Standardization and Quantification of Radionuclide Solid Gastric-Emptying Studies

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The purposes of this investigation were to standardize and validate a simple quantitative method for performing radionuclide solid gastric emptying that can be used for any dual-head γ-camera and to establish reference values. Methods: After eating a solid meal (egg sandwich) labeled with a radionuclide, 20 healthy volunteers (9 male, 11 female) underwent a 90-min gastric-emptying study performed with a triple-head y-camera. Two sets of 3 simultaneous projections were acquired sequentially for 30 s each: anterior, right posterior oblique (RPO), left posterior oblique (LPO), posterior, left anterior oblique (LAO), and right anterior oblique (RAO), and this sequence was repeated continuously for 90 min. Time-activity curves were generated using a gastric region of interest for each of the views as well as the conjugate-view geometric mean (GM) data for the anterior/posterior, LAO/RPO, and RAO/LPO combinations. Quantitative parameters were determined: percentage gastric emptying (%GE) at 90 min, half-time (min) based on an exponential fit, and clearance rate (%/min) based on a linear fit. Reference values were determined on the basis of a 95% confidence interval of the t distribution. The results were statistically analyzed and compared. Results: The %GE reference values were greater for the anterior/posterior GM (\geq 33%) than for the LAO (≥31%) and anterior (≥30%) GMs. The 3 %GE GM methods, the 3 exponential-fit GM methods, and the 3 linear-fit GM methods had high correlation coefficients ($r \ge 0.874$), and with only a single exception, there was no statistical difference among them. The LAO method and LAO/RPO GM mean method correlated strongly (r = 0.900) and had similar mean values (52% vs. 51%) and reference values (29% vs. 30%). All 3 methods of GM quantification also correlated strongly, and there was no significant difference among them. Conclusion: We have described and validated a simple method for radionuclide solid gastric emptying that can be used with a dual-head y-camera. We recommend the anterior/posterior GM method and have established reference values (\geq 33%).

Key Words: gastric emptying; ^{99m}Tc-sulfur colloid; stomach; gastroparesis

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Kadionuclide solid gastric-emptying studies have been performed clinically since 1976 (1). Many investigations published since then have confirmed the clinical utility of such studies for diagnosis of a variety of gastric motility disorders (2). Nevertheless, there is a remarkable lack of standardization of this study and no generally applicable reference values. Among the many reasons for this lack, one important factor is that instrumentation has changed over the years. Although some laboratories still use a single-head γ -camera for this study, many now have dual-head systems.

With single-head cameras, attenuation correction using the geometric mean (GM) method is not easily or accurately performed, since image acquisition by necessity consists of a set of static images that alternate between opposing views. Alternative methods for attenuation correction that allow for continuous image acquisition using a single-head camera have been published (3-5). We first proposed the left anterior oblique (LAO) method (5), and it has subsequently been validated by other investigators (6-9). However, a dualhead system allows for the simultaneous acquisition of conjugate views and thereby the straightforward application of the gold standard GM mean method of attenuation correction.

No generally applicable reference values for solid gastric emptying exist, because the quantitative results depend strongly on the size and content of the meal and on the acquisition and quantification method used. Furthermore, many different methods and parameters have been used for this quantification. Reference values are methodology specific. The purpose of this paper is to describe a simple, validated method for radionuclide solid gastric emptying using a dual-head camera, now available in most nuclear medicine clinics. Various methods of acquisition, attenuation correction, and quantification were directly compared and reference values established, leading to the development of the simple approach that is described.

MATERIALS AND METHODS

Twenty healthy subjects (9 male, 11 female) volunteered to undergo a radionuclide solid gastric-emptying study. The healthy volunteers had no known serious health problems and had been questioned particularly about gastrointestinal or hepatobiliary

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problems. Their ages ranged from 21 to 35 y (mean \pm SD, 28.7 \pm 6.3 y). Patient weight ranged from 52 to 100 kg (mean, 74 \pm 14 kg). These subjects also participated in prior investigations quantifying the lag phase (6) and comparing the LAO view with the GM (*10*). The gastric-emptying study was acquired using a triplehead γ -camera (TRIAD; Trionix).

