JOURNAL OF NUCLEAR MEDICINE 5:1-8, 1964

An Approach to the Scanning of Pulmonary Infarcts[1,2]

James L. Quinn, III, M.D.,[3] Joseph E. Whitley, M.D.,[4]
Allen S. Hudspeth, M.D.,[5] and Finley C. Watts, B.S.

Winston-Salem, North Carolina

INTRODUCTION

The clinical diagnosis of pulmonary infarct is often difficult. The vagaries of radiologic diagnosis (2) have recently been reviewed.

Because it is important to differentiate pulmonary infarcts from other conditions, and because of changing concepts of treatment with even surgical removal of pulmonary emboli a practical present day consideration, more accurate diagnostic procedures are needed.

Williams, *et al* (2,3) have reported the use of pulmonary angiography for the detection of pulmonary emboli in 50 patients with suspected pulmonary emboli. Ariel (1) has reported successful scintiscanning of surgically created pulmonary infarcts in animals employing the intravenous injection of radioactive microspheres. He has also described his experience in applying the technique in humans.

Since some diagnostic aids are inexact and others difficult or potentially harmful to a group of patients who are usually seriously ill, we have attempted to use soluble radioisotopes in an effort to develop a new technique. The investigation has been carried out by studying the distribution of radioisotopes in the circulation of dogs who have had pulmonary infarcts produced by artificial embolization. The production of the embolus is by a simple technique which does not otherwise disturb the circulation of the lungs or adjacent structures, and does not involve thoracotomy.

EXPERIMENTAL DESIGN

1. Mongrel dogs were examined for heart worms *(Dirofilaria immitis)* by peripheral blood smear inspection, and for gross pulmonary disease by chest roentgenograms. The dogs were 10 to 17 Kg in weight, except for a single dog weighing 23 Kg.

---

[1]Departments of Radiology and Surgery, Bowman Gray School of Medicine.

[2]This project was supported by a grant from the Fluid Research Funds of the Bowman Gray School of Medicine.

[3]Fellow, American Cancer Society.

[4]Senior Investigator in Clinical Research, N.C. Heart Association.

[5]Research Fellow, National Institutes of Health (Heart Institute).

2. Radiopharmaceutical. Three compounds were chosen for testing viz. Chromium-51 tagged red cells (CR^{51}-RBC), Iodine-131 human serum albumin ($RI^{131}SA$), and Mercury-203 chlormerodrin ($Hg^{203}CM$) on the basis of availability and proven utility in other scanning procedures.

3. Dosage. To insure adequate tissue radioactivity in this experiment, a dose of 500 microcuries of $Hg^{203}CM$, 250 microcuries $RI^{131}SA$, and 250 Cr^{51}-RBC was used for each experimental animal regardless of weight.

4. Embolus Technique. A simple method of embolization was developed by one of the authors (A.S.H.). It will be reported in detail in a forthcoming article along with the gross and microscopic changes in the lung. It involves the introduction of a piece of Ivalon (TM) surgical sponge into the external jugular system of the anesthetized dog.

5. Study Groups. There were three major and two minor study groups:

Group A. Control—injection of the radiopharmaceutical followed by sacrifice of the dogs at intervals of 1, 4, 8, 12 and 24 hours.

Group C. Older Embolus—embolus followed by the injection of the radiopharmaceutical *one hour* later followed by sacrifice of the dogs at intervals of 1, 4, 8, 12 and 24 hours.

