Clinical Evaluation of a New $^{99m}$Tc-MAA Kit for Lung Scanning

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Lung scanning has been recognized as a clinically useful technique for portraying macroscopic pulmonary perfusion defects since it was first reported by Wagner in 1964 (1). A number of radiopharmaceuticals have been proposed to assess pulmonary perfusion. Although $^{131}$I imposes many limitations as a radiotagging agent, the use of iodinated macroaggregated albumin (I-MAA) has received wide acceptance as the agent of choice. The desirability of $^{99m}$Tc as a scanning agent, especially for static imaging systems, has long been recognized and leads to the ultimate development of $^{99m}$Tc-tagged human albumin microspheres (Tc-HAM) (2). Technetium-99m-labeled macroaggregated albumin (Tc-MAA), although desirable, has not been exploited for lung scanning because of the technical requirements encountered during its preparation (3).

Recently, a lyophilized macroaggregated albumin kit (Macrotec) for preparing Tc-MAA has undergone field trials by E.R. Squibb & Sons. Preparation of Tc-MAA from this kit yields a stable product which on standing may be used without resuspension and rewashing the tagged particles to remove sequestered technetium. Preparation and clinical evaluation of the Macrotec kit was undertaken in our laboratories from July 1972 to February 1973 and is the subject of this report.

Materials and Method

Macrotec ($^{99m}$Tc-Sn-MAA) is a lyophilized, sterile preparation containing 1.5 mg denatured human serum albumin, 0.13 mg stannous chloride (SnCl$_2$•2H$_2$O) and 10 mg normal serum albumin in each vial. The contents are reconstituted with 1–3 ml of eluate containing $^{99m}$Tc-pertechnetate from a molybdenum-technetium generator. For our investigation we reconstituted with 3 ml fixed volume of eluate containing 20 mCi $^{99m}$Tc-pertechnetate and gently swirled the vial to prevent particle fracture. By establishing a fixed volume containing 20 mCi of eluate, we were able to control and reproduce the agent by maintaining the specific activity at 0.075 mg/mCi of serum albumin for each injected dose. Administering less than 0.025 mg/mCi of serum albumin produced lung images that were mottled in appearance due to the inadequate number of particles in the injected volume.

Size specifications require that at least 90% of the particles must range between 10 and 100 microns with none over 150 microns. In our investigation, particle size and concentration were measured by using a phase microscope and standard hemocytometer techniques (Fig. 1). Paper chromatography of the final preparation was carried out to determine the percent labeling of $^{99m}$Tc to the MAA particles. The destructive ascending paper chromatography technique described by Gutowski (4) using Whatman No. 1 chromatographic paper in an 85% methanol-water interface was employed (Fig. 2). Before submission to destructive chroma...
tography, the chromatograph was placed in a cel­
lophane bag to prevent contamination and then
placed on our scintillation camera detector head
where a scintiphoto was made. The resulting pic­
ture permitted a qualitative assessment of tech­
netium to particle binding (Fig. 3).

One hundred subjects presented to the labora­
tory for routine evaluation of pulmonary perfusion
were administered 3 mCi of the Tc-MAA intrave­
rously without premedication. Three of these pa­
tients were selected to be control subjects for de­
termination of clearance time for Tc-MAA from
the lungs, organ distribution, and excretion. Exter­
nal port counts were taken over the lungs and liver
during the 72-hr period postinjection. Urinary ex­
cretion was measured for radioactivity with 24-hr
collection specimens for 3 days. In addition, blood
samples were taken periodically for 24 hr following
injection for measurement of radioactivity. Tem­
perature, pulse, and respiration of all subjects
studied were noted for 24 hr after administration
of the scan agent. Eight-view lung scans, including
anterior, posterior, left and right laterals, with an­
terior and posterior oblique views of both lungs
were obtained with a scintillation camera. Total
accumulated activity per view averaged 500,000
counts and required approximately 1 min with a
3-mCi dose. Selected interesting cases were re­
studied the following day with either I-MAA or
Tc-HAM for comparative lung scan quality using
the identical scanning projections.

Results
Particle preparation. Control studies were per­
formed on each batch of Tc-MAA produced during
the course of this study. Particle size was assessed
with phase microscopy which showed that particles
ranged in size from 10 to 120 microns. The major­
ity of particles produced varied between 20 and 80
microns. Particle configuration was usually in a
strand shape (Fig. 1). Particle concentration per
cubic centimeter of Tc-MAA remained reasonably
constant with the establishment of a standard
method for production as outlined previously. The
concentration of particles ranged between 350,000
and 525,000 particles/cc with an average concen­
tration of 400,000 particles/cc. Since approxima­
tely 0.5 cc of the preparation was required for a
3-mCi dose, the average number of particles per
injection was 200,000.

