolus movements of food through the antrum. The second area is in the distal antrum where rhythmic contractions repel the incoming bolus in a retrograde fashion; 2) The percentage of total proximal and distal antral pixels which are in-phase by DACS analysis correlates well with the overall T1/2 GE. This suggests this quantitative measurement may serve as a new physiologic measurement of antral contractility; 3) In normal subjects, the ratio of in-phase proximal/distal antral pixels significantly increases over time from 30 min to 120 min post meal ingestion. This agrees with early observations of Rees et al which showed that the motility index of the distal antrum decreased in the postprandial period.(*17*) This supports an important role of increasing proximal antrum contractions over time post meal ingestion as the fundus progressively moves solids into the antrum(Figure 5); 4) In a similar fashion, the antral EF in normals increases with time; 5) Finally, univariant and multivariant regressions show that the % total in-phase antral pixels at 30 minutes and the antral EF at 60 appear to be predictors of delayed gastric emptying. We acknowledge that additional multi-institutional clinical studies with more patients will be needed to see if these findings can be confirmed and expanded to help explain symptoms in patients with suspected gastroparesis when conventional GE results are normal.

The final composite of dynamic images used for the Fourier analysis utilized only a subset of the antral contractions(4 cycles) that occur during the 10 minutes of continuous list-mode DACS imaging. We acknowledge that the quality of the Fourier analysis could improve utilizing more gastric contraction cycles. We found however that the current beta software which utilizes existing MIM cardiac phase-amplitude software required typically 10 -15 minutes run time for 4 cycles. When we utilized more than 4 cycles the processing time became greater than 20 minutes which was not practical for the large number of patient studies and imaging time points needing analysis. The lenghty processing time of the current DACS MIM workflow is likely related to the need to reformat all the individual list mode gastric images without the benefit of ECG gating. Such gating which is performed during cardiac MUGA acquisition helps create a single summed cardiac cycle for analysis.

The beta software used for DACS analysis in this study is still under development by MIM and not currently commercially available. We anticipate that as demand for processing DACS data grows the current beta software processing time will be improved. It is our hope that based on the results of this study a final commercial DACS software package with the potential for more widespread availability will make acquisition and processing of DACS available for routine clinical use.

While processing only 4 gastric contraction cycles could be considered a potential limitation of the analysis, this permitted us to select a set of best reformatted, summed antral contraction cycles for measurement of phase, amplitude, frequency and EF across multiple time points. Others have observed with DACS that while most antral contractions appear regular in frequency and amplitude within the time of observation, some antral contractions are irregular(*13*). We found that there is a low occurrence (average of 11%) of irregular antral contractions observed during DACS in normals. Such short periods of spontaneous gastric arrythmias(which may be up to 35%) observed could affect the DACS analysis. Thus, we believe that visual review of the DACS imaging data and selection of an optimum set of gastric cycles prior to final analysis, as performed in this study, is desired and important to exclude not only irregular gastric contractions but also potential patient motion artifacts. Such selection of the regular antral contractions should be performed routinely as a part of DACS analysis. Further characterization of whether short periods of antral dysrhythmias effects overall GE in symptomatic patients will require additional study.

In summary, in this study Fourier phase analysis of proximal and distal antral phasic contractions was added to DACS in addition to measurements of antral frequency and ejection fraction(EF). The study establishes new normal values and demonstrates new physiologic information on antral motility with normal increasing ratio of Proximal/Distal in phase pixels and EF with time post meal ingestion. The % Total proximal and distal in-phase pixels had good correlation with early T1/2 GE values. Further, for symptomatic patients the percent of in-phase proximal and distal antral pixels(at 30 min) and EF (at 60 min) post meal ingestion are potential new parameters to assess for abnormal antral contractility and delayed GE. Utilization of Fourier analysis of DACS has the potential to provide for added understanding of the underlying pathophysiology of antral contractility.

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A beta version of the MIM software was provided for these studies. Natalie Cole, PhD is a software engineer employed by MIM software company. As a salaried employee she has no potential conflicts of interest in terms of any monetary gain for any potential sales of the software or patent ownership.

