Radiopharmacy

Theoretical Considerations in the Preparation of Tc-99m MAA for Pulmonary Perfusion Studies

Geoffrey Levine and Balwinder Malhi

University of Pittsburgh Schools of Medicine and Pharmacy and the Presbyterian-University Hospital, Pittsburgh, Pennsylvania

The results of theoretical calculations in the preparation of Tc-99m MAA for lung perfusion studies using MAA from various commercial manufacturers combined with eluate from various size technetium generators are considered. Kit-generator incompatabilities based on specific activities are specified. Percent of elution yields required to prepare a particular product preparation are calculated.

The use of Tc-99m MAA for lung perfusion imaging in both adults and children is well known and documented (*1–9*). The choice of the number of particles of MAA to be administered per dose for a diagnostically adequate and safe scan is of considerable importance. Too few particles can lead to artifactual perfusion defects, and too many particles can potentially lead to respiratory complications in patients with an abnormal vascular bed. At least four patients may have died from such complications (*10–13*).

The optimal number of particles to administer has been suggested by Rhodes to be in the range of 100,000–150,000 (*8*). Heyman has suggested that a one-year-old infant should not receive more than 165,000 particles, if 500,000 particles are considered safe for the adult (*9*). Allen et al. (*14*) have measured pulmonary artery pressure as an indication of acute particle toxicity and reported elevation of this indicator as the first sign of acute toxicity. This occured 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.

Commercially available MAA may contain 10,000,000 (or more) to 500,000 particles per vial. Technetium generators are available; these cover at least a 50-fold range or more of eluate activity depending on the activity prepared for delivery by the manufacturer and the associated date of shipment, calibration, arrival, or use in the hospital or radiopharmacy (e.g., 10 Curie to 100mCi).

It has been our observation and experience in consultation with nuclear medicine personnel (e.g., physicians, technologists, and radiopharmacists) that the choice of the desired or required number of particles to be administered is often overlooked, not considered, or downgraded in importance.

We discuss several common matching permutations between various MAA products and generator elutions of different total radioactivity as they relate to the clinical choice of the number of particles to be administered to a selected patient. The availability of pertechnetate eluate for a Tc-99m MAA preparation containing the desired number of particles in a given dose is also considered.

Materials and Methods

A list of the mean number of particles of MAA for various commercially available products was reviewed from reference 1. Theoretical calculations were performed using this list to determine the quantity of radioactivity required in order to prepare a "usual" 3-mCi dose of Tc-99m MAA containing a specific number of particles ($0.1, 0.3, 0.5, 0.8, 1.0 \times 10^6$) from the various commercial MAA products. Lastly, calculations were made to determine the percent of stock pertechnetate eluate required to prepare a minimum of a single 3-mCi dose containing the chosen number of particles for administration from various commonly used generator sizes (100, 200, 300, 500 mCi). We have assumed 100% yield of elution for ease of calculation, while recognizing usual yields to be on the order of 75 to 90%. Likewise, the generator designated as 100 mCi at calibration on a Friday would likely be about 450–500 mCi on date of shipment from the manufacturer.

For reprints contact: Geoffrey Levine, Presbyterian–University Hospital, Dept. of Nuclear Medicine, Pittsburgh, PA 15213.

TABLE 1. Activity of Pertechnetate Required for the Preparation of the Chosen Number of Particles per 3-mCi Dose of Tc-99m MAA.

	100,000*	300,000*	500,000*	800,000*	1,000,000*
Mallinckrodt	240.0 mCi	80.0 mCi	48.0 mCi	30.0 mCi	24.0 mCi
New England Nuclear	151.5 mCi	50.5 mCi	30.3 mCi	18.9 mCi	15.1 mCi
Squibb †	120.0 mCi	40.0 mCi	24.0 mCi	15.0 mCi	12.0 mCi
Medi-Physics	27.0 mCi	9.0 mCi	5.4 mCi	3.4 mCi	———‡
Union Carbide	22.5 mCi (unit dose)	7.5 mCi	4.5 mCi	———‡	———‡
	52.5 mCi (multidose)	17.5 mCi	10.5 mCi	6.6 mCi	5.3 mCi

*Chosen number of particles per 3-mCi dose of Tc-99m MAA
†Not in the market place May 1980
‡Line indicates that the preparation cannot be made according to specifications.

Results

Table 1 was designed so that the user of any particular MAA product could determine if the product met the criteria that he had pre-selected, i.e., a given number of particles per 3-mCi dose based on the quantity of pertechnetate available to him. Conversely, one could select the approximate number of particles to be injected and then decide which of the manufacturers' MAA products met his criteria.

