# Experience with Technetium-99m Albumin Colloid Kit for Reticuloendothelial System Imaging

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***The $^{99m}$Tc labeled albumin colloid has been evaluated regarding its particle size, both in vitro and in vivo stability, blood clearance, and efficacy in reticuloendothelial system imaging. The labeling efficiency was always > 99%. The labeled colloid remained stable both in vitro and in vivo for up to 24 hr. The blood clearance curve from four patients had two components: one with a $T_{1/2}$ of 2.48 ± 0.37 min and the other with a $T_{1/2}$ of 271 ± 109 min. Images of the liver, spleen, and bone marrow with $^{99m}$Tc-albumin colloid and $^{99m}$Tc-sulfur colloid showed a similar distribution pattern except that slightly higher splenic uptake relative to the liver was observed with the former. However, $^{99m}$Tc-albumin colloid has the advantage of easy preparation over $^{99m}$Tc-sulfur colloid.***

Technetium-99m sulfur colloid (SC) has been the agent of choice for imaging the reticuloendothelial system since its introduction some 20 yr ago (*1,2*). However, unlike many other kits, $^{99m}$Tc-SC requires several steps of preparation such as adding acid, boiling and adding buffer and, therefore, increases the radiation exposure to personnel in addition to inconvenience. In order to alleviate all these difficulties, a kit* of $^{99m}$Tc labeled microcolloid made of human albumin for reticuloendothelial system imaging has recently been introduced. We have evaluated this colloid regarding its labeling efficiency, size distribution, blood clearance in patients, in vitro and in vivo stability, and also its efficacy compared to that of $^{99m}$Tc-SC. The results are presented in this report.

## MATERIALS AND METHODS

The albumin colloid was supplied as a kit* containing 1 mg albumin colloid, 10 mg normal human serum albumin, 0.17 mg (maximum) total tin (as stannous chloride $SnCl_2$ .2H O), 1.1 mg poloxamer 188, 0.12 mg medronate disodium, and 10 mg sodium phosphate (anhydrous). The $^{99m}$Tc-albumin colloid was prepared by adding 30–40 mCi of [$^{99m}$Tc]pertechnetate in a volume of 3–8 ml to the kit vial and swirling the contents for 1 min.

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### Radiochemical Purity

The radiochemical purity was performed by thin layer chromatography using ITLC-SG paper as the solid phase and methyl ethyl ketone as the solvent. Triplicate experiments were done at different time periods up to 24 hr.

### Colloid Particle Size

The size distribution of $^{99m}$Tc-albumin colloid particles was determined by the use of Nuclepore filters. The size of the filters varied from 0.1 $\mu$m–2 $\mu$m. A 1-ml colloid sample was drawn in a 3-ml syringe, and the activity was measured. The sample was passed through a Nuclepore filter of definite size. [Millipore filters were not used for particle sizing because their pores are tortuous and their thickness is ~ 100 $\mu$m, whereas the pores of Nuclepore filters are cylindrical and their thickness is ~ 10 $\mu$m (*3*).] Ten milliliters of saline were then passed through the filter to wash out any removable activity, and the wash was combined with the filtrate. The activities in the filtrate and the filter were separately measured in a dose calibrator. The percentage of activity retained by the filter gave the percentage of particles greater than the size of the filter. Six experiments were run, and the mean and standard deviations were calculated. In separate experiments, the size of $^{99m}$Tc-SC particles was measured for comparison with that of $^{99m}$Tc-albumin colloid.

### Blood Clearance of $^{99m}$Tc-Albumin Colloid

Into one arm of the patient, 4–5 mCi of $^{99m}$Tc-albumin colloid was injected intravenously. A 4-ml blood sample was collected from the other arm at 2, 5, 10, 15, 20, 30, and 45 min after injection, and the activity in 1 ml of each sample was measured in a NaI(Tl) well counter. Activity was plotted versus time to determine the $T_{1/2}$ of the blood clearance of $^{99m}$Tc-albumin colloid.

### Free $^{99m}$Tc in Plasma

The blood samples collected at 2 min and 45 min after injection were centrifuged at 2,000 g for 5 min, and thin layer

chromatography was done on the plasma using ITLC-SG paper as the solid phase and methyl ethyl ketone as the solvent. The activity at the solvent front was measured and expressed in percentage to estimate the extent of free $^{99m}$Tc.

