# DIAGNOSTIC NUCLEAR MEDICINE

# Computer Analysis of Radionuclide Esophageal Transit Studies

Herbert A. Klein and Arnold Wald

*University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania*

**For detailed examination of the esophageal transit of a swallowed radioactive liquid bolus, three computer-based techniques have been developed: (a) analysis of time-activity curves with decomposition into rapid and residual components, yielding the mean transit time for the former and the residual fraction for the latter; (b) reduction of dynamic image sequences to single condensed images, facilitating subjective assessment; and (c) tracking of the centroid of radioactivity, permitting quantification of retrograde motion. Studies were performed on 12 normal subjects and on six patients with motility disorders. Elevated residual fractions were observed in all the patients, and an abnormal degree of retrograde motion in two. Two normal and two abnormal studies exemplify the variety of patterns observed in condensed images.**

To characterize esophageal motility in health and disease, the fate of a swallow of Tc-99m sulfur colloid in water has been examined through computer analysis of scintigraphic data. Tolin et al. (*1*) quantified the clearance of the material from the esophagus during the initial swallow and multiple subsequent dry swallows. Russell et al. (*2*) characterized the events of the first 50 sec after an initial swallow by means of time-activity curves and determinations of transit time for the whole esophagus and its individual thirds; this work has been expanded by Blackwell et al. (*3*) and Benjamin et al. (*4*). In each of the above investigations, features distinguishing motility disorders were described.

In order to improve the diagnostic value of esophageal scintigraphy, we have incorporated procedures from these previous studies and added new computer-based techniques that provide a more elaborate analysis of the dynamic events (*5*). Three techniques—time-activity curve analysis, condensed images by the method of Svedberg (*6*), and centroid analysis—were developed during a pilot study of normal volunteers and patients.

## SUBJECTS AND TEST PROCEDURE

**Subjects.** Two groups were evaluated with one study per subject: (a) 12 normal volunteers (three men and nine women, mean age 33 yr, range 21 to 50) with no symptoms of esophageal disease; and (b) six patients with evidence of esophageal motility disorders (Table 1). Informed consent was obtained according to the appropriate protocols for our institutions. All subjects fasted overnight and refrained from smoking for 2 hr before the test.

**Test procedure.** With the subject supine, anterior imaging from chin level downward is performed with a scintillation camera having a 38-cm field of view. A Co-57 source marks the cricoid cartilage in a single static view. After a practice swallow of 5 ml of water, the subject, with his head turned to one side, receives a dose of 0.3 mCi (11.1 MBq) of Tc-99m sulfur colloid in 15 ml of water, delivered into the mouth from a syringe with a blunt plastic tip. At a verbal command, the subject turns his head forward and swallows, and the technologist starts the camera and computer. A second swallow is executed after 30 sec, and additional dry swallows at 15-sec intervals thereafter for a total of 40 swallows.

The dynamic computer collection is in frame mode (64 × 64) at 0.2 sec/frame for 30 sec; then at 1 sec/frame

## TABLE 1. CHARACTERISTICS OF PATIENT GROUP

| Patient (age/sex) | Barium esophagram | Esophageal manometry |
|---|---|---|
| **Esophageal reflux** | | |
| 1. 66/M | Reflux, distal spasm, transient stasis | Not done |
| **Achalasia** | | |
| 2. 52/M | Dilated esophagus with tertiary contractions, narrowing at gastroesophageal junction | Simultaneous contractions, incomplete relaxation of lower esophageal sphincter |
| 3. 64/M | Dilated esophagus with tertiary contractions, narrowing at gastroesophageal junction | Simultaneous contractions, incomplete relaxation of lower esophageal sphincter |
| 4. 45/M | Dilated esophagus with tertiary contractions, narrowing at gastroesophageal junction | Simultaneous contractions, incomplete relaxation of lower esophageal sphincter |
| **Unclassified motility disorders** | | |
| 5. 50/F | Normal | Simultaneous contractions, normal lower esophageal sphincter |
| 6. 53/F | Tertiary contractions | Simultaneous contractions, normal lower esophageal sphincter pressure with incomplete relaxation |

during the 15-sec periods of the second, third, and fourth swallows and a predetermined sampling of later swallows; otherwise at 15 sec/frame. Thus, detailed resolution of temporal events following each swallow is obtained in the early part of the study, but only for some of the late swallows.

