

TECHNIQUE FOR THE RAPID PREPARATION OF LUNG SCAN PARTICLES USING ^{99m}Tc -SULFUR AND HUMAN SERUM ALBUMIN

Michael D. Cragin, Milo M. Webber, Winona K. Victory and Daniel Pintauro

Center for the Health Sciences, University of California, Los Angeles, California

Presently applied techniques for the preparation of albumin particles used in technetium lung scintiscanning involve very detailed radiolabeling procedures and often elaborate laboratory appliances plus considerable time (1). In addition, technetium albumin labeling procedures result in varying degrees of recovery and efficiency (1). Recent investigations of a new technetium lung scanning agent developed earlier by one of us have shown the advantages of this new agent over heat-treated, technetium-labeled, human serum albumin as a preferable radiodiagnostic material.

This new diagnostic agent consists of macroaggregates of albumin incorporating particles of technetium-sulfur. It requires four common laboratory reagents and a short preparation time. The suspension can be easily prepared using hypodermic syringes and needles, a serum vial and a heated water bath. This new preparation of lung scanning material thus necessitates fewer manipulations than the conventional technetium albumin labeling procedures, thereby reducing the probability of procedural error and bacterial contamination. The high efficiency of the heated human serum albumin to entrap the technetium sulfur particles eliminates the step of removal of the free technetium with a sterile ion-exchange resin column.

MATERIALS AND METHODS

Technetium-sulfur suspension is made after a modified Patton procedure (2,3). Into a clean, dry, sterile, stoppered serum vial is placed 3.5 cc per technetate solution in saline from a sterile ^{99}Mo - ^{99m}Tc generator. To this is added 1.0 cc of a 10 mg/cc solution of sodium thiosulfate and 1.0 cc of 1 N HCl. All solutions are sterile and pyrogen free, and the procedure is performed aseptically. The vial is vented by inserting a 23-gage needle and is secured in a boiling water bath for 3.5 min. At the end of this time, the vial is cooled in running water for 3.5 min. Then 0.35 cc of a 1:10 dilution or 8.75 mg of human serum albumin which is prepared fresh daily (Courtland Laboratories, 25%) is added to the

vial, followed by the addition of approximately 1.7 cc of a pH 7.4 phosphate buffer (15.26% $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 0.92% $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$) (to bring the pH of the mixture to 5.2). The vial is then placed in a 95°C water bath and agitated for about 90 sec to achieve particles in the range of 50 microns (Fig. 1). Macroscopically, the material has the appearance of snowflakes.

The amount of free technetium in the material when prepared as above was determined by passing an aliquot through a 300-m μ (0.3-micron) Millipore filter. This filter removes from the material the

Received July 31, 1968; revision accepted April 29, 1969.

For reprints contact: Milo M. Webber, Dept. of Radiology, The Center for the Health Sciences, University of California, Los Angeles, Calif. 90024.

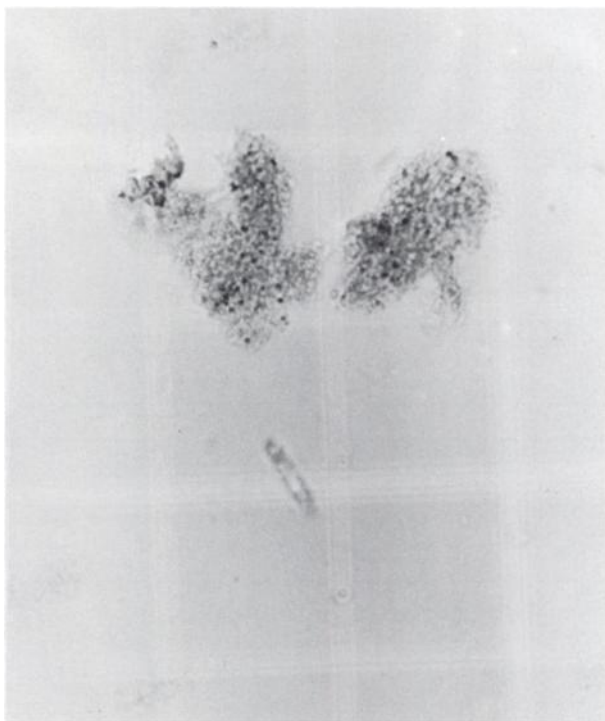


FIG. 1. Two aggregates of human serum albumin showing incorporated radiotechnetium-sulfur (aggregate size approximately 50 microns).

