## RADIOCHEMISTRY AND RADIOPHARMACEUTICALS

# A Conveniently Prepared Tc-99m Resin for Semisolid Gastric Emptying Studies

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**A polystyrene resin, suitable for semi-solid gastric emptying studies, was rapidly (<20 min) and conveniently prepared using commercially available reagents. Using the outlined procedure, Chelex-100 resin bound Tc-99m with greater than 98% labeling efficiency. The resulting Tc-99m Chelex-100 resin demonstrated excellent in vitro and in vivo stability. The clinical application of Tc-99m Chelex-100 resin, mixed with oatmeal, was tested in normal subjects and in various patient groups, including diabetic autonomic neuropathy, pyloric obstruction, postoperative dumping syndrome, and morbidly obese patients before and after gastroplasty.**

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Scintigraphic solid-phase gastric emptying measurements, performed alone or in combination with liquid-phase measurements, provide a clinically useful, noninvasive technique for the investigation of diabetic and other autonomic neuropathies and of gastric retention or dumping syndromes following surgical procedures (*1–3*). In this regard, antral function is believed to be more appropriately studied using radiolabeled solid rather than liquid-phase test meals (*4*). Although liquid-phase gastric emptying studies (*5,6*) can be performed readily using established radiopharmaceuticals (e.g., Tc-99m DTPA, In-111 DTPA), the incorporation of a radioactive label into a solid test meal has proved more challenging. When in the stomach, many colloidal preparations form micelles, which may stick to the gastric mucosa; while other radiopharmaceuticals may elute from the solid phase into the liquid phase (*7,8*). The in-vivo intracellular labeling of chicken liver with Tc-99m sulfur colloid provides a nearly ideal solid marker, but this procedure is cumbersome (*9*). To overcome these problems, recent emphasis has been placed on the use of radiolabeled polystyrene resins for the labeling of solid-phase test meals (*1,7,8,10–12*). Polystyrene resins appear to be ideal for this purpose since they are inert, nontoxic, minimally absorbable and adsorbable in the stomach and intestines, stable in both gastric and intestinal fluids, and capable of being uniformly mixed with solid foods (*7*). Preliminary studies on Tc-99m polystyrene resins involved the use of specially synthesized resins not commercially available (*7–12*). Recently the binding of Tc-99m to commercial resins has also been investigated (*13*). This communication describes the rapid (<20 min) preparation of a Tc-99m polystyrene resin using commercially available reagents; the incorporation of this radiolabeled resin into a small, palatable, semisolid meal; and the subsequent clinical evaluation of this technique.

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## MATERIALS AND METHODS

**Preparation of Tc-99m Chelex-100 resin.** A commercial analytical-grade cation exchange resin, Chelex-100 (sodium form, 50–100 mesh, 300–850 μm diam), was used. This resin, a styrene divinylbenzene copolymer with paired iminodiacetate chelating groups, has a strong affinity for transition metals (*14*). The

**TABLE 1. ESTIMATED RADIATION DOSIMETRY FOLLOWING THE ORAL ADMINISTRATION OF Tc-99m CHELEX-100 RESIN**

| Organ | Rad/mCi |
|---|---|
| Stomach wall | 0.14 |
| Small-intestine wall | 0.26 |
| Upper large-intestine wall | 0.49 |
| Lower large-intestine wall | 0.33 |
| Testes | 0.0045 |
| Ovaries | 0.094 |
| Total body | 0.018 |

following method is used to prepare a single dose of Tc-99m Chelex-100 resin:

1. Weigh 0.5 gram of Chelex-100 resin (no prior preparation required) and place in a clean glass vial. Cover vial with a rubber stopper.
2. Reconstitute a stannous pyrophosphate kit using 2 ml of nonbacteriostatic normal saline, and add total contents of this kit to the resin vial.
3. Shake the resin vial for approximately 1 min, then withdraw the stannous pyrophosphate supernate using a syringe attached to a 26-gauge needle. (The resin particles will not pass through this needle).
4. Rinse the resin three times to remove any remaining stannous pyrophosphate. For each rinse add 2 ml of non-bacteriostatic normal saline to the resin vial, shake well and withdraw the supernate using a syringe and 26-gauge needle.
5. Add 1-2 mCi of pertechnetate (Tc-99m) in 2 ml of nonbacteriostatic normal saline to the resin vial. Shake and then place the resin vial in an ultrasonic water bath for 10 min.
6. To remove any unbound pertechnetate from the final resin, withdraw the supernate with a syringe and 26 gauge needle. Rinse the Tc-99m Chelex-100 resin with an additional 2 ml of normal saline, and withdraw.
7. Labeling efficiency

$$= \frac{\text{activity Tc-99m Chelex-100 resin}}{\text{activity Tc-99m Chelex-100 resin + activity final rinses (Step 6)}} \times 100$$