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KEY POINTS

QUESTION: Does Fourier phase analysis of DACS provide added physiologic information on antral motility which can augment conventional gastric emptying studies for diagnosing gastric dysmotility?

PERTINENT FINDINGS: In normal subjects the ratio of Proximal/Distal in-phase antral pixels and antral EF increases with time following meal ingestion. The % Total Proximal and Distal in-phase antral pixels at both 30 and 60 minutes had good correlation with T1/2 GE. For symptomatic patients, the % Total Proximal and Distal in-phase antral pixels at 30 min and the antral EF at 60 min post meal ingestion have potential to further aid in diagnosing delayed gastric emptying.

IMPLICATIONS FOR PATIENT CARE: New software and associated normal values for antral frequency, in-phase contractions and ejection fraction has been developed which offers the potential for more widespread application of DACS to aid in the diagnosis of abnormal gastric emptying.

References

1. Quartero A, deWit N, Lodder A, Numans M, Smout A, Hoes A. Disturbed solid-phase gastric emptying in functional dyspepsia: a meta-analysis. *Dig Dis Sci.* 1998;43:2028-2033.

2. Knight L, Parkman H, Brown K, et al. Delayed gastric emptying and decreased antral contractility in normal premenopausal women compared with men. *Am J Gastro.* 1997;92:968-975.

3. Orthey P, Dadparvar S, Kamat B, Parkman HP, Maurer AH. Using gastric emptying scintigraphy to evaluate antral contractions and duodenal bolus propagation. *Am J Physiol Gastrointest Liver Physiol.* 2019;318:G203–G209.

4. Urbain J, Vekemans M, Bouillon R, et al. Characterization of gastric antral motility disturbances in diabetes using a scintigraphic technique. *J Nucl Med.* 1993;34:576-581.

5. Camilleri M, Brown M, Malagelada J-R. Relationship between impaired gastric emptying and abnormal gastrointestinal motility. *Gastroenterology.* 1986;91:94-99.

6. Stanghellini V, Ghidini C, Maccarini MR, Paparo GF, Corinaldesi R, Barbara L. Fasting and postprandial gastrointestinal motility in ulcer and non-ulcer dyspepsia. *Gut.* 1992;33:184-190.

7. Wilmer A, Cutsem EV, Andrioli A, Tack J, Coremans G, Janssens J. Ambulatory gastrojejunal manometry in severe motility-like dyspepsia: lack of correlation between dysmotility, symptoms, and gastric emptying. *Gut.* 1998;42:235-242.

8. Orthey P, Dadparvar S, Parkman HP, Maurer AH. Enhanced Gastric Emptying Scintigraphy to Assess Fundic Accommodation Using Intragastric Meal Distribution and Antral Contractility. *J NucMed Tech.* 2019;47:138-143.

9. VanKriekinge S, Germano G. Imaging cardiac dyssynchrony. *Clin Transl Imaging.* 2013;1:353-361.

10. Tougas G, Eaker EY, Abell TL, et al. Assessment of gastric emptying using a low fat meal: establishment of international control values. *Am J Gastroenterol.* 2000;95:1456-1462.

11. Donohoe KJ, Maurer AH, Ziessman HA, et al. Procedure guideline for adult solid-meal gastric-emptying study 3.0. *J Nucl Med Technol.* 2009;37:196-200.

12. Abell TL, Camilleri M, Donohoe K, et al. Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *Am J Gastroenterol.* 2008;103:753-763.

13. Diaz J, Friedman M, Makiyil J, Sarosiek I, McCallum R. Antral scintigraphy identifies patterns of gastric contractility in patients with upper GI motility disorders: Comparison to conventional gastric emptying scintigraphy data. *Gastroenterology.* 2015;148:S515-S516.

14. Spandorfer R, Zhu Y, Mekaroonkamol P, Galt J, Halkar R, Cai Q. Gastric Emptying Before Gastric per Oral Endoscopic Myotomy: Imaging May Inform Treatment. *Gastrointest Endoscopy Clin N Am.* 2019;29:127-137.