The subjects took nothing by mouth after midnight the night before the study, which was the first study performed the next morning. Each subject ingested a ^{99m}Tc (37 MBq)-sulfur colloid–labeled egg-white sandwich (3 fried egg whites, 2 pieces of toast, butter, salt, and pepper [260 kcal, 40 g of carbohydrate, 5 g of fat, and 93 g of protein]) along with 200 mL of water over a period of 5–10 min while seated. Imaging commenced immediately after the subjects had ingested the meal and had lain supine on the table of the triple-head γ -camera.

With the triple-head system, 2 sets of 3 simultaneous projections could be acquired. Each was acquired for 30 s: first, the anterior, right posterior oblique (RPO), and left posterior oblique (LPO) projections; then, after a suitable rotation of the gantry, the posterior, LAO, and right anterior oblique (RAO) projections. This sequence was repeated continuously for 90 min. The data were decay corrected to the start of acquisition. Images were reviewed in cinematic display to assist in placement of the manually drawn regions of interest about the stomach. Time–activity curves were derived for the anterior, posterior, LAO, RAO, LPO, RPO, and for the anterior/posterior, LAO/RPO, and RAO/LPO conjugate views (GM).

Various quantitative parameters were determined using the derived time–activity curves. These included the percentage gastric emptying (%GE) at 90 min (maximum counts – minimum/maximum counts) \times 100, the half-time (t_{1/2}, in minutes) derived from an exponential fit, and the %/min emptying rate from the slope of a linear fit. An anterior/posterior GM inflection point lag phase, defined as the time that the second phase of emptying began, was determined by visual inspection of the gastric time–activity curve. The results were statistically analyzed and compared to determine the similarities and differences of the quantitative methodologies and the advantages of each.

RESULTS

Table 1 shows the results for all 20 subjects. One subject appeared to be an outlier (patient 20), and statistical analysis was calculated with and without this subject. The results were basically the same whether or not this subject was included, although a slightly greater mean %GE and smaller SDs were calculated when this subject was excluded. The statistical results discussed below are for the remaining 19 subjects except when stated otherwise.

A trend was noted when comparing the %GE of the anterior/posterior GM with the anterior and LAO views. The range of reference values was determined on the basis of the 95% confidence interval of the *t* distribution for 19 subjects (18° of freedom). The reference values (± 2 SDs from the mean) were highest for the anterior/posterior GM (\geq 33%), followed by the LAO GM (\geq 31%) and then the anterior GM (\geq 30%). Correlation coefficients between the methods were high: GM/anterior, *r* = 0.874; GM/LAO, *r* = 0.918; anterior/LAO, *r* = 0.924. There was no statistical difference among them.

The 3 maximum/minimum (%GE) GM results had a high statistical correlation: anterior/posterior versus LAO/RPO, r = 0.905; anterior/posterior versus RAO/LPO, r = 0.909; LAO/RPO versus RAO/LPO, r = 0.897. There was no statistical difference among them.

The 3 exponential-fit GM results were compared: anterior/ posterior versus LAO/RPO, r = 0.905; anterior/posterior versus RAO/LPO, r = 0.909; LAO/RPO versus RAO/LPO, r = 0.897. There was no significant difference among them.

The 3 linear-fit GM methods were compared: anterior/ posterior versus LAO/RPO, r = 0.918; anterior/posterior versus RAO/LPO, r = 0.863; LAO/RPO versus RAO/LPO, r = 0.919. There was no statistically significant difference among them. Two subjects were excluded from the results because the time-activity curves were noisy and difficult to fit.

The LAO method and the LAO/RPO GM mean methods were compared: The respective mean %GE values (52% and 51%), SD values (10.7% and 10.3%), and lower limit of reference values (31% and 31%) were nearly identical. The correlation coefficient was high (r = 0.900), and there was no statistically significant difference between the 2 methods.

The 3 methods of GM quantification (maximum/minimum, linear, and exponential) were compared: exponential versus linear (anterior/posterior), r = 0.944; maximum/ minimum versus linear (LAO/RPO), r = 0.809; maximum/ minimum versus exponential (RAO/LPO), r = 0.925. There was no significant difference among them.

Correlation was poor between the lag phase, as defined by the inflection point (10), and the overall %GE (r = 0.26), the anterior/posterior linear rate of emptying (r = 0.23), and the anterior/posterior exponential rate of emptying (r = 0.12).