aggregated human serum albumin which has entrapped the technetium-sulfur suspension and allows the free or unbound technetium and very small particles to pass through. This filtrate is then compared by radioassay to the unfiltered material and "tagging" efficiency determined by the following expression:

% Efficiency =

$$100 \left(1 - \frac{\text{cpm/ml of fluid after filtration}}{\text{cpm/ml of fluid before filtration}} \right).$$

Volume is determined by gravimetric means assuming the specific gravity to be constant.

DISCUSSION

Several preparations of Tc-S+MAA (technetium-sulfur plus macroaggregated albumin) were thus assayed as were a number of commercially available preparations of radioiodinated, macroaggregated human serum albumin (Mallinckrodt/Nuclear) (Table 1). The figures in Table 1 indicate that the "tagging" efficiency of Tc-S+MAA was comparable to that of the commercially available preparations, and in most findings the Tc-S+MAA showed slightly better "tagging" efficiency.

In vivo studies using mice were done to discover what percent of the injected material was concentrated in the lung, liver and blood. We decided to assay the liver since particles of technetium-sulfur

entrapped in MAA which were of insufficient particulate size would be localized in the liver. Hence, this assay of liver tissue would be a test of proper particle size for lung scans. Again, the preparations were compared to the commercially available radioiodinated, macroaggregated HSA. The findings are presented in Table 2. One group of healthy adult male mice was injected with commercial preparations of IHSA-MAA while a second group was injected with preparations of Tc-S+MAA. The lung-scanning agents were allowed sufficient time to localize in both groups, and the mice were sacrificed with sodium pentobarbital. A representative section of lung and liver plus an adequate blood sample were taken and prepared for radioassay.

The findings between Tc-S+MAA and the commercially available IHSA-MAA preparations as noted in Table 2 are comparable except for a notable difference in blood clearance of the two diagnostic agents. Of the two, Tc-S+MAA showed a lower concentration in the blood. It should be noted that all animals were sacrificed after the same amount of time had elapsed post-injection for each animal. Thus Table 2 shows a high concentration of the lung-scanning agent Tc-S+MAA in the lung (98.4%) with the figure comparable to commercial products. Radioassay of liver and blood reveal negligible amounts of Tc-S+MAA and IHSA-MAA.

TABLE 1. ASSAY DATA ON ¹³¹I-MAA AND Tc-S + MAA

Sample number	Tc-S+MAA			¹³¹ I-MAA		
	Before filtration	After filtration	Efficiency (%)	Before filtration	After filtration	Efficiency (%)
1	1,879,011*	32,245*	97.7	8,298,327*	188,706*	98.2
2	5,485,716	18,620	99.7	6,880,440	388,340	94.4
3	4,027,232	18,460	99.6	7,560,077	411,952	94.6
4	2,716,791	16,666	99.4	9,519,859	473,900	95.1
			$\bar{M} = 99.1$			$\bar{M} = 95.6$

* cpm/gm material.

TABLE 2. PERCENT CONCENTRATION OF INJECTED MATERIAL*

Lung		Liver		Blood	
Tc-S+MAA	IHSA-MAA	Tc-S+MAA	IHSA-MAA	Tc-S+MAA	IHSA-MAA
1. 98.7%	93.8%	1. 1.1%	0.3%	1. 0.2%	6.0%
2. 97.9	98.3	2. 1.8	0.8	2. 0.3	0.9
3. 98.4	97.7	3. 1.3	0.9	3. 0.3	1.4
4. 98.8	99.8	4. 1.0	0.0	4. 0.2	0.1
$\bar{M} = 98.4\%$	$\bar{M} = 97.4\%$	$\bar{M} = 1.3\%$	$\bar{M} = 0.5\%$	$\bar{M} = 0.25\%$	$\bar{M} = 2.1\%$

* cpm/gm lung + cpm/gm liver + cpm/gm blood = 100%.