15. Mekaroonkamol P, Tiankanon K, Rerknimitr R. A New Paradigm Shift in Gastroparesis Management. *Gut and Liver.* 2022.

16. Lu K-H, Liu Z, Jaffey D, et al. Automatic assessment of human gastric motility and emptying from dynamic 3D magnetic resonance imaging. *Neurogastroenterology & Motility.* 2022;34:1-14.

17. Rees W, Go V, Maladelada J. Antro-duodenal response to solid liquid and homogenized meals. *Gastroenterology.* 1979;76:1438-1442.

Figures and Figure Legends

Figure 1. User selection of a set of antral contractions for DACS analysis.
This example of a time activity curve(TAC) from a patient study shows that even after use of image motion correction software, patient motion can result in significant motion artifacts in the TAC. The software workflow allows the user to select an optimum subset of image peaks and valleys (as shown between the "start time" and "end time") where the antral contractions are stable and will be used for the DACS processing.

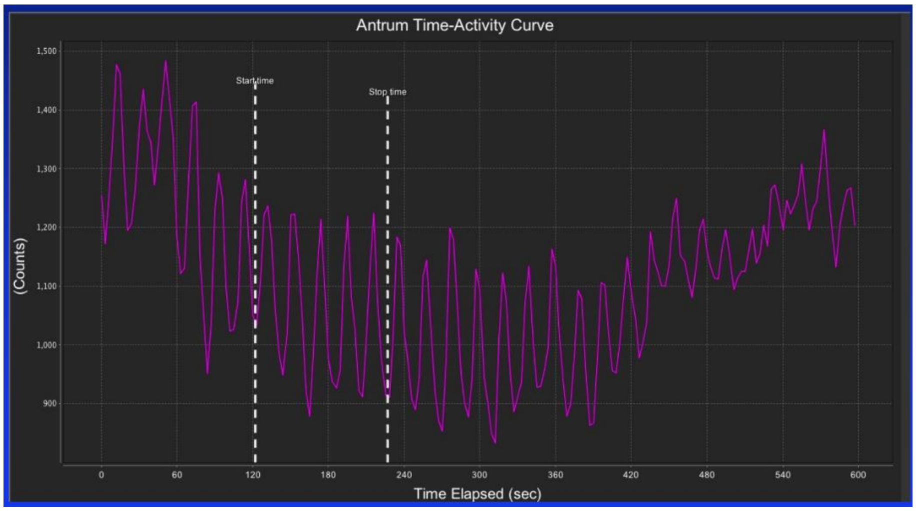


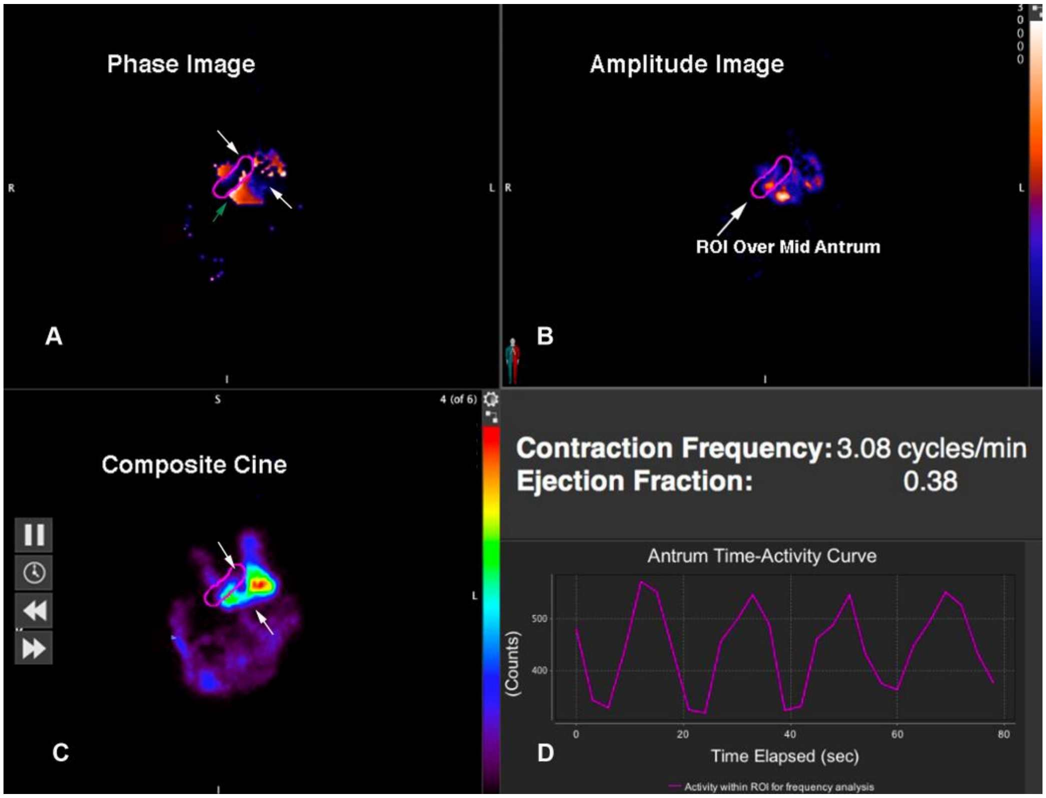
Figure 2. Normal Subject Fourier phase(A), amplitude(B), composite cine image(C), and Frequency & EF (D) results.