**Stability of the Tc-99m Chelex-100 resin.** Several (N = 5) preparations of the Tc-99m Chelex-100 resin (0.5 g, 1100-1900 $\mu$Ci) were mixed with 5-ml volumes of both stimulated gastric juice U.S.P. and simulated intestinal fluid U.S.P., then incubated for 24 hr at 37°C. Since the Tc-99m Chelex-100 resin is to be mixed with a hot meal, its heat stability was also examined following incubation of the resin vial for 10 min in a boiling-water bath. One-hour blood samples and 24-hr urine collections were obtained from five human subjects to monitor in-vivo stability.

**Meal formulation.** One millicurie of the Tc-99m Chelex-100 resin was uniformly mixed with a one-ounce packet of instant oatmeal, one packet (~3.5 g) of sugar, and 100 ml of hot whole milk. This meal has a final volume of 115 ml and provides 178 calories from 8.2 g simple carbohydrate, 17.0 g complex carbohydrate, 3.4 g animal protein, 5.0 g vegetable protein, and 5.4 g fats. The meal is prepared in and eaten from a disposable plastic dish using a disposable plastic spoon.

**Settling behavior of the Tc-99m Chelex-100 resin/oatmeal combination.** Four ounces of the Tc-99m Chelex 100 resin/oatmeal combination was mixed vigorously with simulated gastric juice U.S.P. to a total volume of 600 ml. The mixture was divided into four, 150-ml aliquots, which were permitted to settle. At 15, 30, 45, and 60 min the content of the beakers were aspirated from the surface in 30-ml aliquots, resulting in five layers, each of which was counted for radioactivity. The layers were subsequently dried, weighed and activity expressed as percent of total dry weight.

**Imaging and data processing.** All studies were performed after an overnight fast; tobacco and other drugs were omitted for at least 24 hr. The study population included nine normal, healthy volunteers (7 male, 2 female); 20 morbidly obese patients studied before and

**TABLE 2. SETTLING PROPERTIES OF Tc-99m CHELEX-100 RESIN OATMEAL IN SIMULATED GASTRIC JUICE**

| Aliquot number | Time of settling (minutes) 15 | | 30 | | 45 | | 60 | |
|---|---|---|---|---|---|---|---|---|
| | A* | B† | A | B | A | B | A | B |
| 1 (top) | 0.2 | 6.1 | 0.3 | 5.3 | 0.3 | 4.9 | 0.6 | 6.6 |
| 2 | 0.3 | 6.3 | 0.4 | 6.7 | 0.5 | 5.5 | 0.3 | 5.3 |
| 3 | 1.5 | 10.2 | 12.4 | 18.4 | 3.3 | 15.0 | 0.2 | 4.8 |
| 4 | 43.0 | 26.7 | 45.4 | 21.6 | 50.2 | 35.0 | 43.3 | 18.5 |
| 5 (bottom) | 55.0 | 50.7 | 41.5 | 48.0 | 45.7 | 39.6 | 55.6 | 64.8 |

* A = % of total radioactivity.
† B = % of total dry weight.

**TABLE 3. PARAMETERS OF GASTRIC EMPTYING STUDIED USING Tc-99m CHELEX-100 LABELED SOLID-PHASE TEST MEAL [MEAN ± s.e. (n)]**

| | Time to peak | Emptying half-time | % Residual activity at 1 hr |
|---|---|---|---|
| Normal volunteers | 5.27 ± 2.10 (9) | 43.88 ± 7.45 (9) | 32.77 ± 6.59 (9) |
| Morbid obesity, preoperative | 13.88 ± 1.68 (20) | 63.75 ± 4.45 (20) | 50.30 ± 3.63 (20) |
| Morbid obesity, postoperative | | | |
| Proximal compartment | 2.97 ± 1.03 (18) | 13.32 ± 2.61 (18) | 3.33 ± 1.76 (18) |
| Distal compartment | 14.00 ± 2.55 (20) | 56.47 ± 8.13 (20) | 37.57 ± 5.94 (20) |
| Dumping syndrome | 2.97 ± 0.95 (5) | 16.38 ± 2.17 (5) | 10.60 ± 4.08 (5) |
| Pyloric obstruction | 12.29 ± 3.73 (7) | 143.14 ± 22.76 (7) | 79.00 ± 3.98 (7) |
| Diabetic gastroparesis | 12.00 ± 3.56 (5) | 143.99 ± 36.96 (5) | 74.20 ± 5.99 (5) |

after gastroplasty (Gomez or Mason procedures); 12 patients suspected of physical or functional gastric-outlet obstruction (n = 7) or of dumping syndrome (n = 5) following previous upper gastrointestinal surgery; and five patients with well-documented diabetic autonomic neuropathy. Informed consent was obtained from each subject.

