Technical Factors in Labeling Test Meals to Determine Gastric Emptying Rate

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Objective: This study investigates the behavior of two different radionuclide labels for liquid test meals and the stability of radionuclide labeling of solid meals.

Methods: Technetium-99m DTPA and ^{99m}Tc colloid were compared as labels for liquid test meals in an in vivo investigation of gastric emptying rate. Half emptying time and retention percentages were used as parameters. Stability of solid test meals labeling using ^{99m}Tc colloid on liver paté was determined in vitro. After incubation in gastric acid, samples of the labeled solid meals were incubated in bile with pancreatic juice. After separation, activity of ^{99m}Tc is determined in the solid phase and in the supernatant. Technetium-99m activity was also measured in plasma during gastric emptying measurements for solids in healthy volunteers.

Results: Liquid gastric emptying was faster if DTPA was used. Colloid remained in the stomach longer. There was little dissociation of ^{99m}Tc from the solid test meal into gastric acid and into bile with pancreatic juice. Activity levels of ^{99m}Tc in plasma remained low throughout the emptying study.

Conclusion: We prefer DTPA as the label for gastric emptying study of liquid meals. We suspect that colloid adheres to the gastric wall and falsifies the results. The current labeling of solid test meals is stable in gastric and duodenal environments. Adsorption of ^{99m}Tc into plasma remains very limited. Subsequent resecretion of ^{99m}Tc in whatever form into gastric juice is excluded.

Key Words: gastric emptying rate; labeling stability; technetium-99m DTPA; technetium-99m colloid

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Although radionuclide studies of gastric emptying rate (GER) are easy to perform, several basic elements are critical for the accuracy of these studies. Most of all the radionuclide labeling of the test meal must be stable throughout the duration of the procedure. The radionuclide must remain attached to the phase it is supposed to represent. This is true for both solid and liquid test meals.

The most frequently used and recommended markers for liquid test meals are radiolabeled DTPA and colloid (*1*). Since DTPA is soluble in water, one can expect a different behavior compared to colloid. Colloid particles are much larger and they could match with the size of the foveolae of the gastric mucosa. This could cause a coating effect, and hence misrepresent the gastric handling of the liquid meal. In this study, differences in results using both types of labels were investigated.

Stability of labeling of solid test meals in gastric acid has been studied extensively in vitro (*2–4*). Hepatic intracellular, liver surface as well as liver paté labeling have been compared. Intracellular labeling is very stable, but live chickens are difficult to handle in a nuclear medicine department. Surface labeling of liver chunks does not provide adequate stability of the label. Liver paté is easy to label and the labeling procedure yields high stability in gastric acid.

Nevertheless, stability in the duodenal environment, in which bile and pancreatic enzymes are present, also needs investigation. Possible breakdown of the labeling and subsequent absorption into plasma of the label has not been excluded yet. This could be followed by resecretion of ^{99m}Tc by the gastric mucosa. If this secretion occurs in considerable amounts, GER could be misrepresented by such increased intragastric activity. Therefore, additional experiments were performed to verify and extend the already known guidelines about labeling solid test meals.

MATERIALS AND METHODS

Stability tests for liquid meals were performed in vivo. Six healthy individuals were investigated. The test meal consisted of 100 ml plain tap water labeled with 1 mCi ^{99m}Tc DTPA. Acquisition was performed in postero-anterior directions.

Intragastric activity was measured in a region of interest and plotted against time (*5*). Half-emptying time and retention percentages at 2, 5, 10 and 20 min were determined. The measurement was repeated within one week using ^{99m}Tc stannous colloid as the marker. Statistical analysis, using Wilcoxons' rank sum test for paired data was performed.