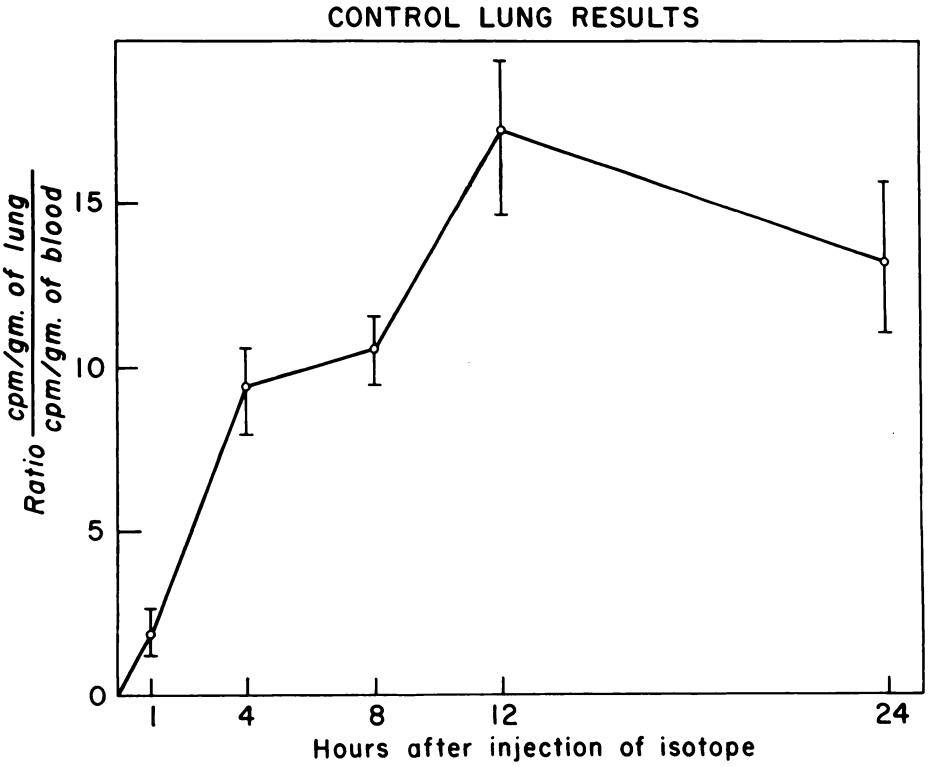

Fig. 1 Group A—Control. Mean radioactivity ratio and range of normal lung in cpm/gm to whole blood in cpm/gm., at intervals of 1, 4, 8, 12 and 24 hours after the intravenous injection of Hg^{203} chlormerodrin.

Group B. Recent Embolus—embolus followed by the injection of the radiopharmaceutical *twenty-four hours* later followed by sacrifice of the dogs at intervals of 1, 4, 8, 12 and 24 hours.

Two or three dogs were used to study each of the above intervals. Two other groups were studied, each consisting of two animals.

Group D. Embolus followed by injection of the radiopharmaceutical *forty-eight hours* later followed by sacrifice of the dogs 24 hours post-injection.

Group E. Embolus followed by the injection of the radiopharmaceutical *94 hours* later followed by sacrifice of the dogs 4 hours post-injection.

6. Necropsy. The animals were electrocuted and dissected. Samples of grossly normal and infarcted lung were removed for microscopy.

7. Tissue sampling. The following tissues were obtained for radioassay in an automatic gamma well counter: lung, normal and infarcted; whole blood; myocardium; liver; spleen and renal cortex.

In order to test the validity of random sampling of lung tissue, a control dog had nine samples taken from each apical and diaphragmatic lobe (three at the peripheral visceral pleural reflection, three in the mid-portion of the lobe and three close to the hilum), and six samples from each cardiac lobe (two peripheral, two mid and two central or hilar). The counts per minute per gram (cpm/gm) of tissue was determined and the values analyzed statistically. The