### COMPUTER METHODS

The methods are explained with reference to the study of a normal volunteer (Figs. 1-3).

**Time-activity curve analysis.** Curves are generated using an esophageal region of interest from cricoid to gastroesophageal junction. Our cases fit the following model of behavior for the initial swallow. A rapid component passes through the esophagus, leaving a residual component of nearly constant counting rate. This model is the basis for decomposition of the raw curve into separate curves describing the behavior of the two components, measurement of the residual component, and determination of the mean transit time (MTT) of the rapid component.

The pattern of the raw curve (Fig. 1, A) begins with a rise in activity, generally reaching a short-lived peak at point Q. This signals passage of the bolus through a proximal region of decreased attenuation, which can be demonstrated with time-activity curves (not shown) obtained when the top level of the esophageal region of interest is lowered. This causes the early peak to diminish and disappear.

Whether preceded by an early peak or not, a roughly constant plateau of activity (points R through T) occurs while the bolus is still entirely within the esophagus. With passage into the stomach, the esophageal activity falls to a lower plateau level (points U through V) representing the remaining material. The boundary points of

the early and late plateaus are user-selected. Let J be the counting rate at point Q, while K and L are the mean counting rates for the RT and UV plateaus. The count-
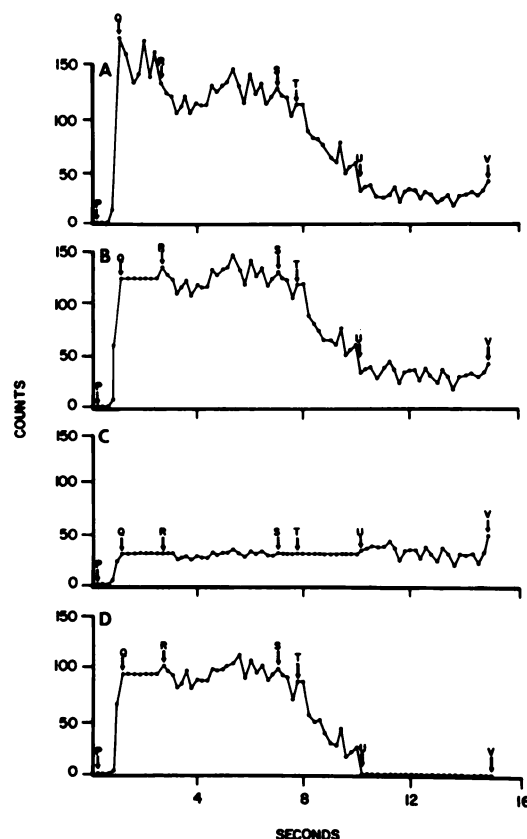


**FIG. 1.** Processing of first-swallow time-activity curve for whole-esophagus. A. Unprocessed curve. B. Early peak truncated to correct for low attenuation in proximal esophagus. C. Isolated theoretical behavior of residual component. D. Rapid component. These curves reveal definite residual component remaining after prompt transit of rapid component. MTT = 7.9 sec; RF(1) = 24% [reduced to RF(2) = 3% after second swallow].

**FIG. 2.** Condensed images of first two swallows. In first swallow (A) we see downward course of tracer, with residual component separating in mid esophagus and moving into more proximal location, while rapid component continues to progress, with broadening and lingering in lower esophagus before entering stomach. Second swallow (B) propels residual component into stomach. No significant esophageal activity can be seen in subsequent swallows (not shown). These images confirm larger than usual residual component remaining after first swallow, but virtually eliminated after second.
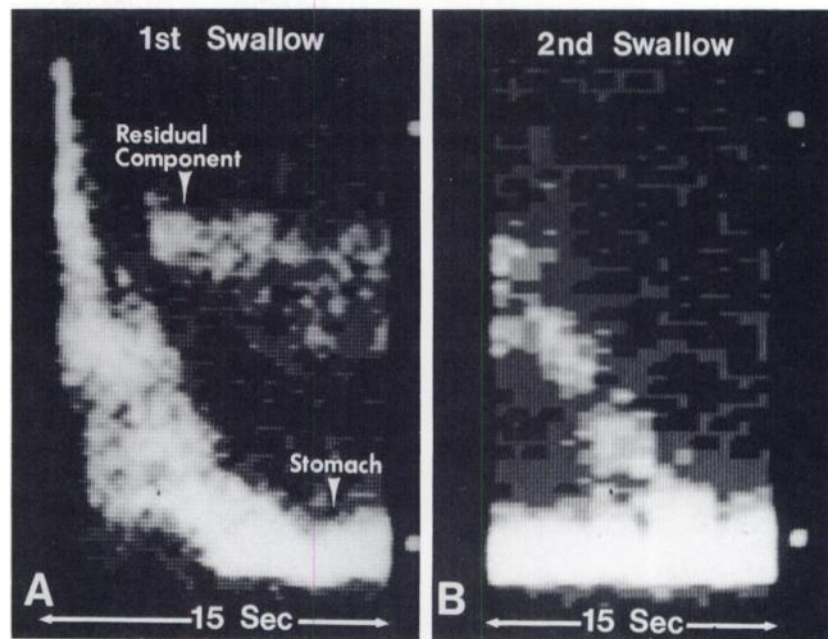
ing rate K is then taken to represent the entire administered bolus, and L the residual component. Thus, the residual fraction of the first swallow [RF(1)] is given by L/K.

