A Simplified Method for Laboratory Preparation of Organ Specific Indium 113m Compounds

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Generator systems producing short lived nuclides from longer lived parents have distinct clinical advantages. They are more economical, result in a lower radiation dose, and can make short lived scanning agents readily available even in areas remote from rapid radiopharmaceutical delivery services. The ^{113}Sn–^{113m}In generator has the additional advantage that, as a transition metal, Indium can be readily complexed into organ specific preparations.[1]

^{113}Sn, a reactor produced nuclide with a 118 day half life, is absorbed on a zirconium or silica gel column. The generator is eluded with 5 to 8 ml of 0.05 N HCl solution at pH 1.3-1.4. The daughter nuclide, ^{113m}In, has a half life of 1.7 hours and emits a 393 Kev monoenergetic gamma ray.

Previous methods[2,3,4,5] for labeling organ specific complexes with ^{113m}In required terminal autoclaving before injection. With the recent introduction of sterile, apyrogenic ^{113}Sn–^{113m}In generators,† we have developed a simplified technique for the laboratory preparation of Indium labeled compounds. This method eliminates autoclaving and titration enabling us to pre-prepare organ specific complexes for blood pool, liver, spleen, brain, kidney and lung scanning.

METHODS AND MATERIALS

(1) Elution of generator

The eluding solution, 0.05 N hydrochloric acid, contains 4.5 ml concentrated HCl diluted in 1,000 ml pyrogen free water. The generator is connected to the elution system with plastic tubing and a three way stop cock (Figure 1). A second plastic tube connects the bottom of the generator to a sterile needle. To elude the generator, we draw 5 to 8 ml of eluding

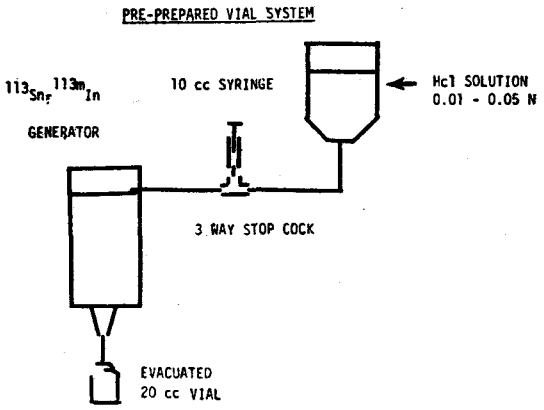


Figure 1. Eluding system for ^{113m}In generator.

† Indicow, Mallinckrodt Chemical Co., St. Louis, Mo.

solution into a syringe connected to the three way stop cock, emptying the syringe through the generator into a 20cc sterile, air tight bottle. Elution is facilitated by removing as much air from the bottle as possible before connecting it to the needle leading from the generator.

(2) Preparation of ^{113m}In-complexes

(a) Blood pool scanning agent-Figure 2

Eight ml of HCl solution is eluded directly into a pre-autoclaved 20 cc bottle as described above. We determine specific activity by counting an aliquot of the eluent against an ^{113}Sn standard. We use 2-4 mCi (intravenous) cardiac and placental pool scanning. The ^{113m}In binds to transferrin, a betaglobulin, and has a biological half life of 8 hours. This material may also be used to evaluate transferrin spaces (i.e. plasma volume).

(b) Liver and spleen scanning agent-Figure 3 and 4

Sodium phosphate buffer containing 76.1 gm $Na_2HPO_4 \cdot 7\ H_2O$ and 4.6 gm $NaH_2PO_4 \cdot H_2O$ in 500 ml of pyrogen free water is autoclaved at 250°F for 15 minutes. Enough buffer is added to the 20 cc sterile vials to adjust the final pH to 3.5 for liver scanning and 6 for spleen scanning. Terminal autoclaving and titration are eliminated. We inject 2-4 mCi intravenously, scanning the liver in the anterior and lateral positions or the spleen in the anterior, posterior and left laterial positions.

The whole body dose following a 2 mCi injection is .90 rad, a reduction from the 5-7 rads per millicurie of ^{198}Au.