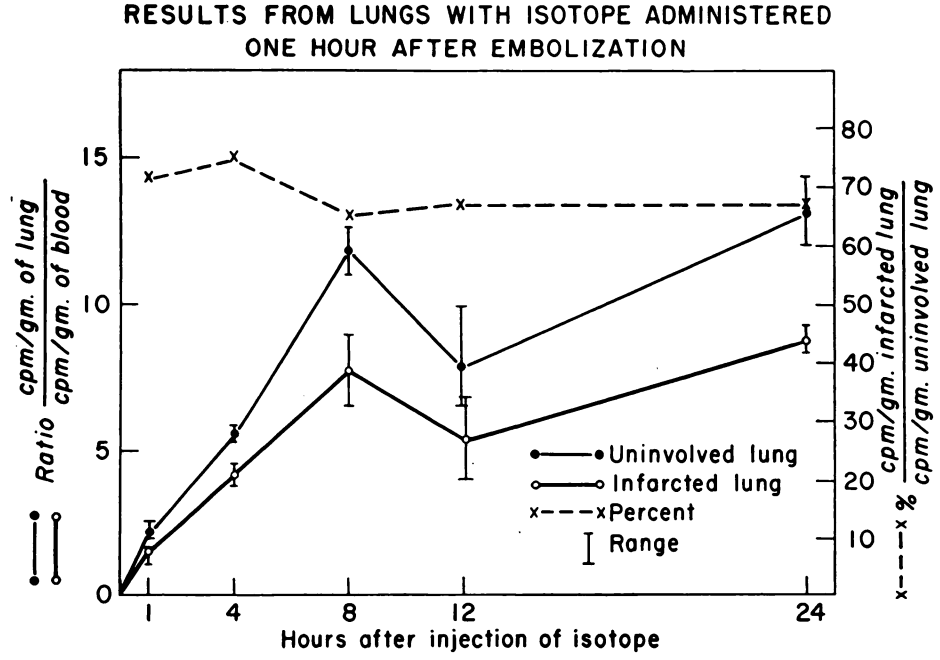

Fig. 2 Group B—Embolization 1 hour prior to isotope injection. Mean radioactivity ratios and ranges of uninvolved and infarcted lung in cpm/gm to whole blood in cpm/gm, at intervals of 1, 4, 8, 12 and 24 hours after the intravenous injection of Hg^{203} chlormerodrin. Dotted line represents ratio of radioactivity of infarcted lung to uninvolved lung.

lobes were compared one to another, the lungs were compared one to another and the samples obtained from the mid-section of all six lobes were compared with the samples obtained from the hilar regions. Statistically there was no difference in activity per gram of tissue between lobes or lungs ($P > 0.5$). The samples obtained from the periphery were compared to the samples obtained from the mid and hilar regions, and the activity levels of the two regions were statistically different ($P < 0.001$). Therefore, random sampling of the lungs was abandoned and the normal and infarcted lobes were each homogenized and analyzed. A kitchen blender was used and a satisfactory homogenate was obtained for radioassay.

8. Sample counting and recording. The tissues were placed in weighed counting vials and the sample weight determined immediately. The tissues were then counted in an automatic gamma ray well-type counter and the cpm/gm of tissue determined. A ratio of the cpm/gm tissue to the cpm/gm whole blood was the determined and this value was used to graphically describe the distribution of the radiopharmaceutical.

9. Scanning. Two animals were subjected to pulmonary embolus, and twenty-four hours later the radiopharmaceutical was administered. Four hours

