# CLINICAL EVALUATION OF AN INSTANT KIT FOR PREPARATION OF $^{99m}$Tc-MAA FOR LUNG SCANNING

Ramesh Chandra, Jack Shamoun, Philip Braunstein, and Oro L. DuHov

*New York University Medical Center, New York, New York*

***A commercially available kit for the preparation of $^{99m}$Tc-MAA for lung scanning has been evaluated in 45 patients. The effective half-life in the lungs of this preparation was found to be 236± 30 min in seven patients. The radiation dose/mCi to the lungs, liver, and kidneys is estimated to be 0.28, 0.08, and 0.16 rad, respectively, from the biological data obtained on seven patients. The preparation is very simple, and the use of $^{99m}$Tc-MAA instead of $^{131}$I-MAA has resulted in improvement of image quality and reduction of the time of study as well as radiation dose to the patient.***

Lung scanning that uses $^{131}$I-labeled macroaggregated human serum albumin ($^{131}$I-MAA) was initially introduced by Taplin, et al (*1*) and Wagner, et al (*2*). This procedure has since become a recognized diagnostic aid in certain pulmonary diseases. The most common radiopharmaceutical used for this purpose still remains $^{131}$I-MAA. Because of the high patient radiation dose and the relatively high gamma-ray energy of this agent, a search by several workers (*3–6*) for a better radiopharmaceutical has led to the successful development of $^{99m}$Tc-MAA. Technetium-99m possesses desirable properties for in vivo imaging, e.g., a 6-hr half-life, a single 140-keV gamma-ray emission, and ready availability. The published labeling techniques (*3–6*) are relatively complex. They usually require the services of a radiopharmacist and are not practical for routine use in the great majority of nuclear medicine facilities.

Indium-113m-labeled $Fe(OH)_3$ macroaggregates (*7,8*) and $^{99m}$Tc-$Fe(OH)_2$ (*9,10*) have also been used for lung scanning. These radiopharmaceuticals possess similar advantages over $^{131}$I-MAA as $^{99m}$Tc-MAA. Even though the preparation techniques are simpler for these radiopharmaceuticals, these macroaggregates are reported to be retained in the lung for a long time, and therefore there are some questions about their long-term safety (*11,12*).

Recently several workers have reported the preparation of simple kits for labeling MAA with $^{99m}$Tc (*13–16*). This communication concerns the clinical evaluation of just such a simple, one-step kit that will be commercially available.

A search of the published literature reveals a lack of details with regard to clinical evaluation and the biological behavior of $^{99m}$Tc-MAA in patients. Much of the published literature is in the form of abstracts. Additional data regarding excretion and effective half-life in the lungs in several patients with this preparation of $^{99m}$Tc are also presented.

## MATERIALS AND METHODS

The MAA kits* were supplied in the form of vials, each containing 0.13 mg stannous chloride, 1.5 mg heat denatured human serum albumin, and 10 mg normal human serum albumin. The labeling of $^{99m}$Tc-MAA was performed by injecting 3 ml of sterile sodium pertechnetate ($^{99m}TcO_4^-$) solution slowly into the vial and then shaking gently by hand for 3–5 min with the vial in a lead container. Labeling efficiency was determined by ascending paper chromatography using Whatman No. 1 paper and 85% methanol. The size of the particles was determined microscopically using a hemocytometer. Forty-five patients who were referred to the Nuclear Medicine Department for lung scanning were injected with 2–3 mCi of $^{99m}$Tc-MAA (0.1–0.5 ml) intravenously in the supine position. The total num-

Received Dec. 27, 1972; revision accepted Mar. 25, 1973.

For reprints contact: Ramesh Chandra, New York University Medical Center, 560 First Ave., New York, N.Y. 10016.