On the assumption that, but for decreased attenuation, the maximum counting rate of the early peak would have the value K, Curve B (Fig. 1) is generated by multiplying the points from the first one (P) through Q by K/J, by reducing to counting rate K all points between Q and R that exceed it, and by leaving all the other points unchanged. This constitutes a simplistic method of correction for variable attenuation of the radioactivity in different portions of the esophagus, a problem that has also been addressed by Helm et al. (7).

The theoretical behavior of the particles of the residual component is next considered and represented in Curve C. During entry into the esophagus, the rapid and residual components are assumed not to be distinguishable, but to contribute to the curve proportionately. In the RT

interval, however, the residual component takes on a mean counting rate of L and persists at that level. Those conditions are met when Curve C is derived, segment by segment, from Curve B as follows. In the RT interval we find a point, S, whose counting rate is closest to the RT average, K. Points from P through S are multiplied by L/K; points between S and U are assigned the counting rate L; and points in the interval U through V are unchanged.

Finally, the residual component is stripped by subtracting Curve C from Curve B. The difference curve (D) represents the rapid component and descends to a zero value. It supplies the data used to compute the mean transit time (MTT) of the rapid component through the entire esophagus by the following area-over-height formula (8):

$$MTT = \frac{\int_0^\infty M(t)dt}{M_{max}},$$

where the numerator is the area under the curve and the denominator is the height of the curve. Specifically, the sum of the counts under Curve D is divided by its mean counting rate in the RT interval. The latter is taken to represent the quantity of the rapid component, and the validity of the formula depends on that premise (8).

In addition, whole-esophagus time-activity curves are generated for the second, third, and later swallows, and are the basis for computing, in analogous fashion, the corresponding residual fractions [RF(2), RF(3), etc.] as percentages of K, the original early plateau counting rate. The study chosen to illustrate the method of this paper shows, for a normal subject, a residual fraction that is unusually high after the first swallow but is virtually eliminated after the second.
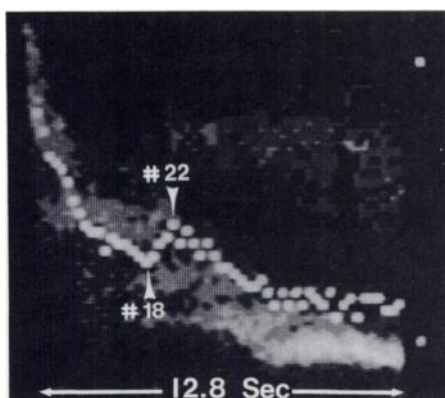


**FIG. 3.** Centroid curve superimposed on condensed image. Greatest retrograde excursion occurs between points 18 and 22 and is associated with separation of residual component. RI = 12%.