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Stability tests for solid meals are performed in vitro. The labeling of liver paté with ^{99m}Tc stannous colloid is consolidated by frying (*6,7*). It was then mixed thoroughly with fresh unlabeled paté. Four 1-g samples of this mixture were incubated in 10 ml fresh canine gastric acid at 37°C and pH2 for 2 hr. Stirring occurred every 15 min in order to mimic gastric motor activity. After separation from gastric acid, the solid phase was incubated in a 10-ml mixture of fresh canine bile and pancreas juice from 1 hr up to 4 hr, after which solid and liquid phase were separated again. Activity of ^{99m}Tc was measured separately in gastric acid, bile with pancreas juice and the solid phase using a gamma counter. Correction was performed for decay of ^{99m}Tc. The sum of all activity, as well as the percentage of activity in both liquids and solid phase, was calculated.

A complementary test was performed in vivo. During the performance of a gastric emptying test for solids (*6*) in three healthy volunteers, a 2-ml blood sample was taken every hour after ingestion of the test meal, up to 4 hr. Activity of ^{99m}Tc was determined in every sample using a gamma counter. These results, expressed in counts per minute (CPM) were converted into mCi after correction for decay:

$$1 \text{ Ci} = 37 \times 10^9 \text{ Bq disintegrations per sec (DPS)}$$

$$1 \text{ Ci} = 2.22 \times 10^{12} \text{ disintegrations per min (DPM)}$$

In the gammacounter, the counting efficiency was 75%. In this case:

$$1 \text{ Ci} = 1.655 \times 10^{12} \text{ counts per min (CPM)}$$

Therefore:

$$1 \text{ CPM} = 0.610^{-12} \text{ Ci.}$$

The activity of ^{99m}Tc in the whole-blood compartment was calculated and expressed as the percentage of the administered dose, which was 1 mCi. The theoretical volume of the blood compartment was calculated using the height and weight of the volunteer. As a control, a 10-ml sample, containing 1 mCi ^{99m}Tc was diluted one million times. The activity of the diluted sample was measured in the same gamma counter.

RESULTS

Table 1 shows that GER for liquids was slower when colloid was used as radiopharmaceutical. The increase of median half emptying time is 11 min. Retention percentages are increased in all cases. After 2 min, the median increase is 13%; after 20 min, this increase rises to 27%. In two cases, $T_{\frac{1}{2}}$ cannot be determined since the colloid curve flattens after a few minutes and remains well above 50% retention. Statistical analysis shows that these differences are significant (p is lower than 0.05 in all instances). Even in this small population, the differences are of such magnitude that they can be considered clinically important.

Table 2 shows that almost none of the radionuclide dissociates from the solid phase. The highest level of activity in gastric acid remains below 1%. Furthermore, the labeling of liver paté with ^{99m}Tc stannous colloid remains quite stable in fresh bile with pancreatic juice. Dissociation of ^{99m}Tc from solid into liquid does not exceed 5% in any case.

TABLE 1
The Results of GER Using Technetium-99m Stannous Colloid and Technetium-99m DTPA

	Emptying time $T_{\frac{1}{2}}$ (min)		
	^{99m}Tc Sn Colloid	^{99m}Tc DTPA	P
$T_{\frac{1}{2}}$	19 (12–<48)*	8 (2–32)*	<0.05
	% Retention		
	^{99m}Tc Sn Colloid	^{99m}Tc DTPA	
R2 min	92 (78–100)	79 (66–86)	<0.05
R5 min	73 (35–100)	45 (31–71)	<0.05
R10 min	66 (39–100)	25 (20–69)	<0.05
R20 min	48 (34–83)	21 (12–55)	<0.05

*Results are presented as median and range.

Table 3 shows that the highest count rate measured in a blood sample is 1239 CPM. Converting this result into Ci yields 743×10^{-12} Ci per 2 ml of blood. In a calculated blood volume of 5600 ml, 2×10^{-6} mCi of ^{99m}Tc is detectable. This result corresponds with 0.2% of the total administered dose of ^{99m}Tc, which is 1 mCi or 1000×10^{-6} Ci. Dilution of a 10-ml sample containing 1 mCi ^{99m}Tc one million times yields 3329 CPM, which is of the same magnitude as 1239 CPM. This confirms the observation that only minimal amounts of ^{99m}Tc are adsorbed into plasma.