DISCUSSION

Many different methodologies for performing solid gastric-emptying studies have been described over the years (2). Reference values have been established with some of these methods; however, the reference range is method specific, depending on the type of meal, the acquisition and processing methodology, the imaging equipment, and the quantitative technique (11-15). Thus, in a clinical setting, a laboratory needs either to establish its own reference values based on the methodology it uses or, alternatively, to closely follow a method described in the literature and use its established reference values.

Much of the earlier literature is not helpful for establishing a standardized procedure in the modern nuclear medicine clinic. Many past studies included such difficulties as the use of single-head cameras, noncontinuous and infrequent image acquisition, alternation of anterior and posterior acquisitions, and complicated quantification. One would like a methodology that allows for easy set-up and acquisition, patient comfort, attenuation compensation, a rapid framing rate, and straightforward and easy-to-understand quantification. The purpose of this study was to compare and analyze various methods of acquisition and quan-

Patient no.		Age (y)	Weight (kg)	_ິ ⊳	т Е	ANT (%)	(%)	LAO/RPO GM (%)	AP GM (%)	RAO/LPO GM (%)	LAO/RPO exp (min)	AP exp (min)	RAO/LPO exp (min)	LAO/RPO lin (%/min)	AP lin (%/min)	RAO/LPO lin (%/min)	Lag (min)
-		36	79	-		56	60	59	60	63	72	73	100	0.6569	0.6654		24
0		21	20	-		49	47	56	53	52	62	54	51	0.6835	0.7202		30
ო		23	83	-		28	39	39	40	36	121	132	148	0.4369	0.4081	0.3734	21
4		25	73	-		40	34	42	39	34	76	149	113	0.5810	0.3790	0.5852	42
Ŋ		27	61		-	54	52	46	48	48	108	85	06	0.4662	0.5304	0.5473	25
9		27	82		-	36	33	31	44	34	111	110	134	0.4560	0.4729	0.4021	48
7		27	68		-	58	53	46	49	50	84	77	69	0.5978	0.6248	0.6477	24
8		33	66		-	66	70	67	67	65	50	53	54	0.8032	0.8457	0.7894	27
6		24	72	-		58	59	58	64	58	74	67	74	0.6184	0.6283	0.6366	21
10		28	89	-		49	55	53	50	51	53	55	46	0.7608	0.7277	0.7972	36
11		25	20		-	65	70	64	67	66	52	55	53	0.5788	0.7634	0.7908	26
12		33	63		-	47	48	50	51	47	88	87	78	0.5531	0.5982	0.5839	34
13		34	100	-		50	52	46	51	46	101	96	118	0.5091	0.5428	0.4465	27
14		42	100		-	38	41	38	38	42	96	94	85	0.5120	0.5139	0.5538	34
15		35	99		-	64	64	62	60	57	67	71	73	0.6703	0.6504	0.6404	26
16		22	68	-		59	61	69	61	58	64	62	58	0.7290	0.7112	0.7453	11
17		18	86		-	49	47	46	45	52	62	59	45	0.7071	0.6815	0.9423	21
18		37	86	-		48	50	51	53	48	87	75	55	0.5637	0.6191	0.6975	29
19		24	52		-	50	53	54	52	48	72	78	79	0.6670	0.6481	0.6051	1
20		32	54		÷	25	25	19	27	21	269	230	280	0.2271	0.2638	0.2165	21
20*	Mean	29	74	6	1	49.5	50.65	49.8	50.95	48.8	88.4	88.1	90.2	0.5889	0.5997	0.6112	27
	SD	9	14			11.5	12	12.4	10.4	11.4	47	42.2	53.6	0.1333	0.1410	0.1763	<u>ග</u>
19†	Mean	29	75	6	10	50.7	52	51.4	52.2	50.3	78.9	80.6	80.2	0.6079	0.6174	0.6343	27
	SD	9	13			10.2	10.65	10.3	0	9.6	21	26.5	30.3	0.1053	0.1200	0.1507	0
20*	Z	lormal le	ower limit	S		25	26	24	29	26	-10	-	-23	0.3090	0.3036	0.241	ø
19 [†]						29	29	30	33	30	35	25	17	0.3868	0.3654	0.7178	Ø
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*Data 1 +Doto f	or total ni	umber (of subject	15 (ZL	fans 0	ects).	dino 01/	104001									
	anterior;	AP = a	ur suujeci interior/po	oster.	rior; e)	te ouur xp = ex	er (19 sur. (ponential	ojects). I fit; lin = lin	ear fit.								

tification in healthy subjects and to establish a simple methodology and reference values that can be used with the dual-head γ -cameras available today in most nuclear medicine laboratories.

