Technical Factors in Gastric Emptying Studies

In recent years there has been renewed interest in radionuclide studies of gastric emptying. Early nuclear medicine studies using only liquid meals have been replaced by combined solid and liquid meals to provide a more physiologic evaluation. Both research and clinical studies have been conducted and have used a variety of labeled food markers to study liquid, semi-solid, solid, or simultaneous liquid and solid phases of gastric emptying. Radionuclide studies are easy to perform, noninvasive, and quantitative, and they deliver relatively low radiation doses.

Several basic points are critical for the accuracy of gastric emptying studies:

1. Radionuclide markers, whether liquid, semi-solid, or solid, must have a high labeling efficiency and be stable throughout the duration of the procedure.
2. Meal size and composition must be standardized for all studies.
3. A standard patient position and posture should be maintained during imaging.
4. Correction techniques should be applied when needed to compensate for radionuclide decay, multiple radionuclide interference, geometry changes, septal penetration, and scatter from high-energy gamma rays.

Radionuclide markers. Liquid markers have been used in gastric emptying studies for many years (*1*,*2*). They must be nonabsorbable and stable for the duration of the procedure. Most liquid markers equilibrate rapidly with a liquid meal and are representative of emptying for that liquid. The most frequently used liquid markers have been radiolabeled DTPA or colloid.

Fiber has been successfully labeled with Tc-99m or I-131 (*3*,*4*) to provide a nonliquid, nonsolid marker for solid or semisolid meals. However, there has been no definitive study establishing that radiolabeled fiber follows the emptying of solid food, which contains particulate matter larger than fiber. A radiolabeled marker should be similar to the food selected for the standard meal.

Many solids have been labeled with radionuclide markers, and it is extremely important that the initial labeling efficiency of the solid marker be high and that it remain stable throughout the procedure. Meyer et al. (*5*) described the use of intracellularly labeled chicken liver, obtained by injection of Tc-99m sulfur colloid into live chickens, as a marker for solid foods. Chicken liver labeled in this way has been shown to have extremely high labeling efficiency and excellent stability when tested in vivo and in vitro. However, although this material is an ideal solid food marker, most laboratories do not find it convenient to handle and inject live chickens. Chicken liver also has been surface-labeled by in vitro techniques (*6*,*7*). Initial labeling efficiency is high, but 14–33% of the sulfur colloid is released from the surface of the liver within one hour of its contact with gastric juice. Technetium-99m sulfur collid incorporated into puréed meat (paté) has only a 4% breakdown in gastric juice after one hour (*7*). The use of puréed meat provides homogeneous distribution of the radiopharmaceutical throughout the material, which can be fried to trap the radionuclide within the meat particles. Similar procedures have used egg (*8*,*9*) as the medium for mixing with the sulfur colloid. The egg is then cooked, yielding high labeling efficiency with moderate stability.

Large-particle solid-phase markers have been shown to empty more slowly than small particulate material (*10*). Therefore, a relatively constant size of solid particles should be maintained. Mastication of particles should be considered a part of normal digestion.

Meal size and composition. The test meal should be selected carefully to match the properties of the marker. Sulfur colloid and DTPA, tagged with Tc-99m, are readily available liquid markers and are easily imaged. Due to actions of the fundus, antrum, pylorus, and gastroduodenal pressure gradient, liquids empty from the stomach mono-exponentially with time (*11*). The emptying of solids and particulates is dependent primarily on the pylorus, which prevents duodenal reflux and restricts the emptying of solids; thus solids empty more slowly from the stomach than liquids (*11*),

in an approximately linear fashion with time (*12–16*).

Liver labeled with Tc-99m sulfur colloid and mixed with a beef stew meal (*5*) provides an excellent solid-phase marker having properties similar to that of the meal. Labeled meat particles are not expected to empty at the same rate as oatmeal or soft bread, because of the different handling of these materials by the stomach. Hunt and Stubbs (*17*) demonstrated that meals of high energy density (cal/g) empty from the stomach more slowly than low-density meals. These results have been confirmed by other investigators, who showed that increased meal size with a corresponding increase in total caloric content also results in slower gastric emptying (*5,13,14*). Thus, it may be difficult to compare sequential patient studies when the test meals differ in volume, composition, or content, even when the same radionuclide marker has been used.

