Tc-99m MAA: A Model for Administering the Desired Number of Particles for Pulmonary Perfusion Studies

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The use of tables derived from a computer program that insures conformity with certain quality control criteria is discussed in detail for Tc-99m labeled macroaggregated albumin (MAA). Conformity with designated criteria assures that a clinically optimal number of MAA-labeled particles will be administered for each radiopharmaceutical dose. Such ramifications as avoiding error, saving time, and reducing radiation exposure to the patient are discussed.

In clinical nuclear medicine, the radiopharmaceutical dose is not determined in the usual pharmaceutical sense because the radiopharmaceutical usually does not exert a detectable pharmacologic effect. Instead, one normally dispenses a radiopharmaceutical in units of millicuries. Some radiopharmaceuticals can, however, exert a pharmacologic effect or otherwise influence the interpretation of the patient's diagnostic procedure. Recognizing this important aspect, all nuclear medicine allied health specialists are now incorporating stricter quality control procedures into the daily routine *(1-15)*.

Albumin particles of suitable size labeled with technetium-99m for use in perfusion lung scanning are an example of a radiopharmaceutical with potentially deleterious pharmacologic effects. Once intravenously injected, the particles eventually act by transiently blocking the pulmonary capillary bed. If too few particles are injected, a spotty or patchy distribution might falsely suggest a perfusion defect *(8,14)*. Rhodes has suggested that the minimum number of particles that should be injected to give an acceptable scan is 40,000—with an optimum number being in the range of 100,000–150,000 particles *(8)*. If too many particles are injected, those patients with respiratory problems may develop complications. In these patients, the vascular bed is abnormal and, therefore, is thought to be unable to compensate for the transient occlusion of a portion of the capillary bed, which occurs when MAA is administered. This may be the mechanism that has contributed to at least two patient deaths *(16,17)*.

Frequently, patients undergoing lung scanning are very ill. Allen et al. *(9)* have measured mean pulmonary artery pressure as an indicator of acute particle toxicity. They reported elevation of this indicator as the first sign of acute toxicity; it occurred when about 100 times the usual lung scan dose was administered. A million particles of 30 μ each administered to dogs with experimentally produced pulmonary hypertension caused no significant effect.

This paper describes a computer program and a series of simple chart outputs to insure that the proper number of albumin particles are administered for a specified quantity of radioactivity, thus insuring patient safety and proper diagnostic interpretation from this standpoint. The number of particles and other criteria are set forth in the manufacturer's protocol *(18,19)*. The benefits and implications of the tables resulting from this computer program as they relate to one particular radiopharmaceutical product—Lungaggregate® (Medi-Physics, Inc., Emeryville, CA)—and lung-imaging radiopharmaceuticals in general are discussed.

Some basic definitions and abbreviations are:

- Radioactivity concentration (RAC) is radioactivity-per-unit volume as in mCi/ml.
- T_0 is time zero, the time at which the radiopharmaceutical is compounded.
- Tc is volume of technetium eluate used to compound the labeled product. Eluate is obtained from a molybdenum/technetium generator.
- MAA is volume of nonradioactive macroaggregated albumin used to compound the labeled product.
- Tc-MAA is technetium labeled macroaggregated albumin.

Materials and Methods

The recommended radiopharmaceutical dosage range (1–3 mCi) and criteria for preparation of Tc-99m-labeled

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(stannous colloid) macroaggregated human serum albumin particles were obtained from product literature *(18, 19)*. The material is prepared in a multidose quantity, so that in each individual dose of the preparation, the radioactivity concentration will be 1–6 mCi/ml and the volume of albumin will be between 0.3 and 1.5 ml. Each milliliter of nonlabeled albumin reagent contains 3×10^5 to 6×10^5 particles *(19)*.