Published investigations have proven the importance of attenuation correction in obtaining accurate solid gastricemptying studies (12, 14, 16). It is necessary to correct for the variable attenuation of the radiolabeled meal as it moves in the stomach from the relatively posterior fundus to the more anterior antrum. Although this effect is likely to be more important in obese patients, it is not uncommon in normal-weight subjects and cannot be predicted beforehand. In the past, many investigations used intermittent imaging, with images acquired every 15–30 min. A relatively rapid framing rate of 60 s produces a statistically reliable time– activity curve and more accurate quantification (10, 13).

The antrum of the stomach is responsible for solid gastric emptying. Two phases of solid emptying have repeatedly been demonstrated (17, 18): an initial delay before emptying begins, the lag phase, and continuous emptying, typically linear. The lag phase is presumably due to the time required for the antrum to grind food into particles small enough to pass through the pylorus. Some have recommended quantification of the lag phase and the rate of emptying, although individual studies have found that the lag phase may be delayed in certain diseases (19,20) and may be shortened by drug therapy, improving emptying (21,22). Other investigators have found that delayed emptying is usually due to a delay in both phases and similarly improves after therapy (23-25). However, the data are contradictory, and other investigators have not confirmed these findings. A likely explanation for this discrepancy may be the very different methodologies used. This is an area needing further investigation using standardized methodology. In this study, we found no correlation between the length of the lag phase and the overall %GE. We do not recommend quantification of the lag phase for routine clinical purposes. The protocol we have described would also be useful for answering such questions in research investigations.

Many publications have used a $t_{1/2}$ of emptying or a fitted exponential curve to calculate a t_{1/2} rate of solid gastric emptying. This makes little physiologic sense, since gastric emptying is usually linear. Many technical problems are involved in using a $t_{1/2}$, such as determining whether time zero is at the start or end of the lag phase. If a rapid framing rate is not used, the length of the lag phase and, thus, time zero may be erroneously determined, resulting in inaccurate results. Although a linear emptying rate makes more sense, few have used this method (17). A modified power exponential has been put forth and used as a reproducible standardized method for establishing the lag phase and a rate of emptying (18). However, we have shown that the lag phase calculated by the modified power exponential does not correspond to other published methods of lag phase calculation (10).

The LAO method for attenuation compensation is not a mathematic correction. Because the stomach contents move roughly parallel to the head of the γ -camera in this projection, the variation in soft-tissue attenuation is minimized. This method was initially described by us in 1989 (5) and has been subsequently validated in other studies (6–9). The present study again validates this method, showing no significant difference between the LAO and LAO/RPO or anterior/posterior GM methods.

The present investigation attempted to establish a simple, straightforward methodology that can be used in any clinic that has a dual-head y-camera. Our investigation showed a high correlation in reference values among all the methods described. The anterior/posterior GM mean method has been the accepted gold standard for attenuation correction. Attenuation correction using the GM method has been validated on a phantom model (12). Others have shown that the GM method compensates for variable attenuation as the meal moves through the stomach by eliminating the artifactual rise in the time-activity curve, with expected improvement in emptying results (3,4,11). Our data show that the anterior/posterior GM method has a smaller SD and higher reference values than do the anterior and LAO methods, other GM conjugate views (LAO/RPO and RAO/LPO), or exponential or linear emptying methods. Although the other GM conjugate view methods would be expected to provide similar results, we found more variability and a considerably larger reference range using these methods than using the anterior/posterior GM method. The reason is uncertain but may be methodologic because of the variability in selection of the appropriate fitted curve due to the multiexponential shape of many posterior, RPO, and LPO timeactivity curves.