**TABLE 2. QUANTITATIVE ESOPHAGEAL TRANSIT INDICES**

| | MTT (sec) | RF(1) (%) | RF(2) (%) | RF(20) (%) | RI (%) |
|---|---|---|---|---|---|
| Normal group (N = 12) | | | | | |
| Mean | 5.9 | 8 | 6 | 4 | 7 |
| Range | 3.4–10.2 | 2–28 | 2–13 | 1–9 | 1–14 |
| Patient group: Cases | | | | | |
| 1. Esophageal reflux | 4.0 | 29 | 29 | 16 | 6 |
| 2. Achalasia | * | 100 | 100 | 100 | 24 |
| 3. Achalasia | * | 100 | 100 | 100 | 12 |
| 4. Achalasia | * | 100 | 100 | 100 | 11 |
| 5. Unclassified | 5.2 | 47 | 47 | 42 | 3 |
| 6. Unclassified | * | 100 | 100 | 10 | 36 |

* No rapid component identified.

**Condensed images.** These allow depiction of an entire dynamic sequence in one image. Because only cranio-caudal and not lateral changes are of interest in esophageal studies, each original consecutive image frame of the first swallow is compressed (by row summation) into a single column, which displays the vertical distribution of radioactivity from pharynx to stomach within a short time interval. The columns are assembled into the condensed image, whose horizontal and vertical dimensions are thus temporal and spatial, respectively. As indicated by the following equation, the nth frame in the dynamic study determines the nth column of the condensed image:

$$A_c(n,y) = \sum_{x=1}^{64} A(x,y,n),$$

where $A_c(n,y)$ is the numerical content of the pixel with horizontal and vertical coordinates n and y, respectively, in the condensed image, and $A(x,y,n)$ is the content of the pixel with coordinates x and y in the nth original frame.

Condensed images are also constructed from later swallows and from the entire multiswallow sequence. Results are illustrated in Fig. 2. In these images, dots at the right mark the levels of the cricoid cartilage and gastroesophageal junction.

The method is due to Svedberg (6), in whose laboratory it was applied to data, in list mode, recording the esophageal transit of radioactive gelatin pellets (6,9).

**Centroid analysis.** As a further condensation of the dynamic information from the first swallow, the vertical component of the center of mass (centroid) of the spatial distribution of radioactivity is plotted as a function of time. The following equation (10) is used:

$$\bar{y}(n) = \frac{\sum_{y=1}^{64} \sum_{x=1}^{64} [A(x,y,n) \cdot y]}{\sum_{y=1}^{64} \sum_{x=1}^{64} A(x,y,n)}$$

where $\bar{y}(n)$ is the value of the nth point in the centroid curve, and $A(x,y,n)$ is the numerical content of the pixel with coordinates x and y in the nth original frame.

Figure 3 shows the centroid curve superimposed on the condensed image to show their relationship. The curve tracks the mean location of the radioactivity. When, as in this case, the bolus divides and distributes mainly into two locations, it assumes an intermediate value.

Upward excursions interrupting the downward course of the centroid curve occur even in normal subjects, and imply retrograde motion. Quantification, to determine whether the normal range has been exceeded, is achieved with a retrograde index (RI), defined as the greatest difference between the level of any centroid point and any preceding point, expressed as a percentage of the length of the esophagus (Fig. 3). The scheme for computing RI excludes the tail end of the centroid curve, arbitrarily defined as the points occurring after the counting rate in the esophageal region has dropped below 0.75k.

**RESULTS**

The results for both groups are summarized in Table 2.

**Normal group.** The tabulated ranges for the several indices encompass the middle 80% of normals, with 70% certainty by the method of nonparametric tolerance limits (11). The distributions are not demonstrably Gaussian.