Anterior abdominal images were obtained with the subject sitting erect in front of a wide-field-of-view gamma camera (low-energy, parallel-hole collimator) interfaced to a computer. Data acquisition began at the onset of meal ingestion, with collection and storage of 20-sec frames for the next hour. Qualitative examination of gastric emptying was based on a series (n = 30) of 2-min analog images. Background-subtracted, decay-corrected, time-activity curves for gastric emptying were obtained using a gastric region of interest defined from the summation of images obtained over the first 5 min of the study. The following parameters were derived from these time-activity curves: time to peak activity, $t_{1/2}$ for gastric emptying, and percent residual gastric content at 1 hr.

**Radiation dosimetry estimates.** The dosimetry estimates presented in Table 1 assume a nonabsorbable, nonadsorbable Tc-99m agent with normal gastrointestinal kinetics/residence times: stomach—1 hr, small intestine—4 hr, upper large intestine—13 hr, and lower large intestine—24 hr.

## RESULTS

Using the outlined procedure, Tc-99m Chelex-100 resin can be prepared in approximately 20 min with an average labeling efficiency of 98.5% (n = 74, range 93.5–99.9%). This high degree of labeling efficiency agrees with previously described studies that involved greater manipulation of the Chelex-100 resin during the labeling procedure (*13*). The in-vitro incubation studies indicate that the Tc-99m Chelex-100 resin is stable, losing an average of only 0.7% of the total activity in simulated gastric fluid U.S.P., 5.1% in simulated intestinal fluid U.S.P., and 0.11% upon heating in a boiling-water bath. The Tc-99m Chelex-100 resin also demonstrated very little decomposition in vivo. An average of only 0.045% of the administered Tc-99m appeared in the blood at 1 hr, with only 0.41% appearing in the 24-hr urine collection.

The Tc-99m Chelex-100 resin/oatmeal test meal was found to be palatable, with no observed adverse reactions. The data presented in Table 2 demonstrate that this resin remains distributed in the solid phase of the test meal upon incubation in simulated gastric juice and following a period of phase separation. The settling properties of the resin closely resemble those of the oatmeal.

Gastric emptying parameters for normal subjects and for patients are presented in Table 3. Note that in the morbidly obese patients treated by means of gastroplasty (Gomez or Mason), the stomach is divided into a small-volume proximal compartment that communicates with the rest of the stomach (distal compartment) by means of a narrow stoma (9–11 mm diameter) (*15*). Of interest is the fact that prompt passage of the test meal occurs from the proximal to the distal compartment. The distal stomach subsequently empties normally. The mechanism whereby gastroplasty results in satiety and thus weight loss remains unknown, but does not appear to be due to delay in gastric emptying. Patients with known dumping syndrome show rapid emptying, whereas in those with pyloric outlet obstruction or obstruction at the site of anastomoses it is delayed. These findings are better demonstrated with the Tc-99m Chelex-100 solid meal than with a Tc-99m DTPA liquid test meal based on that of Chaudhuri (*5*). Diabetic gastroparesis also reveals delayed gastric emptying that may respond to metaclopramide, 10 mg i.v.

## DISCUSSION

The procedure described permits the rapid, convenient preparation of a stable Tc-99m resin using commercially available reagents. The Tc-99m Chelex-100 resin can be incorporated into a palatable, small semisolid test meal containing complex and simple carbohydrates,

animal and vegetable proteins, and fat. The normal emptying half-time (range: 24 to 86 min) for this radiolabeled semisolid test meal is considerably longer than that observed for a 500-ml Tc-99m DTPA/water load (range: 6 to 18 min, unpublished results and Ref. 5). On early images the Tc-99m label can be seen to migrate from the fundus to the body and antrum of the stomach. With Tc-99m Chelex resin/oatmeal, the $t_{1/2}$ of emptying obtained in normal subjects is similar to that observed for other small, solid test meals (*1*,*6*,*9*). The slightly longer $t_{1/2}$ observed in morbidly obese subjects has not been studied. This radiolabeled semisolid meal was found to provide a convenient, safe, and effective diagnostic tool to examine gastric emptying function in diabetic patients and in a variety of postoperative situations. In the latter it sometimes provided different and more useful information than liquid test meals.

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