Two publications have suggested that quantification at 4 h may improve the sensitivity for detecting delayed emptying (26,27). Only 4 (26) and 6 (27) imaging time points were acquired in these 2 studies. One study found delayed emptying in symptomatic patients more frequent at 4 h compared with 2 h and thus concluded that the 4-h study was superior (26). A second multiinstitutional study established reference values using a large number of healthy subjects and proposed their 4-h study as a screening test (27). They did not attempt to demonstrate that the 4-h study was superior to shorter imaging studies, only that the 4-h study is a simple methodology, with reference values based on a large number of subjects. They noted that their method cannot be used to evaluate gastric physiology-for example, the lag phase or the rate of emptying-because of the limited number of imaging time points. Our proposed standardized protocol is also simple to perform, has established reference values, and can also be used to study gastric physiology and be completed in 90 min.

CONCLUSION

We have described and validated a standardized method for solid gastric emptying that can be used with a dual-head γ -camera. We recommend the use of the anterior/posterior GM method and the calculation of an overall %GE at 90 min, which combines the lag phase and the rate of emptying into a single value. Our protocol is described in the Appendix. Abnormal solid gastric emptying was determined to be less than 33%.

APPENDIX

Solid Gastric-Emptying Protocol Using a Dual-Head $\gamma\text{-Camera}$

Preparation: Have the patient take nothing by mouth after midnight. Perform the study early the next morning.

Meal: Have the patient ingest a ^{99m}Tc (37 MBq)-labeled egg sandwich with 200 mL water while upright.

Patient position: Position the patient supine on the γ -camera table.

Instrumentation: Use a dual-head γ -camera, with a lowenergy, general-purpose collimator.

Acquisition: Acquire 1-min frames for 90 min, in anterior and posterior projections.

Processing: Correct for decay, perform GM attenuation correction, draw a region of interest around the stomach, and generate a time–activity curve.

Quantification: Calculate the %GE at 90 min. Solid gastric emptying of less than 34% at 90 min is considered abnormal.

Meal and Preparation

Meal: Fried egg-white toast sandwich.

Materials: Three fresh eggs, butter, salt, pepper, frying pan, and white bread.

Cooking directions:

- 1. Place $\frac{1}{2}$ tsp of butter in the frying pan, and heat the pan on a burner until the butter melts.
- 2. Separate the yolk from the eggs, and add the egg whites to the melted butter.
- Continue heating until the egg whites begin to solidify. Then add 37 MBq of ^{99m}Tc-sulfur colloid and stir while continuing to heat until the egg whites appear nearly solidified.
- 4. Remove the pan from the heat and continue to stir, allowing the residual heat to complete the solidification.
- 5. Transfer to a plastic dish, cover, and mark with a radioactivity insignia.
- 6. Add salt and pepper. Place on 2 pieces of toasted white bread.

Patient instructions: Ingest the sandwich and drink the water as quickly as possible, within 5–10 min.

Technologist instructions: Begin the acquisition promptly after the patient ingests the meal.

REFERENCES

 Meyer JH, MacGregor IL, Gueller R, Martin P, Cavalieri R. Tc-99m-tagged chicken liver as a marker of solid food in the human stomach. *Am J Dig Dis.* 6;21:296–304.