There are only three variables in the Fortran IV program, which was written in level G, and processed on the IBM 370 Model 145 central data computer (a central facility of the University of Pittsburgh Health Center). They are:

- the radiopharmaceutical dose, which is determined in consultation with the nuclear medicine physician and the nuclear medicine technologist;
- the volume of MAA to be labeled; and
- the volume of the $Na^{99m}TcO_4$ eluate of a known RAC, determined using a Capintec CRC-2 or CRC-6A® dose calibrator to measure the amount of radioactivity.

First, the appropriate radiopharmaceutical dose is chosen. Then to prepare the labeled albumin, one must calculate the volume of technetium eluate required to label the MAA to meet designated criteria. If the radioactivity concentration of the technetium eluate is fixed, Table 1 aids in making the best possible choice of various combinations of technetium and MAA that can be used in compounding the radiopharmaceutical. The dose to the patient (mCi) is chosen from the left column. Based on the radioactivity concentration of the Tc-99m eluate found in the right column, the combination of volumes of MAA and Tc-99m eluate is chosen in order to conform with predetermined criteria.

For example, if the patient dose is to be 2.0 mCi and the RAC of the eluate is 12.0 mCi/ml, then the combination of choice from Table 1 would be 2.0 ml of MAA and 1.0 ml of technetium. This would allow the best use of time before too many albumin particles are administered for the 2.0-mCi dose. Additionally, to compute the doses available at T_0, simply multiply the volume of the technetium by the eluate RAC and divide by the radiopharmaceutical dose. In this example, there are six 2.0-mCi doses available at T_0, i.e., 1.0 ml × 12.0 mCi/ml ÷ 2.0 mCi. Six hours later at T_0 +6 hr (one half-life), there are three 2.0-mCi doses available.

Results

Table 1 was prepared from the series of program outputs of which Table 2 is an example. The RAC of the technetium eluates (Table 1) represents the limits of Table 2.

Table 2 as shown is a program output for the choices of 3.0-mCi individual doses when the multidose vial was made, using a combination of 2.0 ml of albumin reagent and 2.0 ml of $Na^{99m}TcO_4$ eluate, which is fixed by a RAC range of 2.1 to 10.0 mCi/ml. The $Na^{99m}TcO_4$–RAC range is only printed when the choice of the technetium-MAA combination (2.0 ml of each in this example) results in a product that satisfies the manufacturer's protocol and criteria for RAC and volume of albumin administered. This will be true regardless of the dose chosen or the combination of albumin and technetium used. Use of the chart allows one to determine if an acceptable quantity of albumin is present in a given dose based upon the volume combination (ml) of Lungaggreagate reagent MAA and Tc-99m eluate. When Tc-99m eluate is of unacceptable radioactivity concentrations, data are not printed. For this output, radioactivity concentrations of 2.1 to 10.0 mCi/ml, when 2.0 ml of MAA and Tc-99m eluate are used, will insure that the proper number of particles are present in each dose of 3.0 mCi.

For example: if at the time of labeling equal volumes (2.0 ml) of MAA and Tc-99m eluate (5.0 mCi/ml RAC) were used, each 3.0-mCi dose of Tc-MAA would be contained in 1.2 ml of the final product containing 0.6 ml of MAA.

TABLE 1. Preparation of Tc-99m MAA.