Figure 2A. Phase Image. Color coded pixels of the Fourier phase analysis. A 2 cm wide region of interest(ROI) is shown drawn over the mid antrum. This is the same ROI obtained from those pixels in the mid antrum with highest amplitude as shown in Figure 2B. The antral peristaltic wave originates at the incisura(paired arrows). Resulting phase image shows those pixels which have similar color-coded, phase angles clustered in the proximal and distal antrum to the left and right of the mid antral ROI. A leading edge of in-phase pixels appears as a band of pixels (shown here with white color scale or 0 degrees phase angle(small green arrow)) in the proximal antrum. To the left of the mid antral ROI a group of pixels appears (approximately 180 degrees from the leading edge(red/orange color scale) corresponding to the retrograde contractions arising in the distal antrum.

Figure 2B. Amplitude Image. Color coded pixels of the Fourier amplitude. This demonstrates a cluster of the high amplitude pixels in the mid antral ROI(arrow) and in the adjacent proximal antrum.

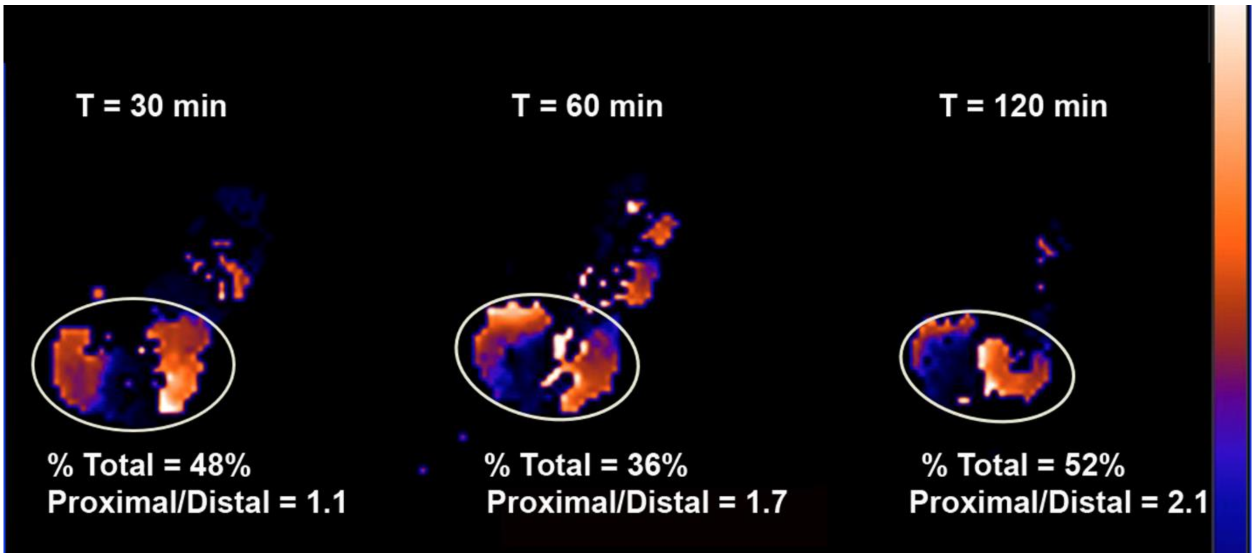
Figure 2C. Cine Display. Single frame only is shown from the cinematic display. Here the colored pixels represent the total counts of the radiolabled solid food activity in the stomach. When viewed as a movie display, the antral peristaltic wave can be seen to originate at the incisura(double arrows) and propagates distally through the antrum across the mid antral ROI followed by retrograde bolus movement back into the proximal antrum.