(c) Lung scanning agent-Figure 5

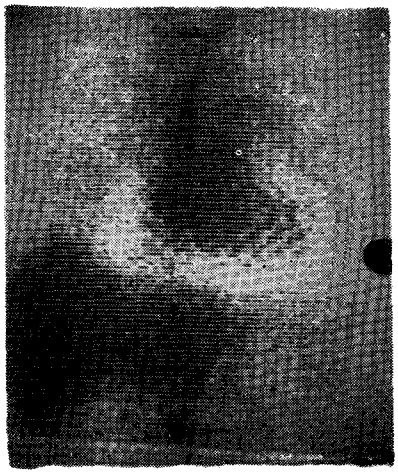
This lung scanning complex is prepared in two steps, requiring two pre-prepared vials. The first contains .15 ml $FeCl_3 \cdot 6\ H_2O$ solution (5% $FeCl_3 \cdot 6\ H_2O$ in 0.05 N HCl) and the second, .17 ml NaOH (10% in pyrogen free water).

The generator is eluded into the first vial with 5 ml of solution. The contents are transferred to the second vial, along with 1 ml of gelatin (20% USP, acid gelatin). We adjust the final pH to 8-8.5 and, assay for specific activity. Particle size should be between 10-60 uc as checked with a hemocytometer. If larger particles are seen, the preparation should be discarded. After thoroughly shaking the vial 2-4 mCi in 0.5 ml solution is drawn up. The syringe is shaken and the dose injected intravenously with the patient supine. 2×10^5 to 4×10^5 particles are injected. Since there are 2.8×10^{11} capillaries in the lungs (Weibel), only one pulmonary capillary in one million is blocked. We scan the patient immediately after injection in the right and left lateral, anterior, and posterior positions.[6]

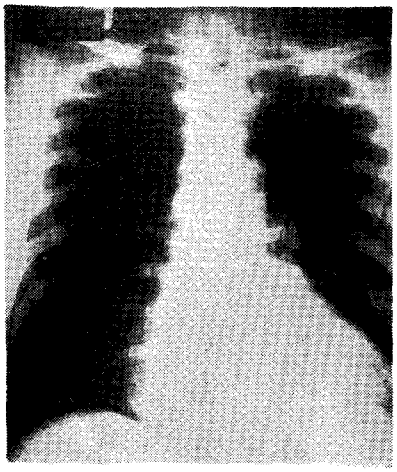
(d) Brain and kidney scanning agent-Figure 6

Since brain scanning is a major part of the clinical load in our department, an easily prepared ^{113m}In labeled compound is extremely useful. We make up a solution containing .762 mg diethylene triamine pentoacetic acid (DTPA) .50 mg acetic acid, 84 mg $Na_2HPO_4 \cdot 7\ H_2O$ and 30.4 mg $Na_3PO_4 \cdot 12\ H_2O$ per milliliter, drawing up 2.1 ml for each sterile 20 cc vial. When ready for use, we elude 8 ml of HCl solution into the vial, assay, and inject 5-10 mCi. We obtain four standard views 20 minutes after the injection. We have found the method reliable and convenient, and have obtained high quality scans comparible to those using ^{99m}Tc pertechnetate.

The same vial can be used for kindney scanning, injecting 5 mCi and waiting 20 minutes before scanning.

