Preparation and Clinical Use of ^{99m}Tc–MAA

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Since its introduction in nuclear medicine (*1*), the advantages of ^{99m}Tc in organ imaging have been well accepted. However, ^{99m}Tc-labeled MAA for lung imaging has not been available on a commercial basis. Therefore we have prepared ^{99m}Tc-MAA in our laboratory for clinical use, modifying the procedures previously described (*2-5*). The procedure is simple and reproducible, yielding a product which results in lung scans of good quality.

Procedure

A 5-cm resin column is prepared in a 12-ml disposable syringe barrel, using Dowex 1X8 exchange resin (ionic form Cl^-, 20-50 mesh). Three to 400 ml of sterile, pyrogen-free water are then flowed through the system at the rate of 10-15 ml/min.

Labeling of the albumin is performed under the hood. Fifty to 100 mCi of concentrated ^{99m}Tc-sodium pertechnetate (1-4.5 ml) is added to a 15-ml disposable beaker. While stirring, 5 mg ferric chloride, 20 mg ascorbic acid, and a sufficient amount of sodium hydroxide (2 *N*) are added to achieve a pH of 8.5-9.0. Twenty-five milligrams of human serum albumin are added and the pH is adjusted to 1.5-2.0 with hydrochloric acid (2 *N*). Stirring is continued for 3 min and pH is readjusted to 7.5-8.0 with sodium hydroxide (2 *N*). The pH is again readjusted to 2.0 with hydrochloric acid (2 *N*). The suspension is allowed to set for 5 min. The labeled albumin is then passed through the Dowex anion exchange resin column at a rate of 2 ml/min into a 50-ml syringe containing 10 ml sterile, pyrogen-free sodium chloride, 2.5 ml acetate buffer (pH 5.4), 0.2 ml 5% of tween 80, and 2-4 drops sodium hydroxide (2 *N*). The beaker is rinsed with sodium chloride and passed through the resin column to obtain a volume of 25 ml in the 50-ml syringe. The plunger of this 50-ml syringe is inserted and the solution forced through a 0.22-micron sterile Millipore filter into a sterile 100-ml vial at a rapid rate without foaming. The vial is vented with a 22-gage needle. The sterile ^{99m}Tc-albumin is then shaken lengthwise in the hot water bath (88-89°C) at 150-200 strokes per minute for 3½ min. The vial is transferred to a 40°C water bath for 1 min, then to an ice water bath for 3 min. The procedure usually requires 25 min.

Quality Control

Particle size. The macroaggregates were examined under the microscopes at low and high power using a hemocytometer and an ocular micrometer. Eighty-three percent of the particles ranged between 10 and 50 microns in diam with 96% between 10 and 75 microns (Table 1).

Organ distribution. Three white mice weighing approximately 20 gm were injected with 0.1 ml of the MAA solution and sacrificed 5 min later. The distribution of radioactivity in the lungs, liver, kidneys, gastrointestinal tract, and carcass minus

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Table 1. Summary of ^{99m}Tc-MAA Radiopharmaceutical (200 Lots)

	Mean	s.d.	Range	
mCi/ml ^{99m}Tc-MAA	3.2	± 0.8	1.2	5.6
pH ^{99m}Tc-MAA	5.4	± 0.1	5.2	5.85
Particle size (%):				
10-25 μ	24	± 12	1	58
25-50 μ	59	± 8	40	79
50-75 μ	13	± 7	1	35
75-100 μ	3	± 3	0	14
100-150 μ	1	± 1	0	4
10–75 μ range	96	± 3	82	100
Organ distribution:				
% lungs	87.8	± 3	79.0	93.4
% liver	2.6	± 0.8	1.1	4.5
% kidneys	0.9	± 0.2	0.5	1.8
% GI tract	2.2	± 0.6	1.1	4.2
% Carcass	6.4	± 1.7	3.4	11.4
Lung: liver ratio	39	± 14	17	85

tail are then determined. The mean lung uptake of 200 preparations was 87.8% with a lung-to-liver ratio of 39:1. Tissue distribution is summarized in Table 1.

Other safety tests. Pyrogen and sterility tests were performed in accordance with the methods described in the U.S.P. The percent unbound pertechnetate was determined by descending paper chromatography in 85% methanol using Whatman No.1 paper. The percent of unlabeled technetium ranged from 0.9 to 4.8%.

Results

Laboratory. We have prepared 200 batches of ^{99m}Tc-MAA using the method described. Fifteen were found unsuitable for clinical use. Four preparations resulted in a lung-to-liver ratio of less than 20:1, with less than 80% in the lungs. Eight batches had more than 3% unbound pertechnetate and three produced aggregates that were greater than 150 microns. Two were due to the reaction of NaOH with the hypodermic needle, and one was a result of an insufficient water level in the shaker bath. Five bottles broke when transferred into the ice water bath. This problem was subsequently solved by cooling in a 40° C bath for 1 min before the ice bath. All batches tested were sterile and pyrogen free.

Clinical. Over 200 rectilinear lung scans were performed using this ^{99m}Tc-MAA. Studies were performed for the following reasons: suspected pulmonary embolism, 128; preoperative evaluation for open-heart surgery, 65; followup for pulmonary embolism, 33; cancer of the lung, 4; subphrenic abcess, 2; coronary artery disease with emphysema, 1; pulmonary metastases, 1. Four of these patients were scanned six times with no adverse reactions. One patient who was allergic to iodine was scanned three times without incident. A total of 164 patients were imaged, several in serious condition. The ages of the patients ranged between 24 and 82 years. Table 2 shows the number of lung scans performed on each patient. The mean dose injected was 2.04 mCi in a mean volume of 1.4 ml. Table 3 provides patient data.

Table 2. Patients Scanned with ^{99m}Tc-MAA

No. of scans	1	2	3	4	5	6
No. of patients	127	24	3	4	2	4

Table 3. Patient Data (234)

	Mean	Range
mCi/dose	2.04	1.00 - 2.30
ml/dose	1.4	0.5 - 3.6
AP count	153 K	70 K - 260 K
LAT count	117 K	60 K - 170 K
Age	52	24 - 82
Weight (kg)	74.5	40.9 - 136.4

Summary

Labeling of human serum albumin with ^{99m}Tc and the subsequent formation of macroaggregates have yielded a very satisfactory product for lung scanning. The agent was safe and relatively simple to prepare. No untoward reactions were noted in over 200 patient scans. As expected, the quality of lung scans was superior to those obtained with ^{131}-I-MAA.

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References

1. Harper PV, Andros G, Lathrop KA: Preliminary observations on the use of six-hour Tc^{99m} as a tracer in biology and medicine. *Semiannual Report to the Atomic Energy Commission*, Jacobson LO, ed, ARCH-18, 1962, pp 76-87

2. Stern HS, McAfee JG, Zolle I: Technetium 99m-albumin. In *Radioactive Pharmaceuticals*. Andrews GA, Kniseley RM, Wagner HN, eds. USAEC Symposium Series 6, CONF - 651111, Springfield, Va, Dept. of Commerce, 1966, pp 359-382

3. Gwyther MM, Field EO: Aggregated Tc^{99m} labeled albumin for lung scintiscanning. *Int J Appl Radiat* 17:485-486, 1966

4. Surprenant EL, Webber MM, Bennett LR: Technetium lung scanning. *Int J Appl Radiat* 20: 77-79, 1969

5. Bowen BM, Wood DE: The radiopharmacist in nuclear medicine—preparation of technetium-99m human serum albumin macroaggregates. *Am J Hosp Pharm* 26: 529-534, 1969