Several techniques have been described using two radionuclides to measure liquid and solid emptying simultaneously (*12–16,18,19*). If the solid phase of the meal is labeled with Tc-99m, the liquid marker for simultaneous use must have an energy different from that of technetium and be suitable for imaging with a scintillation camera. Although the use of multiple radionuclide markers sounds like a cumbersome procedure, it can provide valuable information in both the research and clinical setting. At our institution we occasionally see patients who have disparate emptying of solids and liquids. If a mixed solid and liquid meal were given to a patient using only a liquid marker such as Tc-99m DTPA, the patient may demonstrate normal emptying of the liquid while actually retaining the solids abnormally. Solid food, being more difficult for the stomach to empty, should be the labeled material if only one radionuclide can be used. Several studies have utilized Tc-99m and In-113m simultaneously as solid- and liquid-phase markers respectively (*12,18,19*). Technetium-99m and In-111 DTPA also have been used (*13–16*), as well as a variety of other markers (*20–22*).

Patient position. Some variation in emptying has been shown between upright and supine studies (*18,19*). Since emptying may be affected by posture and gravity, a standard and reproducible imaging geometry must be maintained.

Correction techniques. Techniques for providing correction factors in various aspects of gastric emptying studies must be applied for appropriate situations. In general, there are two types of corrections: (a) those related to the physical properties of the radionuclides and instruments, and (b) those related to changes of the radionuclide distribution within the patient. Physical corrections include those for radionuclide decay, counting interference between multiple nuclides, and septal penetration of the collimator when a high-energy emitter is used. Changes within the patient may involve dissociation of the radionuclide from the marker or changing distribution of the marker within the stomach and duodenum. This may result in changes of depth, attenuation, septal penetration, and scatter.

Because gastric emptying studies may extend over several hours, accurate results may require correction for decay (*12–14,18–22*). Although short-term studies with Tc-99m might not be improved significantly by decay correction, such corrections can be important in patients with extended emptying times. The utilization of In-113m requires decay correction for all data points because of its shorter half-life (100 min). Decay correction can be very important when emptying times fall between the normal and abnormal ranges. Because most gastric emptying procedures are evaluated on the basis of the percent retention of the marker within the stomach, accurate comparison with the initial measurement recorded shortly after food ingestion is necessary.

Several investigators have used In-111 DTPA or In-113m DTPA as liquid markers together with Tc-99m solid markers (*12–16,18,19*). The use of simultaneous markers may require larger amounts of activity of the low-energy radionuclide than for the high-energy radionuclide, to minimize the effects of down-scatter into the low-energy window. An alternative technique estimates the appropriate correction for down-scatter, which can then be subtracted from counts in the low-energy window.

Correction factors for down-scatter interference depend on the window width, the relative amounts of activity used for each radionuclide, and the percentage of scatter into the low-energy window. Correction factors determined from studies on phantoms or patients can be used to calculate down-scatter counts, which in turn must be subtracted from the counts for the low-energy window. Interference corrections should be performed before decay corrections because the two decay rates generally are not equal. If radionuclide energies are closely similar, there may be interference into both low- and high-energy windows, for which correction also can be made (*16*). These

problems have been dealt with for many years in scintillation counting of multiple radionuclides.

After meal consumption, food material may move anteriorly as it descends from the fundus into the antrum, and this may increase anterior counts due to decreased tissue attenuation (*12–14,18–22*). It has long been known (*23*) that the geometric mean of counts from opposing views is insensitive to changing source depth. This technique has been applied successfully to gastric emptying studies (*12–14,18,19,21,22*). The geometric mean (anterior count × posterior count)$^{1/2}$ can be determined easily from anterior and posterior computer images of the stomach. Patients can be imaged from in front, turned immediately to image from behind, and the geometric mean calculated for the respective gastric regions. Corrections for varying depth and attenuation are most important in studies using large meals in normal-sized or obese patients, in whom attenuation may be significant. When this type of correction is not applied, gastric emptying time may appear to be slower than its actual value because of the slight anterior motion and subsequent increased counting rate of the food mass from the anterior view. In our previous studies (*14,24*) the average half-emptying time for a 300-g meal was overestimated by 10.3% by anterior imaging alone, with the highest overestimate being 56.7%.