Figure 2D. Time Activity Curve. This panel shows the time activity curve from the mid antral ROI derived gastric counts which is used to calculate the antral frequency and EF.



Phase Image
A
Amplitude Image
ROI Over Mid Antrum
B
Composite Cine
C
Contraction Frequency: 3.08 cycles/min
Ejection Fraction: 0.38
Antrum Time-Activity Curve
(Counts)
Time Elapsed (sec)
D
Activity within ROI for frequency analysis

Figure 3. Patient With Normal Gastric Emptying and Normal Phase Analysis. Shown are the Fourier phase results at 30, 60, and 120 minutes for a patient with normal conventional gastric emptying results. The ellipse region of interest(white) shows the total antral area used for analysis. The similarly colored clusters of pixels in the proximal and distal antrum are those which have similar phase angles by Fourier analysis. Typically the ratio of proximal to distal in-phase pixels increases from 30 to 120 minutes.



<u>Figure 4.</u> Linear regressions of the %Total compared to the T ½ of Gastric Emptying. A. 30 min(%Total 30min = 0.4630 + -0.0008*T1/2, (R=0.3746, p-value=0.0001)) B. 60 min(%Total 60min = 0.4415 + -0.0005*T1/2, (R=0.2559, p-value=0.0065) C. (%Total 120min = 0.4024 + -0.0003*T1/2, (R=0.1456, p-value=0.1680).