DISCUSSION

It is obvious from current results that the choice of radiopharmaceutical could influence the measurement of GER for liquid test meals. Half-emptying time as well as retention percentages are increased if colloid is used. This increment is statistically significant.

Although the studied group is relatively small, individual differences between results obtained with colloid and DTPA are of such magnitude that they are considered to be important. This observation is explained by the different behavior of the used radiopharmaceutical: DTPA is a small, entirely soluble molecule which is supposed to follow the test meal completely. This is substantiated by the fact that GER, using DTPA, is faster. In contrast, colloid particles are much larger. If their size matchs those of the gastric foveolae, the current observation is explained by a coating phenomenon. Similar observations have been made earlier in dogs where GER for solid meals was measured using resins as carriers for radionuclide labels. The size of particles was held responsible for a coating, and hence a decrease of gastric emptying rate (*8*). Coating of colloid particles on the gastric wall explains an observed retention of activity of ^{99m}Tc in the stomach although

TABLE 2
The Activity of Technetium-99m (in CPM) in the Solid Phase, Gastric Acid and the Bile with Pancreatic Juice

Sample	Activity in solid	%	Activity in gastric acid	%	Activity in bile + P.J.	%	Sum
1	586,808	95.5	3687	0.6	24,247	3.9	614,742
2	527,897	95.0	3268	0.6	24,358	4.4	555,613
3	604,283	95.7	1377	0.2	25,709	4.1	631,369
4	678,627	94.9	1543	0.2	35,337	4.9	715,507

the test meal has already been evacuated for a large part. GER can be greatly misrepresented. It is therefore of great importance to select properly a radiopharmaceutical to obtain accurate GER studies.

Systemic adsorption of ^{99m}Tc during gastric emptying studies using liquids labeled with ^{99m}Tc DTPA does not seem to pose problems. Radionuclide activity could only be detected in small amounts in plasma and tissues, including gastric mucosa, shortly after a GER study (*9*). The DTPA curve more closely fits an exponential curve, which is supposed to represent emptying for liquid meals. For all these reasons, DTPA is preferred for future GER studies for liquid test meals.

Current results, as well as data in the literature, strongly indicate that labeling of solid test meals with ^{99m}Tc colloid on liver paté is efficient and stable (*2–4*). This can be explained by entrapment of the colloid particles into liver paté by frying. We believe that emptying properties of labeled paté are not altered after frying since the caloric content does not change. Furthermore, we have minimized physical changes by thorough fragmentation and mixing of the fried paté with fresh paté. We obtained an almost homogeneous solid phase with particles of similar size, and a similar emptying rate (*10*). Chewing also decreases the size of ingested particles. The stomach allows only small particles to pass the pylorus (*11*).

The current results also indicate that this type of labeling is stable in the duodenal environment. This environment contains bile and pancreas enzymes, which have their lytic activity. This labeling procedure prevents dissociation of ^{99m}Tc into the liquid phase and, hence, possible absorption of significant amounts of radionuclide into plasma. Resecretion by the gastric mucosa of ^{99m}Tc, therefore, can be considered to be negligible. We do not expect a misrepresentation of GER caused by such phenomenon. This is confirmed by the observation that an increase of intragastric activity during the course of the study, as a result of suspected resecretion of ^{99m}Tc, has never occurred in our own series (*6,7,12*).

We conclude that stannous colloid is an excellent choice as a radiopharmaceutical for solid meals, provided it is adequately entrapped in a carrier, such as liver paté, by frying. It has a reasonable preparation time and avoids handling live chickens (*13*).

TABLE 3
The Activity of Technetium-99m in All Samples Obtained from Three Healthy Volunteers

Time after ingestion	Volunteer 1		Volunteer 2		Volunteer 3	
	CPM	10^{-12}Ci (pCi)	CPM	10^{-12}Ci (pCi)	CPM	10^{-12}Ci (pCi)
1 hr	263	158	630	378	147	88
2 hr	207	124	1052	631	253	152
3 hr	311	187	1060	636	292	175
4 hr	224	134	1239	743	278	167

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