Percentage tagging of the particles with tech­
netium-pertechnetate varied between 60 and 95%
as determined by paper chromatography (Fig. 2).
The less efficient tagging was noted in earlier prep­
arations of Tc-MAA. Batches of material obtained
since January 1973 have produced a more uniform
particle with greater tagging efficiency. The overall
average of tagging during our investigation was
80%. Chromatographic analysis is time consuming
and led us to perform scintiphotos of the chroma­
tograph without submitting the study to destruc­
tive methods. It was soon learned that visual in­
spection of the scintiphoto often proved adequate
for the identification of poor tagging. Concentra­
tion of any magnitude in the Macrotec column,
identifiable as technetium-pertechnetate by the
marker column, usually indicated tagging efficien­
cies of less than 70%. Using this method has made
it possible to carry out chromatographic analysis in
approximately 1/2 hr.

Metabolic studies. Three subjects in the present
series were submitted to stationary probe counts
over the lung and liver periodically during the first

FIG. 2. Plotted results of destructive analysis from ascending chro­
matograph. Origin activity confirmed 88% technetium particle tag­
ging.
24 hr postinjection. The half-time disappearance of activity over the lung port varied between 3 and 5 hr. Liver activity rose to a maximum at 6 hr postinjection with a half-time disappearance of 16 hr after maximum liver accumulation. Serial studies of blood activity demonstrated no measurable activity 10 min postinjection. Two percent of the total administered dose appeared at 4 hr and less than 1% of the total activity was noted at 24 hr. Urinary excretion accounted for 25% of the total administered dose at 24 hr, and 40% of the total administered dose by 72 hr. Fecal excretion of activity was not determined.

Scan interpretation. One hundred cases were accumulated during the course of the present study. Retrospective analysis of charts was carried out for all studies not regarded to be normal. Of the cases studied, 42 were interpreted as normal. Subsequent clinical interpretation suggested that 23 studies correlated with the impression of pulmonary embolus. Twenty-eight additional studies had other evidence to suggest chronic obstructive pulmonary disease and two had confirmation of significant pleural effusions. Three cases of pulmonary tumor were verified, and two patients with pneumonia were recognized by abnormal perfusion studies with x-ray and laboratory confirmation of pneumonia.

All studies were performed with the scintillation camera accumulating at least 500,000 counts per picture. Scan time for each view was approximately 1 min which resulted in uniform and even perfusion throughout normal lung tissue. Eight-view lung scans as described previously gave optimal inspection of the lung bases with assurance that perfusion defects could be recognized easily. This technique has been helpful in enabling the interpreter to look en-face at defects in the pulmonary field (Fig. 4). Defects in the midlung field, especially with the lateral and oblique projections, were felt to correlate with bronchovascular structures at the pulmonary hilus. Indentations due to ribs were seen in a few studies and lobar fissures frequently appeared as normal pulmonary landmarks.

A few selected cases were serially restudied with I-MAA using the scintillation camera. Fine detail, as mentioned above, was not seen with this agent, and time per scan view was 10–12 min. Uneven and irregular perfusion distribution as correlated with obstructive pulmonary disease was visible much earlier with Tc-MAA. Serial studies employing Tc-HAM detailed perfusion defects identical to those visualized with Tc-MAA. It was noted, however, that scans performed with Tc-MAA and regarded to be normal often were found to have an irregular and mottled appearance when restudied with Tc-HAM. These cases did not present other clinical evidence to support the diagnosis of chronic obstructive pulmonary disease. We conclude that the larger number of particles employed with Tc-MAA may give a more accurate assessment of subtle and early changes in pulmonary perfusion.

**Conclusion**

Our experience with Tc-MAA has been brief but sufficient to suggest a number of advantages over
the currently available lung perfusion agents. The present kit preparation of Tc-MAA is very stable and does not require complicated procedures for preparation. Stability of the resulting tagged particle is good. There is no necessity for resuspending particles before injection or washing particles to remove free technetium from the product. The efficiency of particle labeling is acceptably high which minimizes unwanted circulatory activity in the field of interest. Interpretation of the Tc-MAA scan is reliable and predictable, making assessment of early obstructive pulmonary changes more certain. The favorable photon yield from technetium and activity available at the present dose of Tc-MAA make multiple views possible with more accurate evaluation of basilar pulmonary defects.

References