### Imaging with $^{99m}$Tc-Albumin Colloid

Approximately 4–5 mCi of $^{99m}$Tc-albumin colloid was injected, and imaging of the liver, spleen, and bone marrow was performed 15–20 min after injection in multiple projections using a large-field-of-view camera with a low-energy all-purpose collimator and an energy window of 140 keV ± 10%. For comparison, imaging was repeated with $^{99m}$Tc-SC in six patients 2 days apart from imaging with $^{99m}$Tc-albumin colloid. Scintigraphs were interpreted by two physicians without the reader's knowledge of which radiopharmaceutical was used for the study.

## RESULTS AND DISCUSSION

The labeling efficiency of $^{99m}$Tc-albumin colloid was 99% or more in 13 preparations. The labeled material remained stable in vitro over 24 hr. The size distribution of the particles from six measurements is shown in Table 1. In two experiments, the size of $^{99m}$Tc-SC particles† also was measured. Ninety-three percent of the $^{99m}$Tc-albumin colloid particles were > 0.4 μm in size (Table 1), compared to only 33% of the SC particles in the same range. In addition, 41% of the albumin colloids were > 1 μm with only 16% of the SC particles in this size range. Thus, the mean size of the $^{99m}$Tc-albumin colloid is larger than that of the $^{99m}$Tc-SC.

The blood clearance of $^{99m}$Tc-albumin colloid in a normal patient is presented in Figure 1. The curve represents two components: (a) one with short $T_{1/2}$, and the other with long $T_{1/2}$. The average short $T_{1/2}$ of blood clearance of $^{99m}$Tc-albumin colloid from four patients was 2.48 ± 0.37 min, representing almost 93% of the injected dose, whereas the longer component had a $T_{1/2}$ of 271 ± 109 min, representing 7% of the injected dose. The longer component may be composed of both free $^{99m}$Tc and larger colloid particles ( > 2 μm or so) that are not removed by the reticuloendothelial system nor by the lungs.

Chromatographic analysis of plasma from five different patients indicated ~ 1.0 ± 0.9% and 23.1 ± 8.2% of free $^{99m}$Tc in the plasma activity at 2 min and 45 min, respectively, after injection. Assuming a plasma volume of 3,500 ml for a standard man and from the measurment of total activity in plasma, it was estimated that ~ 61% and 6% of the injected dose remained circulating in plasma at these time periods. Thus, at 2 min postinjection, 0.6% (1% of 60%) of the injected dose is free $^{99m}$Tc, which is the same as that obtained by chromatography of the initial preparation. On the other hand, at 45 min postinjection, 1.4% (23% of 6%) of the injected dose is free $^{99m}$Tc and the remainder is perhaps $^{99m}$Tc-albumin colloid of larger size particles ( > 2 μm) (see Table 1) or may indicate protein-bound $^{99m}$Tc.

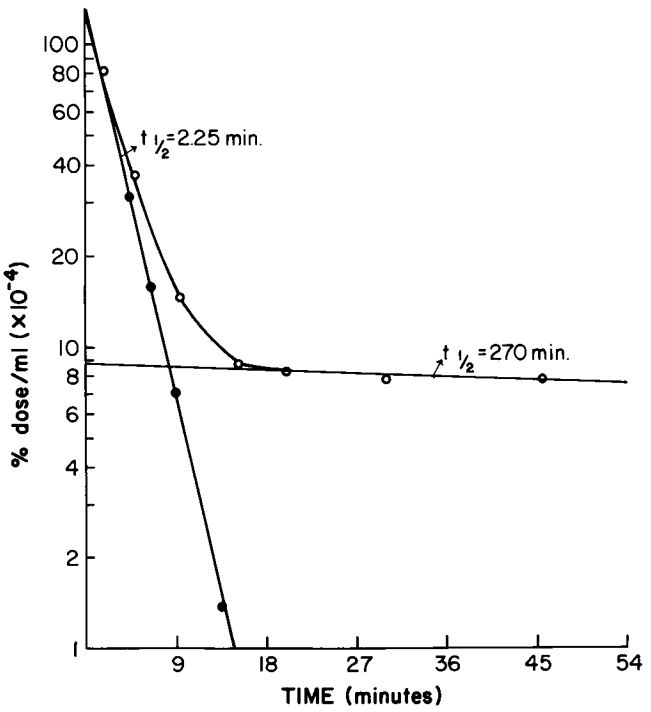


**FIG. 1.** Blood clearance of $^{99m}$Tc-albumin colloid in a normal patient. The curve shows two components: a short-lived component of $T_{1/2}$ = 2.25 min; and a long-lived component $T_{1/2}$ = 271 min.