For example, suppose it was decided to use a Mallinckrodt MAA kit on a Friday in an institution with a 100-mCi size Mo-99/Tc-99m generator. The Mallinckrodt kit contains on the average about 8 million particles per vial. If the physician selected 100,000 particles as the optimum dose (Table 1), then 240 mCi of pertechnetate would be required; this is clearly impossible. If 300,000 particles were selected for administration, then 80 mCi would have to be added to the vial in order that each 3 mCi would be associated with 300,000 particles. Multiple doses could, of course, be drawn. By referring to Table 2(B), one can determine in advance on a Friday (assuming a 100% yield for convenience of calculation only) that 80 mCi would represent 80% of the yield from a 100-mCi generator, but only 16% from the 500-mCi generator. Thus, inventory and scheduling parameters could be considered.

On the other hand, suppose that a dose of 1 million particles was chosen and a Medi-Physics or Union Carbide (single dose) MAA product was selected. In this case, more than enough pertechnetate activity would be available, but there might not be enough particles available to meet the criteria of the dose. A trade-off is that more than one dose of a million particles could not be drawn.

Discussion

We do not mean to advocate one MAA product over another, nor to suggest the number of particles to be used in the lung perfusion study. We do suggest, however, that a minimum approximate number of particles consistent with adequate diagnostic information be chosen in ad-

TABLE 2. Percent of Pertechnetate Elution Yield from Different Size Generators Required to Prepare 3-mCi Doses of Tc-99m MAA Containing a Specific Number of Particles.

TABLE 2(A). 100,000 Particles per 3-mCi Dose

Mfr.	100 mCi*	200 mCi*	300 mCi*	500 mCi*
1	———	———	80.0%	48.0%
2	———	75.7%	50.5%	30.3%
3	———	60.0%	40.0%	24.0%
4	52.5%	26.3%	17.5%	10.5%
5	27.0%	13.5%	9.0%	5.4%
6	22.5%	11.3%	7.5%	4.5%

TABLE 2(B). 300,000 Particles per 3-mCi Dose

Mfr.	100 mCi	200 mCi	300 mCi	500 mCi
1	80.0%	40.0%	26.6%	16.0%
2	50.5%	25.3%	16.8%	10.1%
3	40.0%	20.0%	13.3%	8.0%
4	17.5%	8.8%	5.8%	3.5%
5	9.0%	4.5%	3.0%	1.8%
6	7.5%	3.8%	2.5%	1.5%

TABLE 2(C). 500,000 Particles per 3-mCi Dose

Mfr.	100 mCi	200 mCi	300 mCi	500 mCi
1	48.0%	24.0%	16.0%	9.6%
2	30.3%	15.2%	10.1%	6.0%
3	24.0%	12.0%	8.0%	4.8%
4	10.5%	5.3%	3.5%	2.1%
5	5.4%	2.7%	1.8%	1.1%
6	4.5%	2.3%	1.5%	0.9%

TABLE 2(D). 1,000,000 Particles per 3-mCi Dose

Mfr.	100 mCi	200 mCi	300 mCi	500 mCi
1	24.0%	12.0%	8.0%	4.8%
2	15.1%	7.5%	5.0%	3.0%
3	12.0%	6.0%	4.0%	2.4%
4	5.3%	2.6%	1.3%	1.1%
5	———	———	———	———
6	———	———	———	———

Manufacturers: 1= Mallinckrodt; 2= New England Nuclear; 3= Squibb; 4= Union Carbide multidose; 5= Medi-Physics; 6= Union Carbide unit dose.
*Generator size: Assume 100% elution yield for purposes of calculation.

dition to a specified number of millicuries, and that a conscious decision be made in this regard. We also want to call attention to the particle number problem: the potential mismatch of specific activities based on a manufacturer's kit and the available pertechnetate activity from different size generators.

There is a technique available for the preparation of MAA when there is a kit–generator mismatch. In the case of greater particle-to-activity ratio, some of the particles can be discarded. We have previously discussed such a methodology for the preparation of pediatric doses of Tc-99m MAA. We do not recommend this predilution procedure in the absence of package insert directions because when excess particles are discarded, so is a proportionate quantity of tin that was originally available to reduce the pertechnetate (*2*).

One must also remember that the number of particles in a vial can fall within a fairly wide range as the manufacturers state. The mean particle number was used for calculation in this presentation. Furthermore, a suitable volume consistent with manufacturer directions must be chosen so that an adequate volume can be drawn in an accurate and reproducible fashion when dispensed, without excess trapping in the needle (*15*). For example, if 50.5 mCi of technetium is selected to prepare a vial of 3-mCi doses containing 300,000 particles each (NEN) (Table 1), a volume of 8 ml, as directed, is required even if sterile, preservative-free saline eluant is used for dilution to complete the preparation. In this way the volume drawn for a single dose will be a reproducibly measurable 0.48 ml. Lastly, from an inventory perspective, one must consider what fraction of the stock solution of pertechnetate will be devoted to the preparation of MAA to the detriment of other radiopharmaceuticals required that day. Table 2(A–D) will assist in making this determination. The nuclear medicine department performing a limited number of studies a day, and using the smaller size generator, must be particularly attentive to this problem.

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