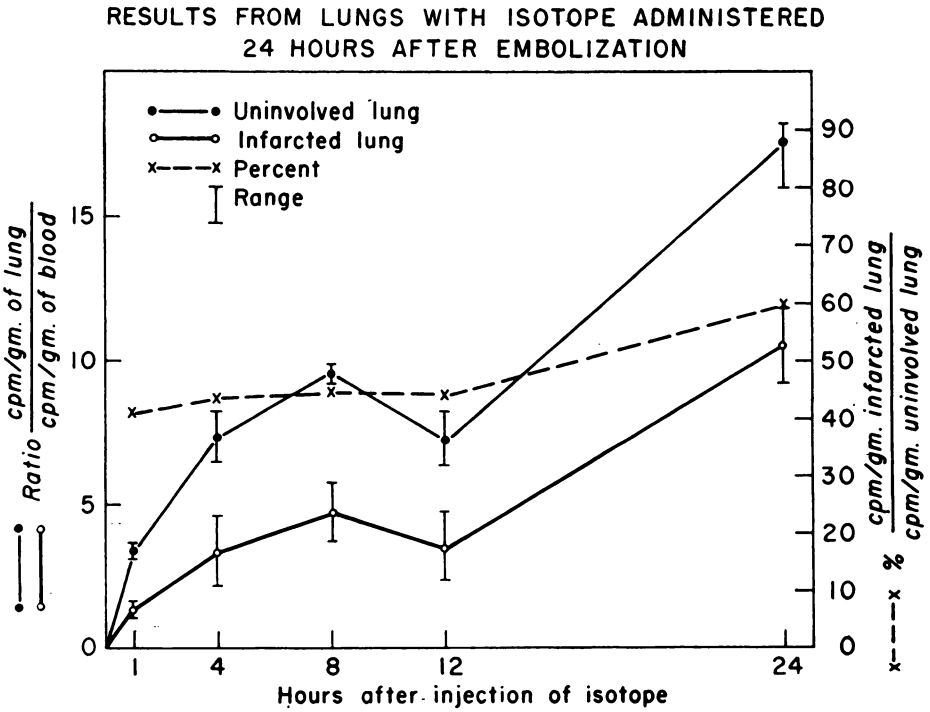

Fig. 3 Group C—Embolization 24 hours prior to isotope injection. Mean radioactivity ratios and ranges of uninvolved and infarcted lung in cpm/gm to whole blood on cpm/gm, at intervals pf 1, 4, 8, 12 and 24 hours after the intravenous injection of Hg^{203} chlormerodrin. Dotted line represents ratio of radioactivity of infarcted lung to uninvolved lung.

post-injection the animals were sacrificed and dissected. The heart and lungs were removed *in toto* and the organ block was scanned.

RESULTS

1. Emboli were released into the circulation of 52 dogs. None of the animals were disabled in any way by the procedure as judged by inspection and observation of their behavior prior to sacrifice. Gross and microscopic changes consistent with hemorrhagic infarction developed in 43 dogs. Of these, 31 were in the right diaphragmatic lobe and 12 were in the left diaphragmatic lobe. No infarct was present in 9 instances. Only 1 large dog (23 Kg) had the embolus in a pulmonary artery without gross changes. The embolus could not be found in the pulmonary arteries of the other 8 dogs. It is presumed that it was lodged in the venous structures leading into the right atrium or in the papillary musculature of the right ventricle.

2. $RI^{131}SA$, Cr^{51}-RBC: There was no significant difference in infarct area and uninvolved lung activity with tagged red cells and $RI^{131}SA$. There was considerable retained blood stream activity with these compounds, making the heart blood pool an interfering factor in regard to scanning. After this initial experi-

