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AN EFFICIENT METHOD FOR FRACTIONAL LABELING OF MICROSPHERES

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The introduction of human albumin microspheres (HAM) is a significant advance in carrier-protein technology for the study of capillary perfusion. However, the recommended labeling procedure is an expensive and inefficient method for the utilization of microspheres and technetium. A procedure is outlined for the fractional labeling of HAM with technetium. This provides a simple, efficient, and economical use of microspheres and technetium allowing for high specific activity particles. It is particularly applicable to nuclear medicine departments with a relatively small patient load.

The introduction of human albumin microspheres (HAM), easily tagged with technetium, represents a significant advance in carrier-protein technology for the study of capillary perfusion (*1*). Microspheres have been commercially available from the 3M Company in kit form for over 2 years. However, in most departments with an average clinical load, if used as directed, there is considerable waste of both technetium and microspheres along with a significant limitation of specific activity. The following technique of preparation provides ^{99m}Tc-HAM of high specific activity and a simple and efficient use of both microspheres and technetium.

METHOD

The tagging vial as received from 3M is double-ended with a large central chamber in continuity with the silver end. A small chamber at the gold end contains ion-exchange resin and a cotton plug and is separated from the large central chamber by a porous frit preventing passage of microspheres. The large chamber contains dry microspheres, a reagent tablet consisting of sodium thiosulfate with a binder, and other chemicals not directly involved in the tagging reaction.

In this method, the same vial is used repeatedly (four to ten times). Consequently, all punctures of the rubber stoppers should be made with 23 gage or smaller needles and should be distributed over the surface of the stopper.

A stock suspension is prepared by injecting 10 ml of sterile 0.9% NaCl through the silver end of a standard 3M vial of HAM (5 mg). When the reagent tablet is completely dissolved, the fluid is withdrawn through the gold end and discarded. Ten milliliters of 3M rinsing and suspending solution (R&S) is then injected through the silver end. The vial is placed in an ultrasonic bath for 1 min. This stock suspension is then stored in the refrigerator in horizontal position to prevent packing of microspheres in the frit. If no other 3M vial is available for tagging, the suspension is withdrawn through the silver end and stored in a standard 10-cc sterile rubber-capped vial and the emptied 3M vial is used for the first series of tagging.

When tagged microspheres are needed, the following steps are taken, with all injections being made through the silver end of the vial.

1. Using a 5-cc syringe, 2.0 or 2.5 ml of the stock suspension of microspheres is injected into an empty 3M vial and the suspending fluid withdrawn through the gold end.

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2. Three milliliters of 0.9% NaCl is injected, mixed by several inversions, and discarded by withdrawal through the gold end.
3. The vial is placed in a lead container with the silver end up for injection of 20–100 mCi of ^{99m}Tc-pertechnetate diluted to 2.5 ml with saline.
4. With a tuberculin syringe, 0.12 ml of 1% sodium thiosulfate (1 gm $Na_2S_2O_3 \cdot 5H_2O$/ 100 ml water) is similarly injected.
5. With a tuberculin syringe 0.25 ml of HCl 1.0 *N* is injected, leaving the needle in the stopper as a vent.
6. The vial is agitated in an ultrasonic bath for 1 min.
7. The vial is boiled in a water bath for 2–6 min with constant agitation.
8. The vial is then cooled in an ultrasonic bath or under running water for 1 min.
9. The vial is returned to the lead shield, the vent removed, and the fluid withdrawn through the gold end.

   The fluid is checked in a dose calibrator and discarded if it contains less than one-third of the original amount of ^{99m}Tc. If greater than one-third, it is possible to increase the ^{99m}Tc tag by injecting this fluid back in the silver end of the vial and repeating the procedure beginning at Step 4.
10. Three milliliters of R&S solution are injected, mixed by inversion, withdrawn through the gold end, and discarded.
11. The microspheres are resuspended in R&S solution by injecting 2.5 ml or more, agitated in the ultrasonic bath for 1 min, and are then ready for use.

After use, the vial is stored in the refrigerator, and the next day that microspheres are needed, the same vial is used again. Through the silver end of the vial the previously tagged microsphere suspension is removed and discarded and the vial is rinsed with 0.9% sodium chloride. The tagging procedure continues as above, starting at Step 1.

DISCUSSION

This method produces ^{99m}Tc-labeled microspheres with high specific activity for 4 or more work days from one vial of 3M HAM. This results in a more economic use of both microspheres and technetium. There has been no change in the tagging efficiency or size of microspheres stored as long as 2 months. However, the R&S solution, which is used as the suspension media, develops a precipitate soon after its expiration date. Therefore, the R&S solution in the stock suspension of microspheres should be replaced if the stock suspension is held over 30 days. The resin in the vial below the frit prevents the loss of ^{99m}Tc during tagging. Thus, any alternate method of cleansing and sterilizing vials should provide for retention of the resin and cotton. Replacement stoppers made of soft rubber will withstand repeated punctures and are therefore preferable to butyl stoppers.

The use of "instant technetium" or saline containing preservatives may cause reduced tagging efficiency. Therefore, generator-produced technetium is used for tagging and IV saline solutions for diluting.

This method has been utilized at this institution since May, 1972, and the use of tagged microspheres in the first 400 cases of myocardial perfusion has been reported (*2*). Since that time over 600 additional myocardial perfusion studies and several hundred pulmonary scans have been performed without untoward effects.

This tagging technique is particularly applicable to nuclear medicine departments where the patient load is relatively small.

REFERENCES

1. WAGNER HN, RHODES BA, SASAKI Y, et al: Studies of the circulation with radioactive microspheres. *Invest Radiol* 4: 374–386, 1969

2. GRAMES GM, JANSEN C, GANDER MP, et al: The safety of the direct coronary injection of radiolabeled particles in 800 patients undergoing coronary angiography. *J Nucl Med* 15: 2–6, 1974