Dose to Patient	Combination		Radioactivity Concentration of Tc-99m
mCi	MAA (ml)	Tc-99m (ml)	mCi/ml
1.0	2.0	2.0	2.1 - 3.3
1.0	2.0	1.0	3.1 - 6.6
1.0	2.0	0.5	5.1 - 13.3
1.0	1.5	2.0	1.8 - 2.5
1.0	1.5	1.5	2.1 - 3.3
1.0	1.0	3.0	2.1 - 2.1
1.0	1.0	2.0	1.6 - 1.6
1.5	2.0	2.0	2.1 - 5.0
1.5	2.0	1.0	3.1 - 10.0
1.5	2.0	0.5	5.1 - 20.0
1.5	1.5	2.0	1.8 - 3.7
1.5	1.5	1.5	2.1 - 5.0
1.5	1.0	3.0	1.4 - 1.6
1.5	1.0	2.0	1.6 - 2.5
2.0	2.0	2.0	2.1 - 6.6
2.0	2.0	1.0	3.1 - 13.3
2.0	2.0	0.5	5.4 - 26.6
2.0	1.5	2.0	1.8 - 5.0
2.0	1.5	1.5	2.1 - 6.6
2.0	1.0	3.0	1.4 - 2.2
2.0	1.0	2.0	1.6 - 3.3
2.5	2.0	2.0	2.1 - 8.3
2.5	2.0	1.0	3.4 - 16.6
2.5	2.0	0.5	6.7 - 30.0
2.5	1.5	2.0	1.8 - 6.2
2.5	1.5	1.5	2.1 - 8.3
2.5	1.0	3.0	1.4 - 2.7
2.5	1.0	2.0	1.6 - 4.1
3.0	2.0	2.0	2.1 - 10.0
3.0	2.0	1.0	4.1 - 18.0
3.0	2.0	0.5	8.1 - 30.0
3.0	1.5	2.0	1.8 - 7.5
3.0	1.5	1.5	2.1 - 10.0
3.0	1.0	3.0	1.4 - 3.3
3.0	1.0	2.0	1.6 - 5.0

TABLE 2. Program Output for Preparation of Tc-99m MAA.

To Prepare Labeled MAA Using 2.0 ml of MAA and 2.0 ml of Tc-99m																				
	Radioactivity Concentration of Tc-99m in mCi/ml from Generator																			
RAC of Eluate	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	3.0	3.1	3.2	3.3	3.4	3.5	3.6	3.7	3.8	3.9	4.0
Final Volume of Tc-99m MAA Injected for 3.0 mCi Dose	2.8	2.7	2.6	2.5	2.4	2.3	2.2	2.1	2.1	2.0	1.9	1.9	1.8	1.8	1.7	1.7	1.6	1.6	1.5	1.5
	Tc-99m MAA																			
Volume of MAA Injected for 3.0 mCi Dose	1.4	1.4	1.3	1.3	1.2	1.2	1.1	1.1	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8
	MAA																			
To Prepare Labeled MAA Using 2.0 ml of MAA and 2.0 ml of Tc-99m																				
	Radioactivity Concentration of Tc-99m in mCi/ml from Generator																			
RAC of Eluate	4.1	4.2	4.3	4.4	4.5	4.6	4.7	4.8	4.9	5.0	5.1	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9	6.0
Final Volume of Tc-99m MAA Injected for 3.0 mCi Dose	1.5	1.4	1.4	1.4	1.3	1.3	1.3	1.3	1.2	1.2	1.2	1.2	1.1	1.1	1.1	1.1	1.1	1.0	1.0	1.0
	Tc-99m MAA																			
Volume of MAA Injected for 3.0 mCi Dose	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.5	0.5	0.5	0.5	0.5	0.5
	MAA																			
To Prepare Labeled MAA Using 2.0 ml of MAA and 2.0 ml of Tc-99m																				
	Radioactivity concentration of Tc-99m in mCi/ml from Generator																			
RAC of Eluate	6.1	6.2	6.3	6.4	6.5	6.6	6.7	6.8	6.9	7.0	7.1	7.2	7.3	7.4	7.5	7.6	7.7	7.8	7.9	8.0
Final Volume of Tc-99m MAA Injected for 3.0 mCi Dose	1.0	1.0	1.0	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
	Tc-99m MAA																			
Volume of MAA Injected for 3.0 mCi Dose	0.5	0.5	0.5	0.5	0.5	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
	MAA																			
To Prepare Labeled MAA Using 2.0 ml of MAA and 2.0 ml of Tc-99m																				
	Radioactivity Concentration of Tc-99m in mCi/ml from Generator																			
RAC of Eluate	8.1	8.2	8.3	8.4	8.5	8.6	8.7	8.8	8.9	9.0	9.1	9.2	9.3	9.4	9.5	9.6	9.7	9.8	9.9	10.0
Final Volume of Tc-99m MAA Injected for 3.0 mCi Dose	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
	Tc-99m MAA																			
Volume of MAA Injected for 3.0 mCi Dose	0.4	0.4	0.4	0.4	0.4	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
	MAA																			