A representative study of a 22-yr-old male is shown in Figs. 4 and 5. Time-activity analysis of the first swallow demonstrates prompt transit of virtually the entire bolus into the stomach, with only a negligible residual component (Fig. 4). This is confirmed in the condensed image, which also shows distal slowing and spreading but no division of the bolus within the esophagus (Fig. 5).
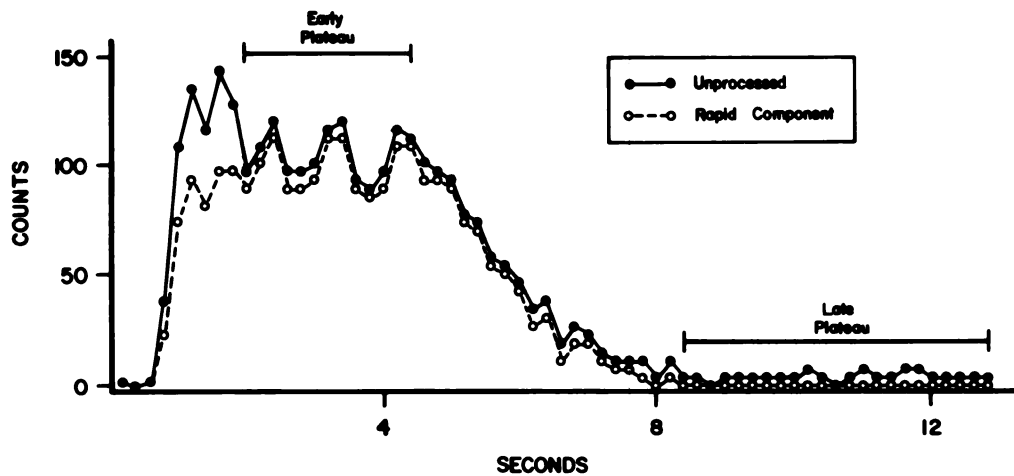
**FIG. 4.** Normal first-swallow time-activity curves for whole esophagus. Computer processing results in curve depicting behavior of rapid component. MTT = 5.0 sec; RF(1) = 2%.

The centroid curve (not shown) reveals a small retrograde excursion (RI = 7%).

**Patient group.** The first two cases are illustrated as follows:

*Case 1 (esophageal reflux).* The first-swallow time-activity curves (not shown) reveal a substantial residual component but prompt transit of the rapid component. The condensed images (Fig. 6) show division of the bolus as the residual component is generated in the first swallow (A). The pattern differs from that of some normal subjects (Fig. 2) because the residual activity is not reduced by the second swallow. Rather, a repetitive pattern of undulation, with no net change of location or quantity, is observed in consecutive swallows (Fig. 6B, C). After a relatively effective swallow (the 12th), the residual component decreases and shifts to a more proximal location, and the undulation is eliminated. The change of pattern is clarified by a condensed image constructed to encompass the entire 40-swallow sequence (D).

*Case 2 (achalasia).* First-swallow time-activity curves are shown in Fig. 7. No movement of tracer out of the esophagus is detected in the curve for the whole organ (A); i.e., there is no rapid component. Curves obtained from the individual thirds of the esophagus (B–D), as described by Russell et al. (2), exhibit an irregular pattern unlike that seen when orderly aboral progression of the bolus occurs. A reciprocal relationship is noted: two peaks of activity occur in the proximal third, at eight and 14 sec, at the expense of activity in the distal third, defining two distinct episodes of retrograde motion.

A better appreciation of the oscillations of activity between the proximal and distal esophagus is obtained from the condensed image (Fig. 8). The centroid curve (Fig. 9) also clearly demonstrates the retrograde motion and reveals an abnormal RI. An oscillating pattern continues through the entire study, with negligible appearance of activity in the stomach.