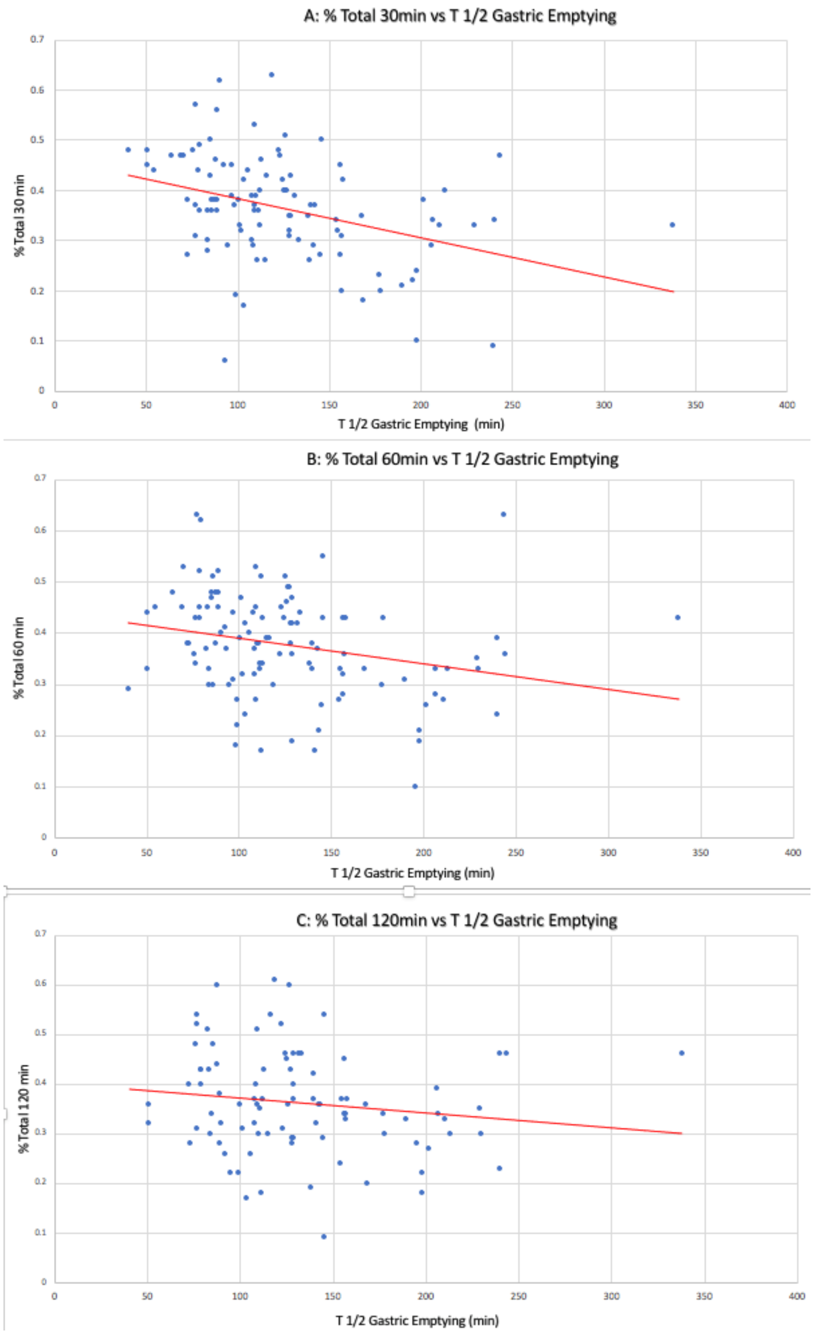


Figure 5. Patient With Abnormal Gastric Emptying and Abnormal Phase Analysis . Shown are the Fourier phase angle images for a patient with delayed gastric emptying(T1/2 emptying = 188 min). The ellipse ROI as in Figure 4 again shows the total antral area used for analysis. There is a lack of synchronous in-phase proximal and distal antral pixels at 30 and 120 min compared to the normal pattern (Figure 4). At 60 minutes there is a cluster of proximal antral phasic activity but no coordinated distal phasic contractions.