The use of a high-energy gamma emitter, such as In-113m (392 keV), requires special correction techniques. Two papers in this issue of the *Journal* (*21,22*) describe and test correction techniques used with In-113m. At 392 keV there is less difficulty with attenuation, but scatter and penetration of collimator septa create additional problems. These studies suggest that for sources at depth, corrections for septal penetration, and scatter based on gastric region-of-interest size should be applied. Although it is not clear which of the two factors (scatter or septal penetration) is the more significant problem, their data indicate that the combined correction can approach 30–40% when small regions of interest are used for In-113m, and about 10% for Tc-99m. Logarithmic functions determined from phantom studies were used to correct for crosstalk from In-113m into the Tc-99m window, and septal penetration and scatter for the In-113m photons. Dual-window imaging was performed to determine a peak-to-scatter (P:S) ratio, which was then used to estimate source depth and thence to correct for attenuation, septal penetration, and scatter.

VanDeventer, and Meyer et al. used a unique approach to test their correction techniques. They used dual-labeling of either two liquid or two solid phases simultaneously and assumed that correction techniques were adequate when gastric emptying curves for the two radionuclides could be superimposed. VanDeventer's study used a liquid glucose meal containing both In-113m DTPA and Tc-99m DTPA. They found that significant errors could result with In-113m if corrections for septal penetration and scatter are omitted. Correction techniques based on either the geometric mean or peak-to-scatter ratios proved adequate. They also attempted to compare their gamma-camera data with simultaneously obtained data from gastric intubation, but technical difficulties prevented a definitive correlation.

In the study by Meyer et al. (*22*) volunteers were fed meals consisting of chicken liver intracellularly labeled with both In-113m and Tc-99m. Again, peak-to-scatter ratios and geometric means were used to determine correction factors. Depth was first determined by a computer calculation, then additional corrections based on region-of-interest size were applied to correct for down-scatter, septal penetration or scatter, and the size of the region of interest. Meyers (*22*) states that, "Superimposition of the two emptying curves indicate that corrections for septal penetration, down-scatter, and anteroposterior movement of the liver were valid." This study again indicated a potentially significant source of error related to septal penetration and scatter, especially for In-113m. The authors concluded that the P:S ratio provides a convenient alternative to the geometric mean for calculation of source depth and related correction factors.

The use of peak-to-scatter ratios to correct for source depth and attenuation was first described by Hine (*25*) and by Genna (*26*) for application to whole-body counting, and was also investigated by one of us (JAS) for application to linear profile scanning (*27*). It was noted in this study that the P:S ratio was more sensitive than the geometric mean to variations in source volume and other distribution effects. In particular, the P:S ratio can be altered by scatter from sources lying entirely outside the field of view of the detector, which could lead to erroneous results. Both the geometric mean and the P:S technique require an additional image, either for posterior photopeak counts, or for anterior scatter counts. Thus, while the P:S technique may be a suitable alternative for gastric emptying studies, provided the problems alluded to above are not significant, it is not clear that it offers any special advantages over the geometric-mean technique.

SUMMARY

Gastric emptying studies are useful not only for the study of gastric physiology, but in the management of individual patients. They can be performed with a variety of radionuclides, labeled markers, and meals. A carefully standardized procedure provides a valuable correlative study for supplementing radiographic and intubation tests. Attention must be given to the selection of radionuclide markers, meal size and composition, imaging geometry, and the application of appropriate correction factors used in concert with proper application.

We feel that, gastric emptying studies should be performed with a meal size of approximately 300 g, composed of equal parts of solid and liquid food materials. A meal of this size can be consumed by most patients. It should contain a stable solid-phase Tc-99m marker, preferably labeled liver or paté. It may also be advantageous to add In-111 DTPA as a marker for the liquid phase and to image both the Tc-99m and then the In-111 (247 keV) photopeaks with a 360–400 keV collimator. If the Tc-99m/In-111 activity ratio is 6:1 or greater, down-scatter of In-111 counts into the Tc-99m window is minimized and indeed down-scatter correction may be unnecessary, depending on the properties of the individual scintillation camera and collimator. Corrections for septal penetration and scatter are necessary with high-energy nuclides (e.g., In-113m). Although depth and attenuation corrections might not be significant in most slender to normal-sized patients, half-emptying times may occasionally be overestimated by up to 56% without this correction (*24*). Obese patients almost always require depth and attenuation corrections. Hence, as a general rule, depth and attenuation corrections should be used.

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