## DISCUSSION

Several recent investigations have demonstrated the usefulness of radionuclide studies of esophageal transit, in which the subject swallows a small volume of Tc-99m sulfur colloid in water (1–4). This approach has been recommended to evaluate disorders of esophageal motility, because of several advantages over established methods. These include speed, simplicity, and noninvasiveness compared with manometry; and swallowing of physiological material, ease of quantification, and low radiation burden compared with contrast radiography. We have elaborated the nuclear approach with three new computer techniques. Our method of time-activity curve analysis differs from that of Russell et al. (2), who proposed that transit time be measured as the time from initial entry of the bolus into the esophagus until total clearance from the organ. In our experience, the end point selection is complicated by the fact that the first-swallow curves do not fall to zero even with normal subjects; there is always a finite, if small, RF(1). This may be due to a lack of quantifiable clearance of the esophagus in a single swallow, adherence of some of the
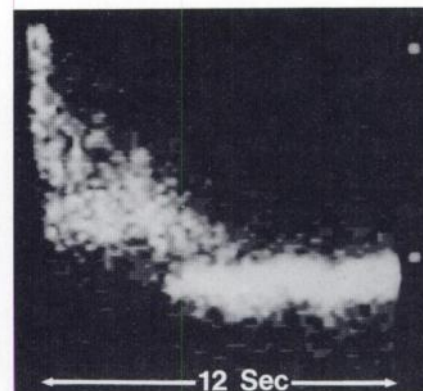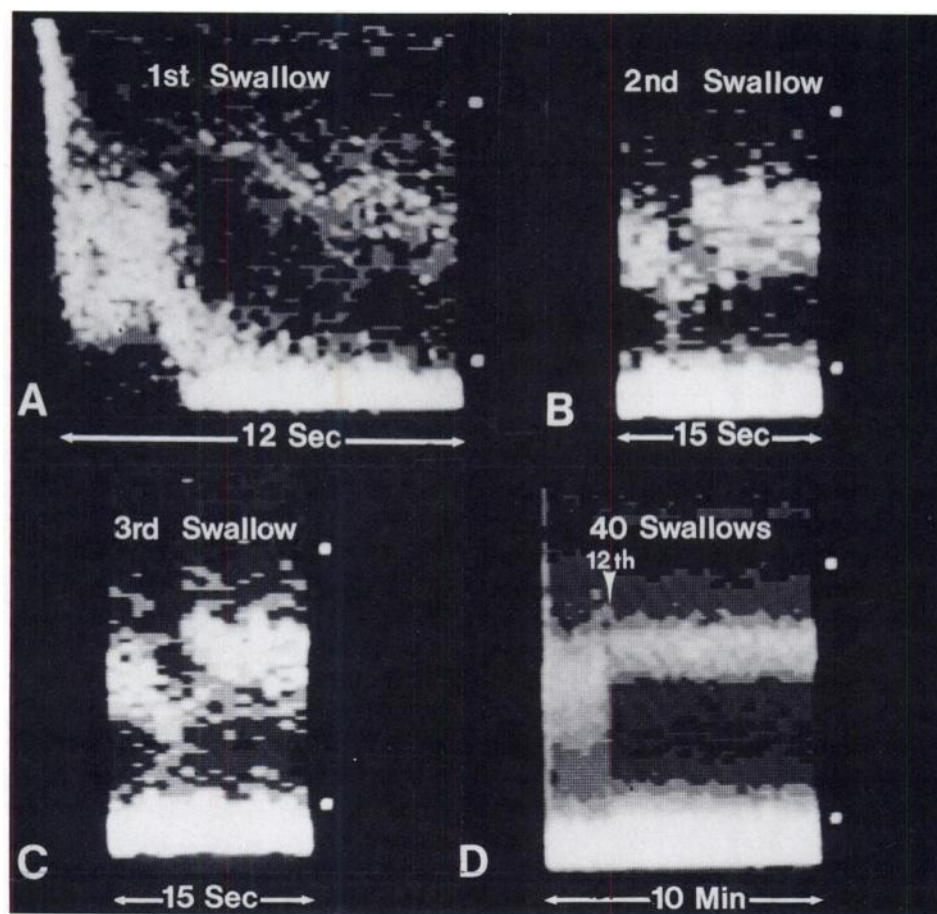


**FIG. 5.** Normal condensed image of first swallow.

**FIG. 6.** Case 1. Condensed images of first three swallows (A–C) and entire 40-swallow sequence (D).
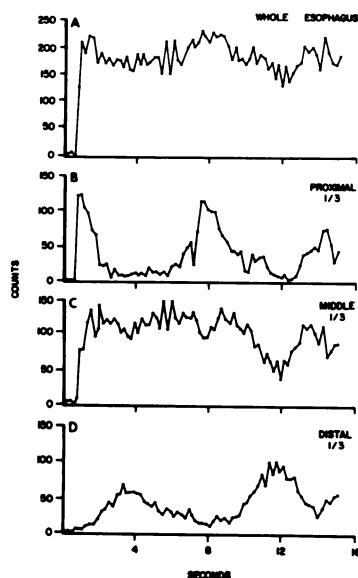


**FIG. 7.** Case 2. First-swallow time-activity curves for whole esophagus (A) and individual thirds (B–D). No rapid component is identified. Although bolus is retained quantitatively in esophagus, Curve A does not assume constant value, but has peaks of activity coinciding with those in Curve B, corresponding with episodes of retrograde motion. This is explained by decreased attenuation in proximal segment.

radiopharmaceutical to the esophageal mucosa (7), or septal penetration and scatter due to activity in the stomach. Our method results in a rapid-component curve that descends to zero; this serves as the basis for application of the theoretically valid area-over-height equation (8) to calculate the *mean* transit time through the whole esophageal region of interest. The problem of end point selection is obviated, and the formula appropriately yields different results for two curves with different shapes but the same interval between end points. Thus, all other things being equal, if a curve has a prolonged plateau terminating with a steep descent, the MTT is longer than in the case of a gradual descent.