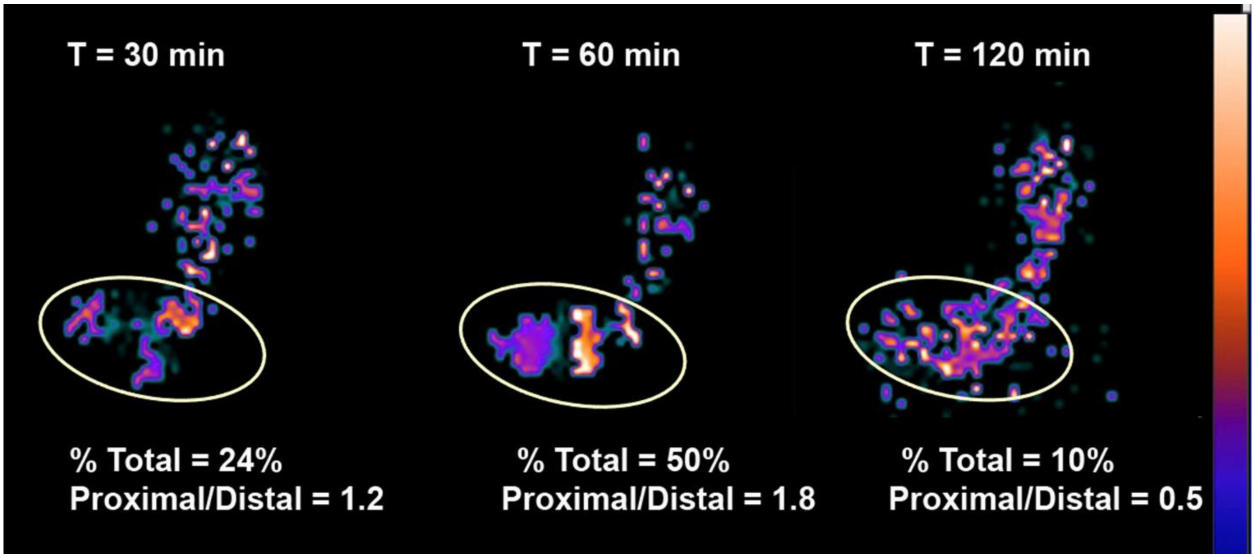


Table 1: Descriptive summary and 90% percentile intervals based on the healthy volunteers for conventional imaging parameters

Variable	*n*	*Median (Range)*	*p-value†*	*(5%, 95%)*
% Total @30min	19	45% (31%, 63%)		(31%, 63%)
% Total @60min	22	40% (17%, 63%)	0.11	(19%, 62%)
% Total @120min	13	51% (32%,61%)		(32%, 61%)
Prox/Distal @30min	19	1.67 (0.36, 6.62)		(0.36, 6.62)
Prox/Distal @60min	22	1.89 (0.71, 4.71)	0.035	(0.88, 3.15)
Prox/Distal @120min	13	2.65 (1.25, 6.38)		(1.25, 6.38)
EF @30min	21	23% (8%, 44%)		(14%, 36%)
EF @60min	22	27% (19%, 42%)	0.022	(19%, 40%)
EF @120min	14	32% (11%, 41%)		(11%, 41%)
Freq (cycle/min) @30min	21	3.08 (2.58, 3.45)		(2.67, 3.33)
Freq (cycle/min) @60min	22	2.86 (2.40, 3.57)	0.11	(2.76, 3.48)
Freq (cycle/min) @120min	14	2.91 (2.42, 3.20)		(2.42, 3.20)

†p-value for testing the time effect of each variable.

Table 2. Associations of DACS Abnormalities as Defined by Not in 90% Percentile Intervals of The Normal Controls with Conventional Gastric Emptying (CGE) Diagnosis in Patients and Healthy Volunteers (table entry=N (%) for the first three columns).

DACS Grouping by: Abnormal (1st row) vs Normal (2nd row)	**Overall (n=121)**	**Abnormal CGE Patients (n=53)**	**Normal CGE Patients + Healthy Volunteers (n=68)**	**p-value†**	**Raw Odds Ratio rOR (95% CI)‡**
By % Total 30min				**0.001**	
<31% or >63%	30 (27.5%)	21 (43.8%)	9 (14.8%)		4.49 (1.81, 11.15)
[31%, 63%]	79 (72.5%)	27 (56.3%)	52 (85.2%)		Reference
By % Total 60min				0.17	
<19% or >62%	9 (7.6%)	6 (11.8%)	3 (4.5%)		2.84 (0.68, 11.97)
[19%, 62%]	109 (92.4%)	45 (88.2%)	64 (95.5%)		Reference
By % Total 120min				0.21	
<32% or >61%	34 (35.1%)	21 (41.2%)	13 (28.3%)		1.78 (0.76, 4.16)
[32%, 61%]	63 (64.9%)	30 (58.8%)	33 (71.7%)		Reference
By Prox/Distal 30min				1.00	
<0.36 or >6.62	7 (6.4%)	3 (6.3%)	4 (6.6%)		0.95 (0.20, 4.46)
[0.36, 6.62]	102 (93.6%)	45 (93.8%)	57 (93.4%)		Reference
By Prox/Distal 60min				**0.017**	
<0.88 or >3.15	39 (33.3%)	23 (46.0%)	16 (23.9%)		2.72 (1.23, 5.99)
[0.88, 3.15]	78 (66.7%)	27 (54.0%)	51 (76.1%)		Reference
By Prox/Distal 120min				0.83	
<1.25 or >6.38	37 (38.9%)	20 (40.8%)	17 (37.0%)		1.18 (0.51, 2.69)
[1.25, 6.38]	58 (61.1%)	29 (59.2%)	29 (63.0%)		Reference
By EF 30min				0.48	
<14% or >36%	25 (24.8%)	12 (29.3%)	13 (21.7%)		1.50 (0.60, 3.72)
[14%, 36%]	76 (75.2%)	29 (70.7%)	47 (78.3%)		Reference
By EF 60min				**0.011**	
<19% or >40%	24 (22.6%)	16 (34.8%)	8 (13.3%)		3.47 (1.33, 9.06)
[19%, 40%]	82 (77.4%)	30 (65.2%)	52 (86.7%)		Reference
By EF 120min				0.26	
<11% or >41%	15 (18.3%)	10 (23.3%)	5 (12.8%)		2.06 (0.64, 6.68)
[11%, 41%]	67 (81.7%)	33 (76.7%)	34 (87.2%)		Reference
By Freq 30min				0.047	
<2.67 or >3.33	11 (10.9%)	8 (19.5%)	3 (5.0%)		4.61 (1.14, 18.57)
[2.67, 3.33]	90 (89.1%)	33 (80.5%)	57 (95.0%)		Reference
By Freq 60min				0.32	
<2.76 or >3.48	10 (9.4%)	6 (13.0%)	4 (6.7%)		2.10 (0.56, 7.93)
[2.76, 3.48]	96 (90.6%)	40 (87.0%)	56 (93.3%)		Reference
By Freq 120min				1.00	
<2.42 or >3.20	11 (13.4%)	6 (14.0%)	5 (12.8%)		1.10 (0.31, 3.95)
[2.42, 3.20]	71 (86.6%)	37 (86.0%)	34 (87.2%)		Reference