* Macrotec, courtesy of E. R. Squibb & Sons, Inc., Princeton, New Jersey.

ber of MAA particles is estimated to be between 60,000 and 300,000 per injected dose. An Anger camera with a medium-energy diverging collimator was used for imaging. Four views—anterior, posterior, and right and left laterals—were obtained in most instances. A total of 200,000 counts per view was collected. In addition, on seven patients data were also collected by counting with an external probe over the lungs, liver, and kidneys at various time intervals postinjection for up to 3 days. From these patients urine was also collected for three successive 24-hr periods following injection of the radiopharmaceutical. Blood activity was measured at 15 min, 4 hr, and 24 hr postinjections. In all patients, temperature, pulse, and respirations were monitored before the start of the procedure and then 1, 8, 16, and 24 hr after injection. The patients were also closely observed for any evidence of side effects during this 24-hr period.

## RESULTS AND DISCUSSION

Microscopic examination of $^{99m}$Tc-MAA revealed that most of the particles (over 90%) ranged in size between 15 and 75 microns. On two occasions, larger particles (up to 250 microns) were also observed. Further gentle agitation for about 3 min was quite effective in eliminating these oversized particles. The $^{99m}$Tc-MAA preparations contained approximately 500,000 macroaggregates per ml. The specific activity of the preparations varied between 2 and 6 mCi/mg of human serum albumin, depending upon the specific activity of $^{99m}TcO_4^-$ used. The labeling efficiency of $^{99m}$Tc to MAA was found to be greater than 90% for the more than 15 preparations tested.

Results of external counting over the lungs are shown in Fig. 1. These represent the averages of seven patients. The data can be fitted into a single exponential with an effective half-life of 236 ± 30 min. The biological half-life of MAA in the lungs using the above effective half-life works out to be 11.5 ± 4 hr. This value is slightly higher than that determined by DeLand (*17*) using $^{131}$I-MAA (9 hr). As monitored with an external probe, the accumulation of radioactivity in the liver and kidneys is shown in Fig. 2. The data in these curves (average values in the same seven patients) have been corrected for physical decay. The accumulation in the liver and kidneys of various breakdown products of $^{99m}$Tc-MAA approaches a broad maximum at about 20 and 10 hr, respectively. These findings are compatible with those of $^{131}$I-MAA and support the view that macroaggregated albumin particles are broken down into microaggregated albumin particles and free technetium. The microaggregates are largely

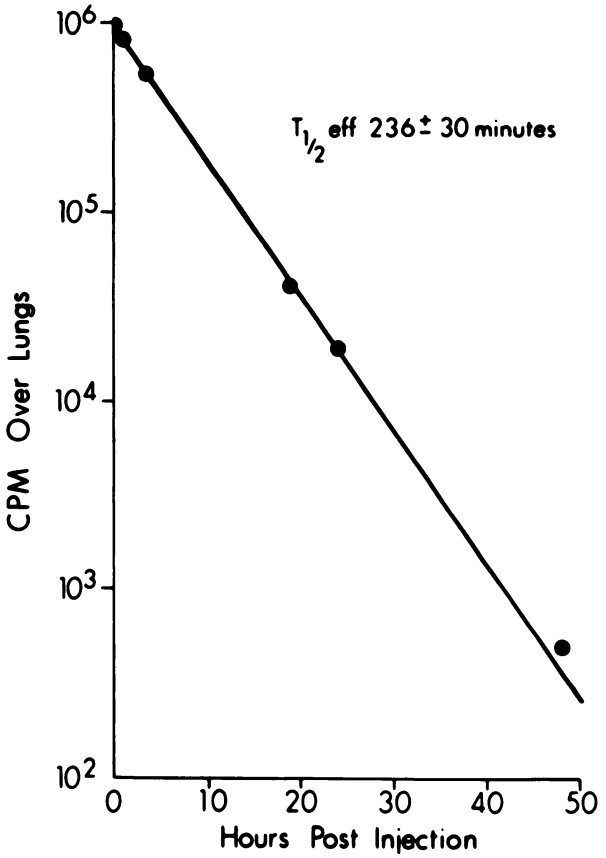


**FIG. 1.** Counts per minute (cpm) over lungs as function of time. Data were obtained with NaI(Tl) detector placed over lungs and are averages of seven patients without any correction of physical decay.