The transit times of our normal group (5.9 ± 1.9 sec, mean ± s.d.) are not greatly different from those of Russell et al. (2) (7.7 ± 1.7 sec) and others who advocate similar end point-related definitions (3,4). However, some of our normal subjects had high RF(1) values (maximum 28%) and would have been abnormal by the criteria of other investigators (2–4) because of the failure of their curves to descend to a baseline within the allowed time. This appears to be an unexplained discrepancy in the behavior of the normal groups, and also illustrates the difference in definition of transit time.
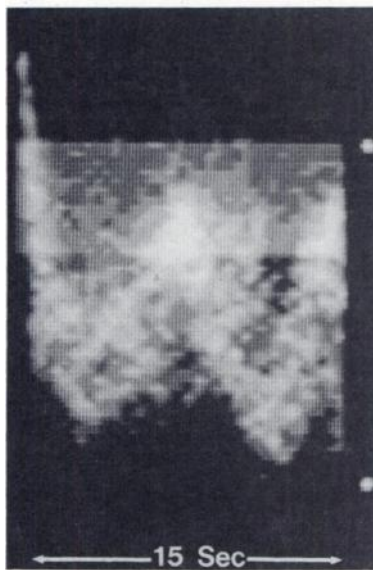
**FIG. 8.** Case 2. Condensed image of first swallow. Time-activity curves may be recovered from dynamic image data stored in this form. Thus, application of conventional profile program to horizontal rectangular region, enhanced in this figure, yields curve for proximal third of esophagus.

Our normal subjects, like those of Tolin et al. (*1*), showed good clearance (i.e., low residual fraction) after multiple swallows.

All six in our patient group had elevated residual fractions after the initial and subsequent swallows, and two had elevated RI values as well. Only the two studies with RF(1) of less than 100% had an identifiable rapid component and a calculable MTT that was within normal limits. All of these studies would presumably have been abnormal by previously described criteria, because

of failure to clear the esophagus in multiple swallows (*1*), and because the elevated RF(1) would be interpreted as a prolonged transit time using the definition proposed by other investigators (*2–4*).

The ability of condensed images to depict normal transit patterns has been shown in Figs. 2 and 5. Figure 6 is abnormal, division of the bolus in the first swallow being followed by a distinctive repetitive undulating pattern of ineffectual deglutition in subsequent swallows. In instances when time-activity curves generated for individual thirds of the esophagus appear abnormal but do not readily lend themselves to a more precise description, the condensed image improves the perception of the specific fate of the tracer, as demonstrated by the antegrade and retrograde motion in Fig. 8.

In conclusion, drawing on a model of rapid and residual components of a swallowed liquid bolus, we have developed and adapted new computer methods for esophageal scintigraphy, in the hope of ultimately improving diagnostic accuracy. Since our methods incorporate detailed examination of the swallowing process with the generation of several quantitative indices, they may clarify the findings that are specific to particular esophageal motility disorders. Possible applications of this approach include the evaluation of minor motor disorders of the esophagus, the effects of various drugs on esophageal function, and the diagnostic use of provocative agents to evaluate symptoms suggesting esophageal dysfunction.
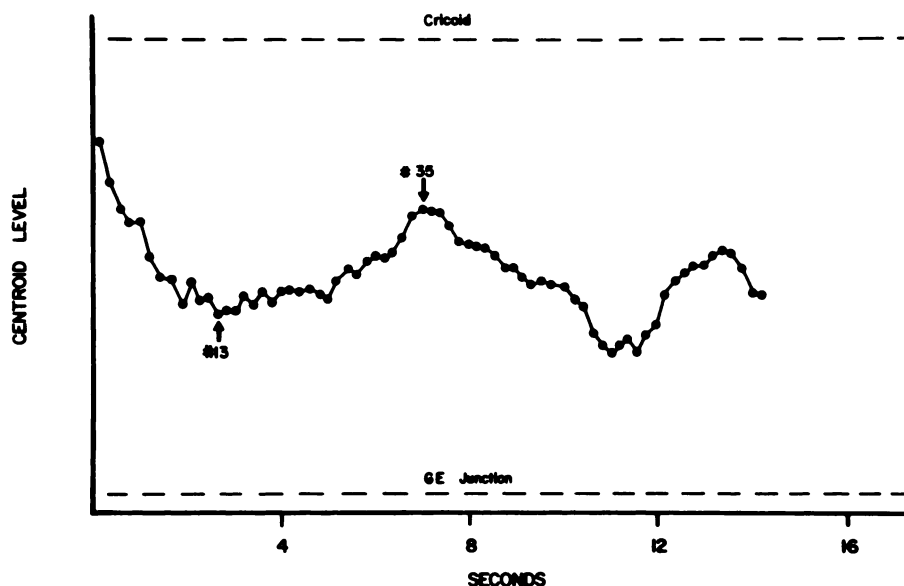
**FIG. 9.** Case 2. Centroid curve. Greatest retrograde excursion occurs between points 13 and 35.