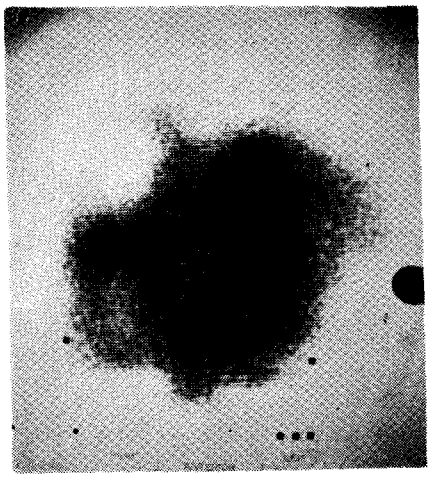


A. Blood pool scan of a patient with large pericardial effusion.

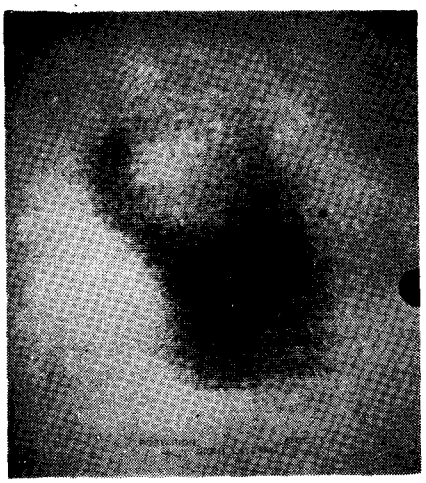


B. Chest X-ray of the same patient.

Figure 2. Blood pool scan



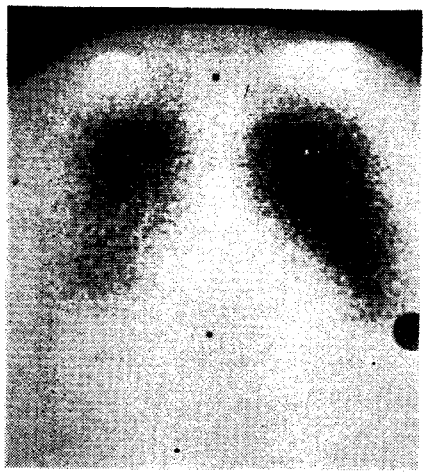
A. Anterior liver scan with multiple space occupying lesions.



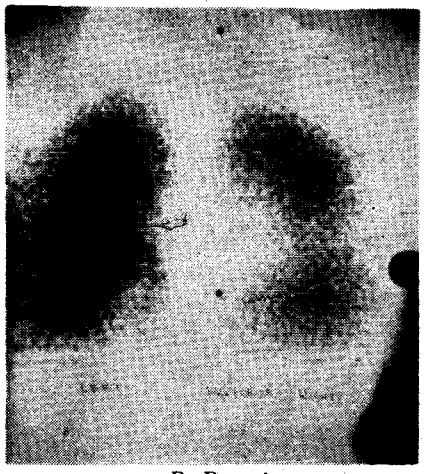
B. Right lateral view of same patient.

Figure 3. Liver scan

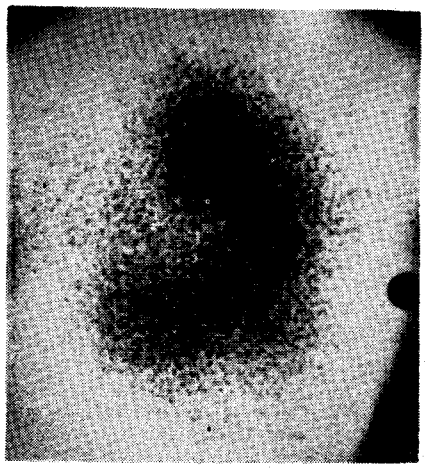
Figure 4. Spleen Scan: Posterior view. An enlarged spleen is shown on the left with uniform activity.