removed by the liver. Some of the free technetium is excreted and some appears to be taken up by the kidneys. Kidney uptake is supported by our counting data as well as by visualization of the kidney after 3 hr in patients who were specially imaged to show this. It is worth noting that the breakdown products of $^{131}$I-MAA are not taken up in the kidneys. Urinary excretion data in these patients are shown in Fig. 3. Only 50–60% of the injected dose was found to be excreted in 72 hr. This is consistent with the long biological half-life of the decay products observed in the kidneys and liver (Fig. 2). The radioactivity detected in the blood at 15 min, 4, and 24 hr did not reveal much variation and was always less than 0.015% of the injected dose per 100 ml of blood. The 24 hr activity (counts/ml) ranged between ½ and ⅔ of the 4-hr value.

Using the above data, our estimates for the radiation dose to the lungs, kidneys, and liver are 0.28, 0.16, and 0.08 rad/mCi of $^{99m}$Tc-MAA, respectively. The estimated doses to the lungs, liver, and kidneys were obtained by using the absorbed fraction method as outlined in MIRD Pamphlet No. 1. The cumulated concentration in the lungs was obtained from the

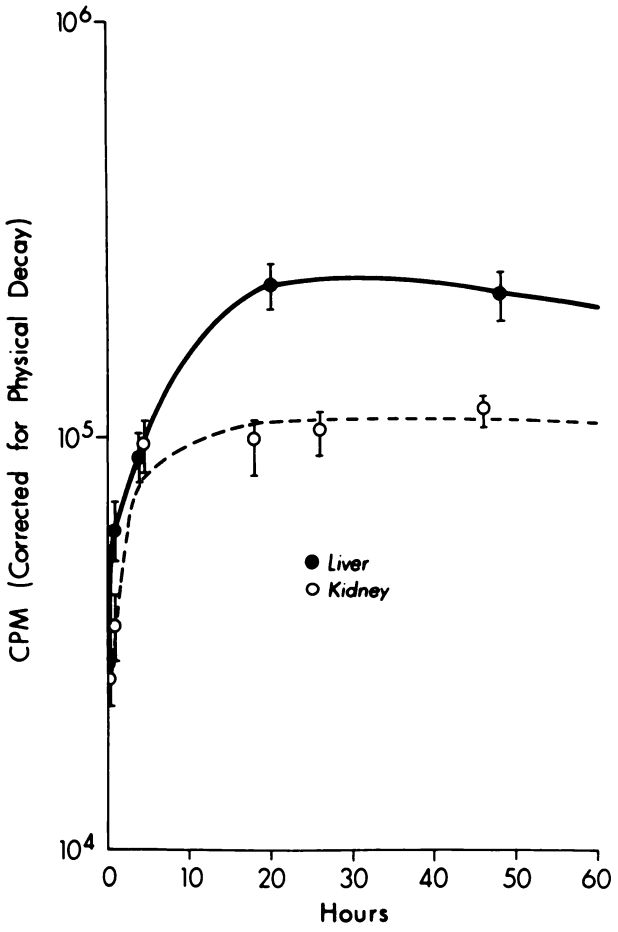


**FIG. 2.** Counts per minute (cpm) over liver and kidneys as function of time. Data were obtained with NaI(Tl) detector placed over liver and kidneys, respectively, and are averages of same seven patients. Data in this case have been corrected for physical decay.