### REFERENCES

1. TOLIN RD, MALMUD LS, REILLEY J, et al: Esophageal scintigraphy to quantitate esophageal transit (quantitation of esophageal transit). *Gastroenterology* 76:1402–1408, 1979
2. RUSSELL COH, HILL LD, HOLMES ER, et al: Radionuclide transit: a sensitive screening test for esophageal dysfunction. *Gastroenterology* 80:887–892, 1981
3. BLACKWELL JN, HANNAN WJ, ADAM RD, et al: Radionuclide transit studies in the detection of oesophageal dysmotility. *Gut* 24:421–426, 1983
4. BENJAMIN SB, O'DONNELL JK, HANCOCK J, et al: Prolonged radionuclide transit in "nutcracker esophagus." *Dig Dis Sci* 28:775–779, 1983
5. KLEIN HA: Esophageal motility: computer analysis of scintigraphic studies. *J Nucl Med* 24: P98, 1983 (abst)
6. SVEDBERG JB: The bolus transport diagram: a functional display method applied to oesophageal studies. *Clin Phys Physiol Meas* 3:267–272, 1982
7. HELM JF, DODDS WJ, PELC LR, et al: Effect of esophageal emptying and saliva on clearance of acid from the esophagus. *N Engl J Med* 310:284–288, 1984
8. LASSEN NA, PERL W: *Tracer Kinetic Methods in Medical Physiology.* New York, Raven Press, 1979, pp 76–101
9. KJELLÉN G, SVEDBERG JB, TIBBLING L: Computerized scintigraphy of oesophageal bolus transit in asthmatics. *Int J Nucl Med Biol* 8:153–158, 1981
10. RICHARDSON M: *Fundamentals of Mathematics.* New York, Macmillan Company, 1958, pp 228–229
11. OWEN DB: *Handbook of Statistical Tables.* Reading, MA, Addison-Wesley Publishing Company, 1962, p 321

---

## Information Processing in Medical Imaging
## 9th International Conference

**June 10–14, 1985**        **Washington, D.C.**

### Announcement and Call for Papers

The Scientific Review Committee welcomes abstracts on all aspects of computer and mathematical analysis and processing of in vivo digital images (nuclear medicine, CT, ultrasound, NMR, etc.). The conference objective is to share in advances that have been made in these fields; constructively criticize the presented work; develop directions for future efforts. The format of the program is structured to foster this objective with approximately 45 minutes for papers plus ample discussion time for each presentation. Full papers will be published in book form.

The total conference attendance is limited to fewer than 100 participants—either authors or co-authors of submitted papers or those researchers who wish to take an active part in the ensuing discussions. All attendees must register in advance. Abstracts must be less than 2 pages long, including supporting data, typed on 8½" by 11" paper, single spaced, in camera ready form. Limited financial support may be available in certain circumstances.

Send abstracts to, or request further information and registration forms from:

Stephen L. Bacharach, Ph.D.
National Institutes of Health
Building 10, Room 1C401
Bethesda, MD 20205 USA

Abstract deadline: December 10, 1984.

---

## Erratum

Please note that the abstract "Perfusional Techniques for Screening Antibodies (Ab) in Living Tissue" appearing in the May 1984 issue of the *JNM,* Vol. 25, Number 5, page P9 should be included in the Author Index under the following authors' names:

G.L. DeNardo, A.W. Saxe, S.J. DeNardo, A. Epstein, C. Suey.