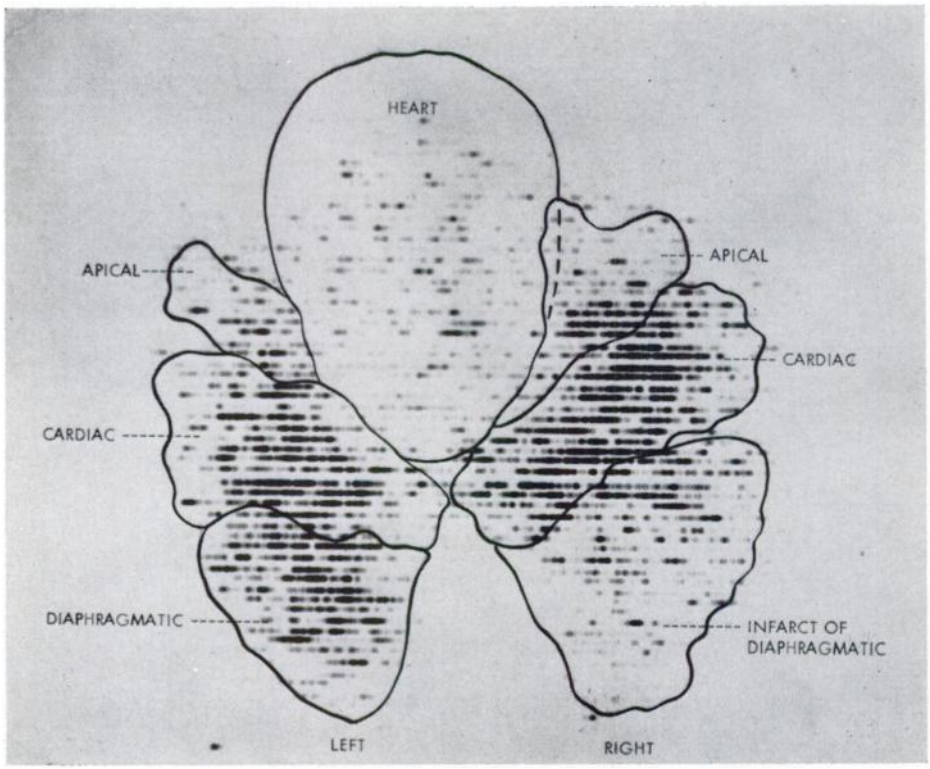

Fig. 4 Photoscan with superimposed line drawing of block dissection of heart and lungs demonstrating diminished activity in association with an infarct of the right diaphragmatic lobe. The normal to infarcted tissue activity ratio was approximately 2:1.

ence was verified with 3 animals in each group all further attention was concentrated on Hg^{203} chlormerodrin.

3. Hg^{203} Chlormerodrin: The chlormerodrin was the only compound in this group which had significant uptake differences in the infarct as opposed to uninvolved lung, and in addition the blood activity was low after one hour.

A. Lung. In the control Group A, pulmonary activity rose and was relatively constant from the 4th through the 8th hour, with a peak at 12 hours and a slight fall at the 24 hour interval (Fig. 1). The embolus Groups B and C behaved much the same, peaking at 8 and 24 hours for both the normal and the infarcted tissue. In Group B, the percentage activity in the infarct area as compared to uninvolved lung maintained a level of 65-75 per cent from one through 24 hours (Fig. 2). In Group C this value remained constant from the first

TABLE I

MEAN ACTIVITY RATIO OF TISSUE TO WHOLE BLOOD AS MEASURED IN COUNTS PER MINUTE PER GRAM.

	Hour	*Lung*			*Heart*	*Liver*	*Spleen*	*Kidney*
		Infarct	*Normal*	*Ratio*				
Group A*	1		1.94		0.39	1.29	1.30	64.
	4		9.24		1.40	5.42	8.81	282.
	8		10.8		1.35	8.21	11.2	451.
	12		17.2		2.05	16.1	14.4	691.
	24		13.3		1.86	17.4	12.3	512.
Group B*	1	1.54	2.14	0.72	0.54	2.02	1.58	62.
	4	4.20	5.29	0.75	0.99	6.06	4.46	210.
	8	7.75	11.9	0.65	1.36	7.26	9.66	380.
	12	5.36	2.92	0.68	0.70	8.79	7.64	215.
	24	8.88	13.2	0.67	1.02	22.4	10.4	566.
Group C*	1	1.42	3.44	0.41	0.61	1.76	4.90	77.
	4	3.42	7.36	0.46	0.84	4.22	9.86	183.
	8	4.76	9.58	0.50	1.40	9.82	10.8	438.
	12	3.50	7.25	0.48	1.15	15.7	16.8	315.
	24	10.6	17.6	0.60	1.46	22.0	15.6	704.
Group D*	24	6.74	17.8	0.38	1.32	22.0	12.0	326.
Group E*	4	2.92	7.86	0.37	1.08	6.87	9.27	280.

*See Experimental Design 5, for Group Definition.

until the 12th hour at around 45 per cent, and by 24 hours had risen to 60 per cent (Fig. 3). The activity in the infarcted areas of the lung in Groups D and E (emboli 48 and 94 hours old) was around 37 per cent that of uninvolved lung. Infarcted and uninvolved lung segments were submitted to radioactive assay in both the natural and dessicated state. The activity differential of the infarcted lung to normal lung in the wet state was approximately the same when aliquots of lung were dried, supporting the thesis that the activity differential was not dependent on the edema associated with the infarct.

B. Heart. The activity curves in Groups A, B, and C were quite similar to lung with activity peaks at 4 and 12 hours in Group A, and at 8 and 24 hours in Groups B and C (See Table I). The absolute radioactivity levels in the normal myocardium are sufficiently low that they would probably not interfere with lung scanning.

C. Kidney Cortex. The activity curve in the renal cortex parallels that of the myocardium in Groups A, B and C (Table I). The absolute activity differential of kidney cortex to myocardium is approximately 300/1. The activity in the kidney cortex is much higher than in the kidney medulla. The cpm/gm tissue activity differential of cortex over medulla is in the order of 6-10/1.