Discussion

When using the eluate from the Squibb Minitec mid-week 100-mCi generator to prepare the labeled macroaggregated albmunim, the undiluted (5 ml) technetium eluate RAC has been in the range of about 55 to 15 mCi/ml, depending upon the day of the week. When using the NEN 300-mCi generator, the eluate RACs are somewhat lower owing mainly to the larger (20 cc) eluate volume. It is not difficult to see that for a given patient dose, the combination of MAA and technetium will vary greatly, depending as it does on the eluate RAC. Hence, on a Monday morning using 2.0 ml of Tc-99m eluate (30 mCi/ml) from a 300-mCi NEN generator combined with 1.0 ml of albumin would result in a particle administration of as few as 15,000–30,000 for each 3.0-mCi dose.

By observation (Table 2), it is also clear that the lower the RAC of the Tc-99m eluate on the chart, the greater the amount of nonradioactive material injected will be. Since the half-life of Tc-99m is six hours, one can calculate the length of time the preparation can be used.

For example: if the eluate RAC is 4.2-mCi/ml at 9:00 a.m., the final product should not be used after 3:00 p.m.—because greater than 1.5 ml of albumin (more than the desirable chosen number of particles) will be administered.

In general, then, one can use the computer-produced charts to (a) determine the amount of MAA in an individual patient dose; (b) determine the final volume of Tc-MAA to administer in the individual patient dose; (c) determine the best combination of MAA and Tc to use for a given radiopharmaceutical dose; and (d) calculate the maximum number of doses available at T_0.

Using this program, all combinations of Tc and MAA that would result in a finished radiopharmaceutical not meeting established criteria are automatically rejected and, therefore, excluded from every chart.

We have found it advantageous to split the MAA reagents into two aliquots for labeling, using nitrogen-filled or evacuated 5-ml multidose vials. One preparation is made early in the day and the other vial is kept for the afternoon patients or late emergencies. This allows additional flexibility in providing a choice of individual radiopharmaceutical doses for individual patients.

In addition to quality control and conformity to product criteria, another function of nuclear medicine personnel is to keep track of patient radiation dose and minimize it whenever possible. Once a procedure has been established, it is all too easy to fall into the pattern of administering the same dosage, or using the same product in lieu of another (Table 3) even when a lower dose should or could be given, because it is inconvenient to perform the required calculation.

Conclusion

Proper use of this computer program model, which we have developed and described, insures conformity with es-

TABLE 3. Number of Particles of Macroaggregated Albumin in Various Commercial Products.

Manufacturer	Trade Name	Particles in Each Reaction Vial
3M	Microspheres	greater than 0.9×10^6
NEN	Pulmolite	$3.6 - 6.5 \times 10^6$
Mallinckrodt	Technescan-MAA	$6.0 - 10.0 \times 10^6$
Squibb*	Macrotec	$3.0 - 5.0 \times 10^6$
Medi-Physics, Inc.	Lungaggregate	$(0.3 - 0.6 \times 10^6$/ml)
		$0.6 - 1.2 \times 10^6$ ampoule
Union Carbide	MAA	$0.5 - 1.0 \times 10^6$ single dose
		$1.0 - 2.5 \times 10^6$ multidose

*Not commercially available in May 1979.

tablished criteria, decreases risk of calculation error, and eliminates the time required to perform repetitive calculations. Availability of the calculated data adds an incentive to decrease the administered radiopharmaceutical dose to the patient and simultaneously decreases a patient's radiation dose. Additionally, this program prevents the administration of too few particles, which could lead to an inadvertent misdiagnosis.

The reader is cautioned that while this methodology is entirely appropriate for any of the commercially available lung imaging kits, the calculations in the tables in this paper can only be applied to the Lungaggregate reagent kit.

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