average effective half-life given in Fig. 1. The cumulated concentration in the liver and kidneys was obtained by assuming that the breakdown products of $^{99m}$Tc-MAA were rapidly taken up by the liver or kidneys, or were excreted. This assumption is supported by the observation that the amount of the radioactivity in the blood is small at all times. The respective fractions of liver and kidney uptakes, and excretion were estimated to be 0.5, 0.3, and 0.2, respectively, on the basis of our external counting data and the distribution data in rats (*18*). The cumulated activity in liver and kidneys is then calculated by

$$\tilde{A}\ \text{liver} = 0.5\ Ro \times 1.44 \times \frac{T_{1/2}\ \text{eff. lungs.} \times T_{1/2}\ \text{phy.}}{T_{1/2}\ \text{bio. lung}},$$

$$\tilde{A}\ \text{kidney} = 0.3\ Ro \times 1.44 \times \frac{T_{1/2}\ \text{eff. lungs.} \times T_{1/2}\ \text{phy.}}{T_{1/2}\ \text{bio. lung}},$$

where Ro is the initial activity in the lungs (1,000 $\mu$Ci), $T_{1/2}$ eff. lung and $T_{1/2}$ bio. lung are the effective and biological half-lives of $^{99m}$Tc-MAA in the lungs, respectively, and $T_{1/2}$ phy. is the half-life of $^{99m}$Tc. The derivation of these equations is straightforward.

As anticipated, the quality of images obtained in a given time with this material was felt to be superior to that of images obtained with $^{131}$I-MAA and essentially comparable to those obtained with $^{99m}$Tc-microspheres. In some of the earlier scans a distinct blotchiness was evident, particularly on the lateral projection; this is presumed to have been due to the presence of extra large particles in the preparation as described above. It was not noticeable when extra care was taken to agitate the vials sufficiently. The time taken to accumulate 200,000 counts for each view was in the range of 2–3 min. This represents a significant saving in time per patient examination when compared to $^{131}$I-MAA in which each view (30,000 counts) takes roughly 10–12 min. Improved sensitivity should be obtainable with the low-energy divergent collimators that are expected to be commercially available. This might make it feasible to obtain images free of respiration artifacts.

In none of the 50 patients was there evidence of significant change in temperature, pulse, or respiratory rate; indeed, there were no detected clinical symptoms or signs attributable to the $^{99m}$Tc-MAA preparation during the 24 hr of close observation following injection. Subacute toxicity studies in dogs showed no evidence of pathological changes in the lungs, liver, or kidneys (*18*). The MAA part of the preparation is essentially the same as that used in

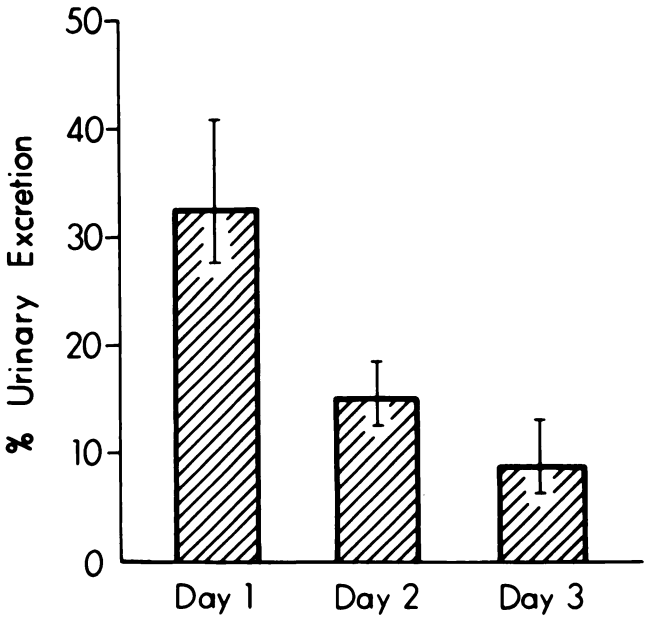


**FIG. 3.** Average urinary excretion of $^{99m}$Tc for three successive 24-hr periods in seven patients.

$^{131}$I-MAA; Taplin, et al (*19*) reported finding no evidence of immunological reactions to $^{131}$I-MAA.