D. Liver and Spleen. The activity as measured by cpm/gm of liver and spleen are quite similar to the lung (Table I). Initially, splenic activity is higher than liver activity per unit weight. In Groups A and B the liver activity became higher than the splenic activity between the 8th and 12th hours; in Group C this occurred between the 12th and 24th hours.

E. Scanning. The photoscan outlined an area of decreased activity in the infarcted right diaphragmatic lobe (Fig. 4). The tissue activity per gram of the infarcted lobe was 45 per cent of normal lung.

DISCUSSION

The ideal radiopharmaceutical for the scanning of pulmonary infarcts would:

1) concentrate rapidly at a significantly different level in infarcted and uninvolved lung tissue;

2) be so selective in the organs in which it concentrates as to present a low radiation background when other organs are compared to the lungs;

3) must rapidly clear from the blood stream if the infarct isotope concentration is lower than that in the blood;

4) give a low radiation dosage to the patient with a suitable gamma energy for scanning;

5) be non-toxic.

From the superficial investigation made with $RI^{131}SA$ and RBC-Cr^{51}, they do not fulfill enough of the above criteria to warrant further investigation.

From the data on experiments with Hg^{203}-CM, several generalities are obvious. The infarct from a one hour old embolus reacts to chloromerodrin differently than the infarct that is association with a 24 hour old embolus. An infarct one hour after embolization will attain approximately 70 per cent of the activity level of uninvolved lung, while the infarct from a 24 hour old embolus will take

up only about 40 per cent as much activity as uninvolved lung. The activity of the heart and the blood clears rapidly and is negligible one hour after the injection of chloromerodrin with respect to scanning.

The activity of the spleen and liver parallels that of the lung, per unit weight, but will undoubtedly interfere because of the greater total mass of these organs with lower lobe scanning *in vivo*. In addition, when the kidney is situated near the diaphragm, its 300/1 activity differential would also interfere with detection of basal infarcts. The differential in radioactivity between the infarcted and uninvolved lung in cpm/cc in the aerated state would undoubtedly differ from that calculated in cpm/gm from homogenized lobes. If significant atelectasis exists in the infarct, the possibility of obtaining the necessary differential for a diagnostic scan would be lessened, as the cpm/cc for infarcted and normal lung would more closely approach each other even though their cpm/gm would still be approximately 1:2.

SUMMARY AND CONCLUSIONS

1. A simple embolus technique for producing pulmonary infarcts in mongrel dogs is described. It was successful in 43 of 44 instances where the embolus could be located within the pulmonary artery system.

2. Three radiopharmaceuticals viz. Cr^{51} tagged red blood cells, I^{131} human serum albumin and Hg^{203} chlormerodrin were evaluated as to their possible efficiency in detecting such infarcts. Chlormerodrin was the only one found to be promising.

3. Successful scans of the pulmonary infarct outside of the chest were obtained. No attempt was made to scan the lungs inflated or within the chest.

4. Hg^{203} chlormerodrin is not likely to be a satisfactory compound for detecting pulmonary infarcts in clinical practice, particularly in regard to scanning the lower lobes of the lungs, due to interference from liver, spleen and renal activity.

5. The described experimental technique is probably satisfactory for initial screening of other radiopharmaceuticals for possible use in the detection of pulmonary infarction.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the assistance of R. W. Prichard, M.D. in the preparation of the manuscript and review of the pulmonary tissue; J. W. Eubanks, D.V.M. and J. R. Pick, D.V.M. for assistance in animal necropsy and slide preparation and A. R. Edwards for assistance in sample weighing and counting.

REFERENCES

1. ARIEL, I. M., (as quoted in Highlights of the Society of Nuclear Medicine meeting): *J.A.M.A.* **183**:32, 1963.
2. WILLIAMS, J. R. and WILCOX, W. C.: Pulmonary Embolism, Roentgenographic and Angiocardiographic Considerations. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* **89**:333, 1963.
3. WILLIAMS, J. R., WILCOX, C., ANDREWS, G. J. and BURNS, R. R.: Angiography in Pulmonary Embolism. *J.A.M.A.* **184**: 1963.