**TABLE 1. Size Distrubtion of $^{99m}$Tc-albumin Colloid Particles**

| Size (μm) | % Colloid Particles |
|---|---|
| < 0.1 | 6 |
| 0.1 – 0.4 | 1 |
| 0.4 – 0.6 | 8 |
| 0.6 – 0.8 | 22 |
| 0.8 – 1.0 | 22 |
| 1.0 – 2.0 | 34 |
| > 2.0 | 7 |

Thirty-one randomly selected patients suspected of having liver disease were imaged with $^{99m}$Tc-albumin colloid after obtaining informed consent. Of these, six patients were repeated with $^{99m}$Tc-SC 48 hr apart. The scintigraphs of the liver, spleen, and bone marrow of a normal patient obtained with $^{99m}$Tc-albumin colloid and $^{99m}$Tc-SC are shown in Figure 2. Technetium-99m-albumin colloid, as expected, exhibits a normal distribution of the tracer in the liver, spleen, and bone marrow (Fig. 2B) similar to that of $^{99m}$Tc-SC (Fig. 2A) except that $^{99m}$Tc-albumin colloid definitely shows a higher uptake in the spleen relative to the liver. This pattern of increased accumulation of $^{99m}$Tc-albumin colloid has been observed in almost all normal patients and can be erroneously attributed to the presence of mildly diffuse liver disease or splenic disease. The increased splenic uptake may be caused by the larger size of $^{99m}$Tc-albumin colloid particles, as noted by others (*4*). If one can accept this higher spleen-to-liver ratio index

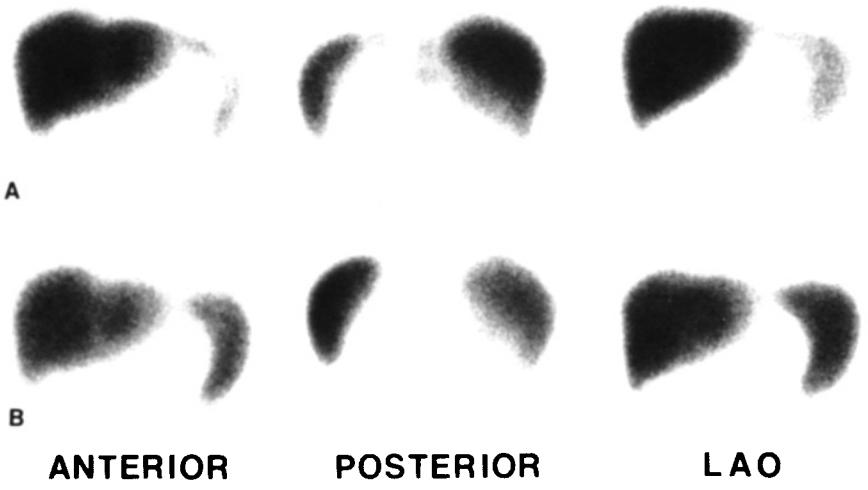


**FIG. 2.** Scintigraphs of the liver, spleen, and bone marrow in a normal patient with (A) $^{99m}$Tc-SC and (B) $^{99m}$Tc-albumin colloid in anterior, posterior, and left anterior oblique projections. The scintigraphs were obtained 48 hr apart. Higher splenic uptake relative to the liver is seen with $^{99m}$Tc-albumin colloid than with $^{99m}$Tc-SC.

as a normal variant, the $^{99m}$Tc-albumin colloid can be a satisfactory substitute for $^{99m}$Tc-SC.

Use of albumin microcolloid labeled with $^{131}$I (*5,6*) and $^{99m}$Tc (*6*) for reticuloendothelial imaging was reported previously, but only limited success was obtained. In addition, there are disadvantages of using $^{131}$I in imaging because of its high energy photons and higher radiation dose. Although $^{99m}$Tc-SC is used routinely, its method of preparation is inconvenient and adds unnecessary radiation exposure to personnel during preparation. The $^{99m}$Tc-albumin colloid supplied as commercially available kits can be a reasonable substitute for $^{99m}$Tc-SC. The cost may be a factor in deciding to use it routinely. The ease and convenience of preparation, however, makes it a more desirable colloid kit and may outweigh the cost factor.

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## FOOTNOTES

*Microlite, Du Pont Company, No. Billerica, MA.
†Mallinckrodt, St. Louis, MO.

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