Radiopharmacy

A Methodology for Preparing Pediatric Doses of Tc-99m MAA for Pulmonary Perfusion Studies

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We present methodologies for preparing pediatric doses of Tc-99m MAA from commercial kits and discuss them by illustrative example calculation.

The use of Tc-99m labeled macroaggregated albumin (Tc-99m MAA) and human albumin microspheres (Tc-99m HAM) for lung perfusion and other studies is well known (*1–3*). The potential consequences of too many or too few administered particles per study have been investigated and discussed in both normal and disease states (*4,5*). Webster et al. (*6*) have reviewed the diagnostic use of Tc-99m MAA in pediatrics as well as methodologies for determining the desired quantity of radioactivity to administer to infants and children. Heyman (*7*) and Davis and Taube (*8*) have addressed the toxicity and safety factors associated with lung perfusion studies using radiolabeled particles, specifically in regard to pediatric doses. They have suggested splitting vials of Tc-99m MAA while preparing doses of 17,000 and 21,000 particles, respectively, for the newborn.

Once the desired number of albumin particles to administer for a study is chosen, package insert directions for preparing the radiopharmaceutical for infants and children in a reasonable volume of administration are not provided. It has been suggested (*9*) that the optimal number of particles to administer to the adult is in the range of 100,000–150,000 particles. For the newborn, the number should not exceed 50,000 particles. The one-year-old infant should not receive more than 165,000 particles if 500,000 particles are regarded as safe for the adult (*7,8*).

We describe four possible methods for preparing Tc-99m MAA. However, three of these four methods are unacceptable for preparing a *pediatric* lung perfusion dose because of unattainable specific activities (radioactivity/particle); volume limitations; and lack of package insert directions.

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A recommendable procedure (method 1), which is utilized at our institution, is described in detail.

Materials and Methods

Method 1: Prepare a vial of MAA using sterile, bacteriostat-free normal saline eluant. Withdraw and discard those particles of MAA that are in excess and not required. Add an appropriate quantity (radioactivity) and volume of pertechnetate stock solution, and saline to meet the criteria established for the final patient preparation.

Method 2: Dilute the radioactivity concentration (RAC, mCi/ml) of the sodium pertechnetate stock solution so that the specific activity chosen for the clinical study to be performed (mCi/mg or mCi/particle) will be obtained in the final product. This procedure erroneously assumes that the desired number of particles will be withdrawn with the desired quantity of radioactivity. This is assumed to be accomplished by using a small volume of high RAC stock solution, adding it to a vial of sterile normal saline eluant, and withdrawing an appropriate volume that can then be added to the vial of MAA.

Method 3: An alternative to method 2 is to add a small amount of the high RAC pertechnetate to the vial of MAA for labeling, and then diluting the labeled material with saline eluant.

Method 4: Simply add the Tc-99m pertechnetate to the MAA vial and take an appropriate aliquot in terms of radioactivity. This method, like method 2, erroneously assumes the correct number of particles will be removed with the appropriate radioactivity. Additionally, it erroneously assumes a measurable volume (*10*).

Results and Discussion

Let us prepare a dose of Tc-99m MAA for an infant or small child. We decided for this example that the dose should be in the 0.75- to 1.0-mCi range and the radioac-

tivity should be associated with between 10,000 to 15,000 particles.

The macroaggregated albumin product (Pulmolite®) contains 3.6×10^6 to 6.5×10^6 particles/vial. The RAC of the pertechnetate stock solution at 8 a.m. is 36.0 mCi/ml. The dose is to be administered at 2 p.m.

Method 1:

a) Add 5 ml of normal saline eluant to a new vial of Pulmolite and shake gently until suspended.
   This step simply dilutes the albumin to attain a sufficient working volume.

b) Remove 4.6 ml of MAA in saline and discard, leaving 0.4 ml in the vial (5 million particles in 5 ml is equivalent to 400,000 particles in 0.4 ml).
   Our goal is to be able to dilute the MAA particles left in the vial to a concentration of about 100,000 particles or less per ml. The total volume of the MAA vial must be kept in mind.

c) Add 27.0 mCi of pertechnetate to the 400,000 particles in 0.4 ml at 2 p.m. Add sufficient saline eluate solution to make 4.0 ml.
   Thus: MAA (0.4 ml) + pertechnetate (1.5 ml) + saline (2.1 ml) = 4.0 ml.
   The reciprocal specific activity (particles/mCi) is the determining factor in deciding how much pertechnetate to add. In this case:

$$\frac{400{,}000 \text{ particles}}{27 \text{ mCi}} = 14{,}815.$$

d) Calculate the volume to be administered:

$$\frac{27 \text{ mCi}}{4 \text{ ml}} = \frac{1 \text{ mCi.}}{x \text{ ml}}$$

$$\therefore$$

$$x = 0.15 \text{ ml.}$$

Therefore, at 2 p.m. each 0.15 ml will contain 1 mCi, which is associated with 14,815 particles.