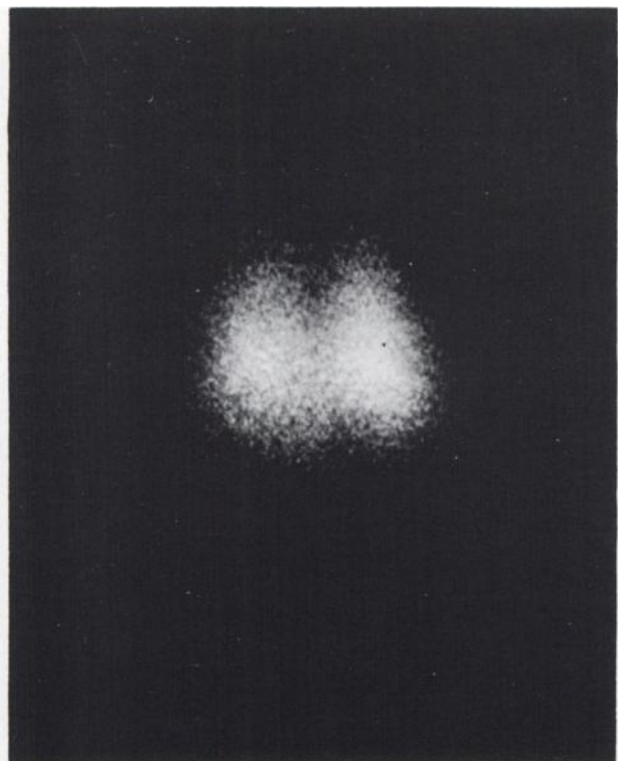


FIG. 2. Scintiscan of rabbit lungs after injection of macroaggregated human serum albumin incorporating radiotechnetium-sulfur.

The true test of a scanning agent, however, is in the quality of the scan or scintiphoto. Rabbit lung scintiphotos using Tc-S+MAA (Fig. 2) and dog lung scintiphotos also done with Tc-S+MAA (Fig. 3) are of excellent quality because a dose of a millicurie or more can be used. No accumulation is seen in the liver.

SUMMARY

The primary advantage of macroaggregated albumin incorporating particles of technetium-sulfur suspension as a radiodiagnostic agent in lung scintiscans is the simplicity with which it is prepared. This

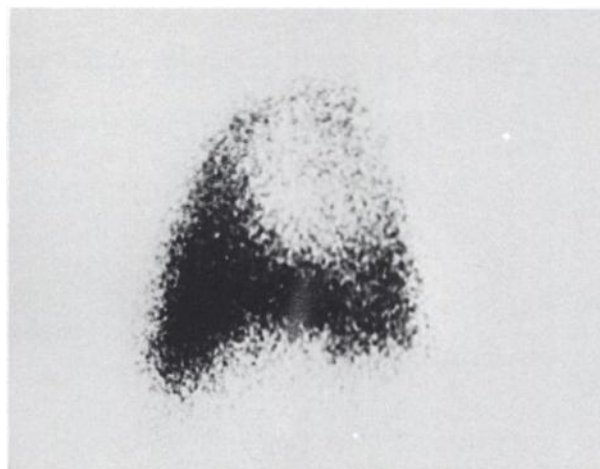


FIG. 3. Scintiscan of dog lungs after injection of macroaggregated human serum albumin incorporating radiotechnetium-sulfur.

preparation requires only a minimum of laboratory equipment and expense plus few steps to achieve an efficient diagnostic agent. The quality of the lung scintiscan in animals is excellent. It is possible that this agent will be very useful as a tracer in human lung scans.

ACKNOWLEDGMENT

We thank Joe Bennett for his help in performing this work. This study was supported in part by AEC Contract AT(04-1) Gen-12 between the U.S. Atomic Energy Commission and the University of California, Los Angeles.

REFERENCES

1. MCAFEE, J. G., STERN, H. S., FUEGER, G. F., *et al.*: 99m technetium labeled serum albumin for scintillation scanning of the placenta. *J. Nucl. Med.* 5:936, 1964.
2. PATTON, D. D., GARCIA, E. N. AND WEBBER, M. M.: Simplified preparation of technetium sulfide for liver scanning. *Am. J. Roentgenol.* 97:880, 1966.
3. WEBBER, M. M., VICTERY, W. K. AND CRAGIN, M. D.: Stabilizer reaction free 99m Tc-sulfur suspension for liver, spleen and bone marrow scanning. *Radiology* 92:170, 1969.