## CONCLUSION

The predictable advantages of using $^{99m}$Tc-labeled particles (as opposed to $^{131}$I) for lung scanning have been described by others. This study confirms the advantages from the point of view of patient radiation dose, time required per examination, and the quality of the resultant image. Unfortunately, the difficulties in the adequate preparation of such labeled particles have limited their use. With this type of kit, $^{99m}$Tc-MAA particles may be prepared quickly and simply, and no extra equipment of any kind is required. This should bring the capability of using $^{99m}$Tc in lung scanning to most facilities.

## REFERENCES


*1.* TAPLIN GV, DORE EK, KAPLAN H: Colloidal radioalbumin aggregates for organ scanning. Scientific exhibit, 10th annual meeting Society of Nuclear Medicine

*2.* WAGNER HN, SABISTON DC, MCAFEE JG, et al: Diagnosis of massive pulmonary embolism in man by radioisotope scannnig. *New Eng J Med* 271: 377–384, 1964

*3.* PETERSON CC, BONTE FJ: Technetium-99m macroaggregated albumin: A new lung scanning agent. *Int J Appl Radiat* 18: 201–202, 1967

*4.* STERN HS, ZOLEE I, MCAFEE JG: Preparation of technetium ($^{99m}$Tc) labeled serum albumin (human). *Int J Appl Radiat* 16: 283–288, 1965

*5.* BENJAMIN P: A rapid and efficient method of preparing $^{99m}$Tc human serum albumin: Its clinical application. *Int J Appl Radiat* 20: 187–194, 1969

*6.* DWORKIN HJ, GUTKOWSKI RF: Rapid closed system production of $^{99m}$Tc albumin using electrolysis. *J Nucl Med* 12: 562–565, 1971

*7.* STERN HS, GOODWIN DA, WAGNER HN, et al: $^{113m}$In—A short lived isotope for lung scanning. *Nucleonics* 24: No 10, 57–59, 1966

*8.* POTCHEN EJ, ADATEPE M, WELCH M, et al: Indium-In 113m for visualizing body organs. *JAMA* 205: 208–212, 1968

*9.* BOYD RE, ACKERMAN SA, MORRIS JG, et al: Lung scanning using $^{99m}$Tc-labeled macroaggregated ferrous hydroxide (Tc-MAFH) as the perfusion agent. *J Nucl Med* 10: 737–739, 1969

*10.* DAVIS MA: $^{99m}$Tc-iron hydroxide aggregates: Evaluation of a new lung scannnig agent. *Radiology* 95: 347–352, 1970

*11.* BARKER SL, GUSMANO EA, SMITH TD, et al: Retention of $^{113m}$In-$^{59}$Fe-ferric hydroxide in the mouse. *J Nucl Med* 12: 5–7, 1971

*12.* GOODWIN DA: Comments by the author: Lung retention of labeled ferric hydroxide macroaggregates used in lung scanning. *J Nucl Med* 12: 580–581, 1971

*13.* ALVAREZ J, MASS R, ARRIAGA C: Experience in humans with multilabeled lung scanning agent. *J Nucl Med* 13: 409, 1972

*14.* DEUTSCH ME, REDMOND ML: Unitary freeze-dried kits for preparation of technetium-labeled human serum albumin. *J Nucl Med* 13: 426–427, 1972

*15.* ROBBINS PJ, FORTMAN DL, LEWIS JT: A kit for the rapid preparation of $^{99m}$Tc-macroaggregated albumin. *J Nucl Med* 13: 463–464, 1972

*16.* SUBRAMANIAN G, ARNOLD RW, THOMAS FD, et al: Evaluation of an instant $^{99m}$Tc-labeled lung scanning agent. *J Nucl Med* 13: 790, 1972

*17.* DELAND FH: The fate of macroaggregated albumin used in lung scanning. *J Nucl Med* 7: 883–895, 1966

*18.* BRUNO G: Personal communication, New Brunswick, NJ, ER Squibb & Sons, Inc.

*19.* TAPLIN GV, JOHNSON DE, DORE EK, et al: Suspensions of radioalbumin aggregates for photoscanning the liver, spleen, lung, and other organs. *J Nucl Med* 5: 259–275, 1964