The essential elements to be kept in mind are:

- Although we assumed an approximate mean value of 5 million particles per vial, the range is 3.6 to 6.5 million particles/vial so that we may be in error by as much as 30%, high or low.
- When the final patient dose is drawn from the vial, the volume must be large enough to be measured accurately. In a small volume dose, an error in measurement represents a greater percentage of error than the same error in measurement would be in a larger volume dose. Also, if the syringe is not flushed, a considerable volume of the dose might be trapped in the needle (*10*). Additionally, care should be taken to prevent clotting in the syringe so that artifactual hot spots in the lung can be avoided.
- If the number of particles/ml of the final preparation is less than 100,000, then for a dose of about 15,000 particles, a reasonable volume with associated radioactivity can be drawn in a relatively accurate fashion (confirmed by measurement in the dose calibrator).
- The amount of radioactivity to be added to the vial can be calculated by examining the reciprocal of the specific activity expressed as particles/mCi.

In this case, given a range of 10,000–15,000 particles, 40.0 to 26.6 mCi is required.

Method 2:

Despite the fact that the RAC or total amount of activity to be added would be suitable, the reciprocal specific activity would not meet our criteria. This is because the particles/ml (concentration) could not be diluted enough within the vial provided. The final dose volume to be withdrawn must also be measurable.

Hence, to withdraw a dose greater than 0.1 ml and containing 10,000 particles in 0.1 ml would require a vial volume of 50 ml (5,000,000 particles/10,000 particles in 0.1 ml = 50 ml); this is clearly not possible within the vial provided.

The transfer of MAA from one vial to another can cause problems because tin-reduced kits are normally packed under nitrogen to decrease the possiblity of oxidation. We recommend that reagents not be transferred from the original vial to another unless we know some of the characteristics of the receiving vial such as the composition of the glass and seal including the septum.

Method 3:

The problems associated with method 3 are similar to method 2 except that in this case the pertechnetate solution is diluted in the reaction vial. The cold MAA cannot be diluted enough within the vial provided.

Method 4:

This method represents the worst possible case of methods 2 and 3. Suppose 25 mCi in 1.0 ml of pertechnetate was added to the vial (8-ml capacity) containing 5×10^6 particles. Then a 1.0-mCi dose would represent 200,000 particles and be present in a clearly unacceptable 0.04-ml volume. The preparation of an adult dose according to the package insert calls for dilution to an 8-ml volume. The pediatric dose would require even more dilution. For example, the dilution of 5×10^6 particles in 8 ml leaves 625,000 particles/1ml, so that, regardless of the activity added, the number of particles desired for a minimally acceptable volume will always be exceeded.

Conclusion

In all cases, the individual preparing a patient dose should attempt to adhere as closely as possible to the manufacturer's package insert directions or authorized procedures. In this case there is no authorized manufacturer's procedure for preparing a pediatric dose. Additionally, the legal ramifications of preparing a product not in accordance with package insert directions must be considered in light of one's own professional credentials. However, cer-

tain circumstances do arise, such as this one, that require deviation. Before deviating, caution is always advised. In our case, for example using method 1, when the excess particles are discarded, so is a proportionate quantity of the tin that was originally available to reduce the pertechnetate. The consequence of too little stannous ion, should it occur, would likely be excess free pertechnetate, partially reduced forms of pertechnetate, or partially oxidized forms of Tc-99m MAA. We always perform chromatography on the end product prescription and discard the unused material to prophylactically prevent its usage in an adult patient. When prediluting the lung agent in order to achieve a reduced particle count, bacteriostat-free normal saline eluant rather than normal saline should be used. This concern stems from the fact that the use of normal saline does not take into account the varying redox potential of diluents of different origin and the varying levels of divalent tin that might be occurring on a lot-to-lot or an agent-to-agent basis (*11*).

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References

1. Neilsen PE, Kirchner PT, Gerber FH: Oblique views in lung perfusion scanning: Clinical utility and limitations. *J Nucl Med* 18: 967–972, 1977

2. D'Altorio RA, Cano JY: Congenital absence of the left pericardium detected by imaging of the lung: Case report. *J Nucl Med* 18: 267–268, 1977

3. Dworkin HJ, Gutkowski RF, Porter W, et al: Effect of particle number on lung perfusion images. *J Nucl Med* 18: 260–262, 1977

4. Allen DR, Nelp WB, Cheney F, et al: Studies of acute cardiopulmonary toxicity of Sn-macroaggregated albumin in the dog. *J Nucl Med* 15: 567–571, 1974

5. Levine G: Tc-99m MAA: A model for administering the desired number of particles for pulmonary perfusion studies. *J Nucl Med Technol* 7: 33–36, 1979

6. Webster WW, Alpert NM, Brownell GL: Radiation doses in pediatric nuclear medicine and diagnostic x-ray procedures. In *Pediatric Nuclear Medicine*, James AE, Wagner HN, Cooke RE, eds, Philadelphia, W.B. Saunders Co., 1974, pp 34–58

7. Heyman S: Toxicity and safety factors associated with lung perfusion studies with radiolabeled particles. (Letter to Ed) *J Nucl Med* 20: 1098–1099, 1979

8. Davis MD, Taube RA: Toxicity and safety factors associated with lung perfusion studies with radiolabeled particles. (Letter to Ed) *J Nucl Med* 20: 1099, 1979

9. Rhodes BA, Croft BY: Methods of localization. In *Basics of Radiopharmacy,* St. Louis, C.V. Mosby Co., 1978, pp 33–51

10. Levine G, Crawford J, Carroll RG: Sequestration of radiopharmaceutical in spinal needle dead space during cisternography. *J Nucl Med Technol* 6: 153–154, 1978

11. Green AM: Personal communication, New England Nuclear, 1980