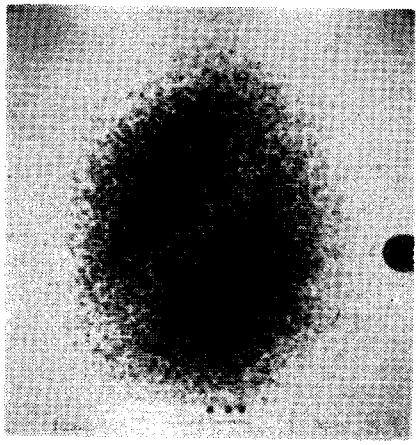
A. Anterior



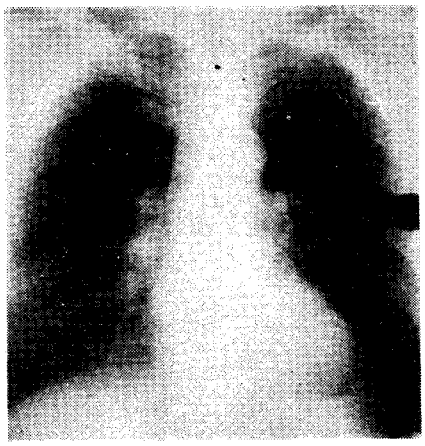
B. Posterior



C. Right lateral

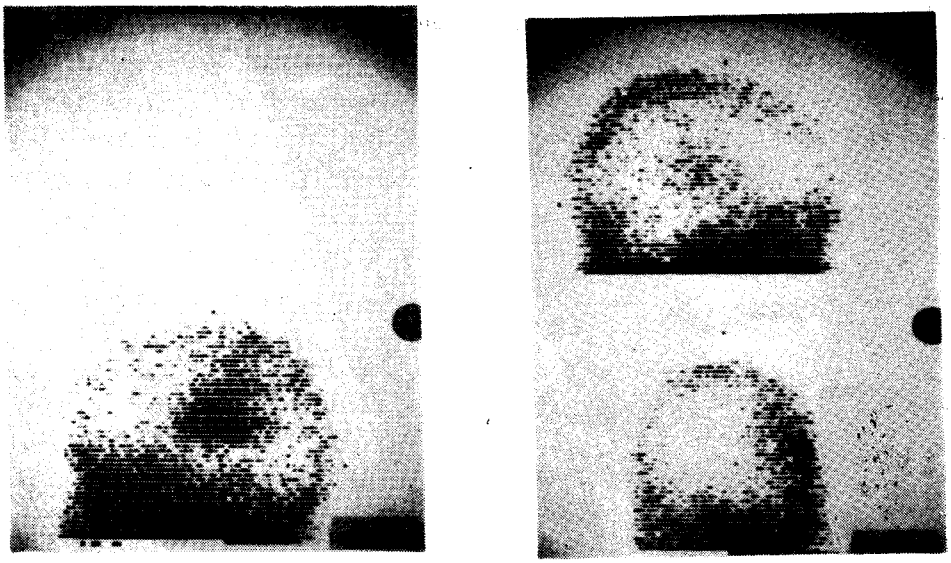


D. Left lateral



E. Chest X-ray

Figure V. Lung scan from a patient with pulmonary emboli. Lateral views. Notice the large band-like perfusion defect in the R.L. view (Fissure sign).



A. Left lateral

B. Right lateral (top), Anterior (bottom)

Figure 6. Brain scan: Recurrent meningioma left parietal lobe

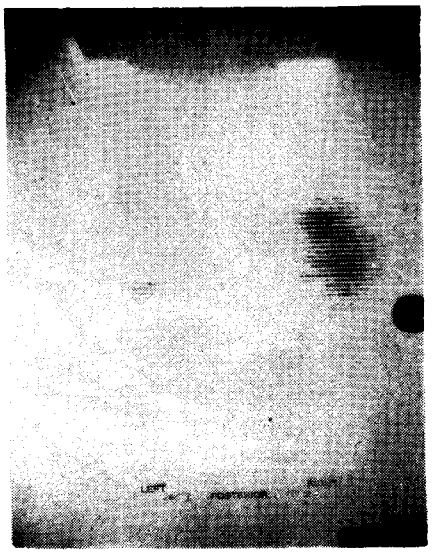


Figure 7. Kidney Scan with ^{113m}In-DTPA complex: Posterior view showing a large hydronephrotic kidney on the left and a normal kidney at right.

CONCLUSION AND SUMMARY

A simplified preparation of ^{113m}In labeled compounds for multiple organ scanning is presented. Clinical experience in more than 500 patients have led us to conclude that these preparations result in scanning images of comparible quality to previously available radiopharmaceuticals. This short lived, broad spectrum scanning agent eliminates the need for storing many different nuclides in the clinical laboratory (which may decay before the clinical need for their use arises) and since the generator has a long effective life (e.g.~5 months) there is no need for frequent radiopharmaceutical delivery. These considerations markedly decrease the radionuclide cost per scan, e.g. in our laboratory, the expense per brain scan for Indium-113 m is approximately 1% that of Mercury 197 or 203.

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