- Ziessman HA. The gastrointestinal tract. In: Harbert JC, Eckelman WC, Neumann RD, eds. *Nuclear Medicine: Diagnosis and Therapy*. New York, NY: Thieme Publishers; 1996:585–670.
- Collins PJ, Horowitz MB, Shearman DJ, Chatterton BE. Correction for tissue attenuation in radionuclide gastric emptying studies: a comparison of a lateral image method and a geometric mean method. Br J Rad. 984;57:689–695.
- Meyer JH, VanDeventer G, Graham LS, Thomson J, Thomasson D. Error and corrections with scintigraphic measurement of gastric emptying of solid foods. *J Nucl Med.* 1983;24:197–203.
- Fahey FH, Ziessman HA, Collen MJ, Eggli DF. Left anterior oblique projection and peak-to-scatter ratio for attenuation compensation of gastric emptying studies. J Nucl Med. 1989;30:233–239.
- Ziessman HA, Harkness BA, Fahey FH. Comparison of the LAO and geometric mean methods for attenuation correction of gastric emptying studies [abstract]. *J Nucl Med.* 1992;33(suppl):833P.
- Yung BC, Sostre S, Yeo CJ, Pitt HA, Cameron JL. Comparison of left anterior oblique, anterior and geometric mean method for gastric emptying assessment of postpancreaticoduodenectomy patients. *Clin Nucl Med.* 1993;18:776–781.
- Ford PV, Kennedy RL, Vogel JM. Comparison of left anterior oblique, anterior and geometric mean methods for determining gastric emptying times. J Nucl Med. 1992;33:127–130.
- Maurer AH, Knight LC, Charkes ND, et al. Comparison of left anterior oblique and geometric mean gastric emptying. J Nucl Med. 991;32:2176–2180.
- Ziessman HA, Atkins FB, Vemulakonda US, Tall J, Harkness B, Fahey FH. Lag phase quantification for solid gastric emptying studies. *J Nucl Med.* 996;37: 1639–1643.
- Moore JG, Christian PE, Coleman RE. Gastric emptying of varying meal weight and composition in man: evaluation by dual liquid and solid phase isotopic method. *Dig Dis and Sci.* 1981;25:16–22.
- Christian PE, Moore JG, Sorenson JA, Coleman RE, Weich DM. Effects of meal size and correction technique on gastric emptying time: studies with two tracers and opposed detectors. J Nucl Med. 1980;21:883–885.
- Christian PE, Datz FL, Moore JG. Confirmation of short solid-food lag phase by continuous monitoring of gastric emptying. J Nucl Med. 1991;32:1349–1352.
- Tothill P, McLoughlin GP, Heading RC. Techniques and errors in scintigraphic measurements of gastric emptying. J Nucl Med. 1978;19:256–261.
- Ziessman HA. Keep it simple—it's only gastric emptying. In: Freeman LM, ed. Nuclear Medicine Annual 2000. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:233–260.
- Moore JG, Christian PE, Taylor AT, Alazraki N. Gastric emptying measurements: delayed and complex emptying patterns without appropriate correction. *J Nucl Med.* 1985;26:1206–1210.
- Camerilli M, Malagelada J-R, Brown ML, Becker G, Zinsmeister AR. Relation between antral motility and gastric emptying of solids and liquids in humans. *Am J Physiology*. 1985;249:G580–G585.
- Siegel JA, Urbain JL, Adler LP, et al. Biphasic nature of gastric emptying. *Gut.* 1998;29:85–89.
- Loo FD, Palmer DW, Soergel KH, Kalbfleisch JH, Wood CM. Gastric emptying in patients with diabetes mellitus. *Gastroenterology*. 1984;86:485–494.
- Horowitz M, Collins PJ, Cook DJ, Harding PE, Shearman DJ. Abnormalities of gastric emptying in obese patients. *Int J Obesity*. 1983;7:415–421.
- Horowitz M, Harding PE, Chatterton BE, Collins PJ, Shearman DJ. Acute and chronic effects of domperidone on gastric emptying in diabetic autonomic neuropathy. *Dig Dis Sci.* 1985;30:1–9.
- Urbain JL, Vantrappen G, Janssens J, Van Cutsem E, Peeters T, DeRoo M. Intravenous erythromycin dramatically accelerates gastric emptying in gastroparesis diabeticorum and normals and abolishes the emptying discrimination between solids and liquids. J Nucl Med. 1990;31:1490–1493.
- Wright RA, Krinsky S, Fleeman C, Fleeman C, Trujillo J, Teague E. Gastric emptying and obesity. J Gastroenterol. 1983;84:747–750.
- Ziessman HA, Fahey FH, Collen MJ. Biphasic solid and liquid gastric emptying in normal controls and diabetics using continuous acquisition in LAO view. *Dig Dis Sci.* 1992;37:744–750.
- Buysschaert M, Moulart M, Urbain JL, et al. Impaired gastric emptying in diabetic patients with cardiac autonomic neuropathy. *Diabetes Care*. 1987;10: 448–452.
- Guo J-P, Maurer AH, Fisher RS, Parkman HP. Extending gastric emptying scintigraphy from two to four hours detects more patients with gastroparesis. *Dig Dis Sci.* 2001;46:24–29.
- 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.