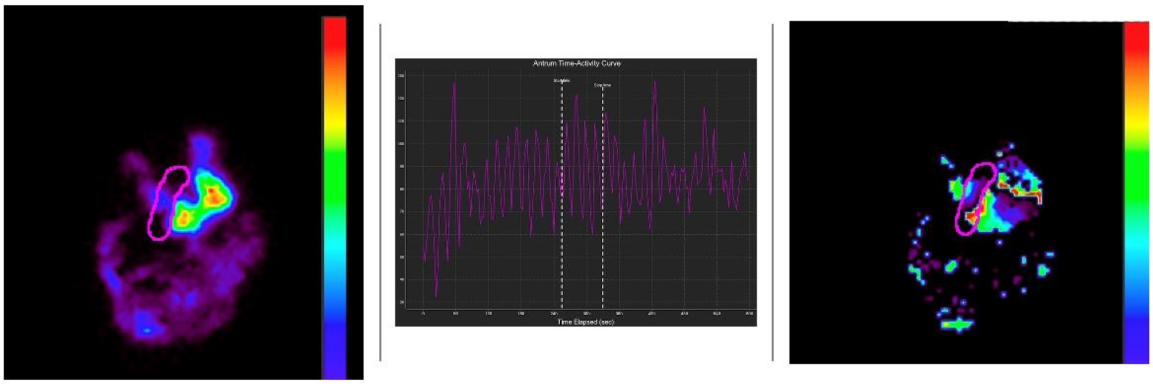
†p-value for testing the association of a DACS abnormality with the standard clinical diagnosis based on Conventional Gastric Emptying (CGE) Imaging using the Fisher's Exact test.
‡Raw Odds Ratio of being diagnosed as Abnormal by Conventional GE comparing the DACS Abnormal to the Normal.

Table 3. Multivariable Logistic Regression Identifying the Best Subset of DACS Abnormality Parameters Associated with Standard Clinical Diagnosis Using Data from All Subjects (N=121)†

DACS Abnormality Variables	**Adjusted Odds Ratio aOR (95% CI)**	**p-value**
By % Total 30min-- <31% or >63% vs [31%, 63%]	3.30 (1.21, 9.00)	0.02
By EF 60min-- <19% or >40% vs [19%, 40%]	2.97 (1.08, 8.21)	0.036

†24 subjects had missing data on at least one of the variables and hence dropped out of the model.

Graphical Abstract



ROI Mid Antrum | Selected Contractions | Final Phase Analysis