

Lung Scanning With Colloidal RISA^{1,2,3}

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Pulmonary artery occlusions were first visualized by scintillation scanning techniques using Hg²⁰³ labelled insoluble ceramic microspheres by Haynie, Calhoun, Nasjleti, Nofal and Beierwaltes (1). The suggestion was made that soluble microspheres would be more desirable for this purpose because the small arterioles filtering out the microspheres would be occluded for only a short period of time. We here present the use of colloidal I¹³¹ labelled human serum albumin (colloidal RISA) as a source of gamma emitting particles for the visualization of the intact pulmonary vascular bed following the suggestion of Taplin (2).

Colloidal RISA

Colloidal RISA was prepared by the technique of Taplin (2). Commercially available RISA⁴ was diluted to a 1 per cent albumin solution, adjusted to a pH of 5.7, then heated with agitation for 20 minutes at 75°C. The supernatant was removed and one half that volume of saline was added to the flocculate. The usual scanning dose was about 75 μ c of I¹³¹, with a maximum of 100 mg of albumin and a volume of 5-10 ml. Particle size was usually 10-50 microns in diameter.

Dogs

The colloidal RISA was injected into the saphenous veins of mongrel dogs weighing approximately 12 kg (25 lbs) during sodium pentothal anesthesia.

Scanning

Using a photo-dot scanner, equipped with a 3 \times 2 inch sodium iodide crystal and a 19 hole collimator⁵, scans were carried out with anesthetized dogs in the prone position. Scans were begun about 15 minutes after injection of the colloidal RISA, starting from below the level of the lowest rib and proceeding cephalad to about the level of the base of the skull. Maximum count rates varied from 2,000 to 8,000 cpm over the lung areas just prior to starting the scan.

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⁴Squibb Biological Laboratories, New Brunswick, N.J.

⁵Pickering Magnascanner, Picker X-Ray Corporation, White Plains, N.Y.

Twelve to twenty-four hours post injection, no discernable activity above body background was found in the chest area. One dog was sacrificed 15 minutes after the injection of colloidal RISA and then scanned.

Biological Half-Life

Blood samples were drawn and stools and urines were collected quantitatively in metabolism cages on three dogs for 10-12 days. All urine and stool counts were performed on the last day of collection.

Tissue Counting

Two animals were sacrificed 10 minutes after injection of colloidal RISA, and various tissues were counted for relative radioactivity determinations in a scintillation well-type counter.

Operations

Pulmonary arterial occlusions were produced at thoracotomy by ligatures around various branches of the pulmonary arteries; the lungs were then re-expanded and an air tight closure effected. Scans were performed at time intervals varying from 1/2 hour to five days after operation. Chest x-rays were taken before and after surgery and at one or two day intervals thereafter. Ligations of the arteries to the following lobes were performed: Right upper, middle and lower lobes and left upper and lower lobes.

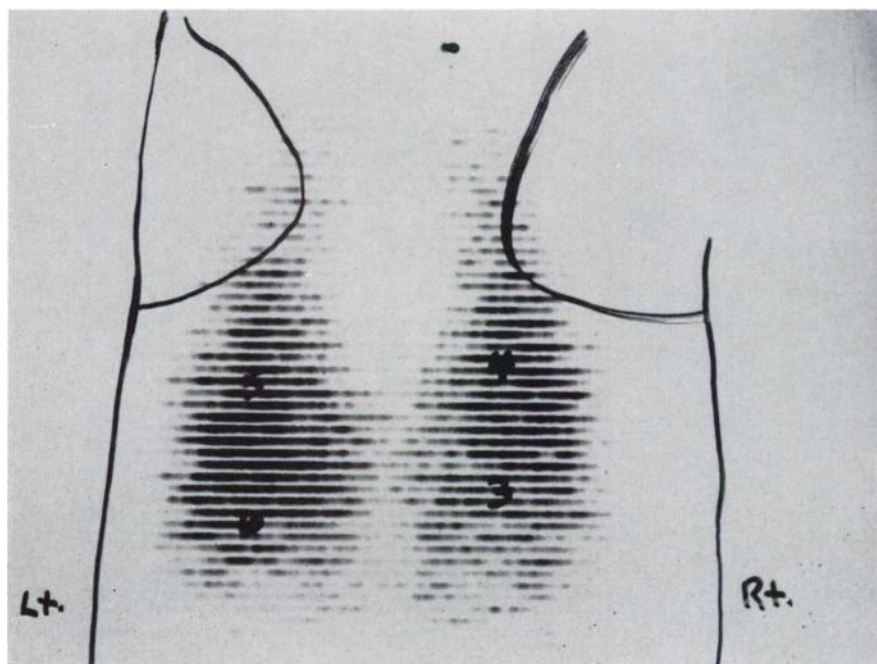


Fig. 1. Normal dog lung scan.

Toxicity Studies

Doses of up to 2 gms of colloidal human serum albumin were administered intravenously to five dogs and the dogs observed for evidence of dyspnea or death.

Pathological Examinations

All lungs scanned were submitted for gross and microscopical pathological examination.

RESULTS

Scans

Several normal dog lung scans were recorded at the outset. An example of these is presented in Fig. 1. Scans following ligation of the right upper lobe (Fig. 2), right middle lobe (Fig. 3), right lower lobe (Fig. 4), left upper lobe (Fig. 5), and left lower lobe (Fig. 6) are presented. All scans demonstrated an area of decreased radioactivity concentration distal to the arterial occlusion. In every instance it is noted that the cardiac area had significantly less activity than nearby normal lung and with the technique used, no significant uptake was encountered in the liver and spleen areas. After 12-24 hours, most of the radioactivity appears to have cleared from the lung area and has appeared in the liver and spleen areas (Fig. 7). The one dog that was sacrificed 15 minutes after injection of colloidal RISA and then scanned failed to show significant activity outside the chest area.

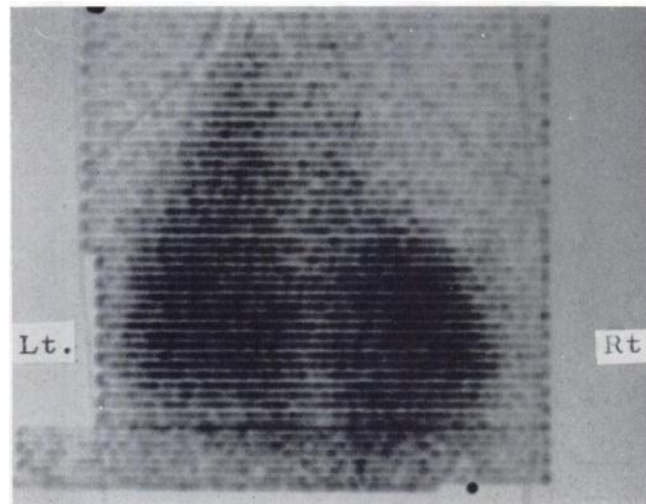


Fig. 2. Lung scan. Right upper lobe pulmonary artery ligation.

Biological Half-Life

The biological half-life of the I^{131} from colloidal RISA is shown in Figure 8. The half-life appears to be between $1\frac{1}{2}$ and 2 days whether or not the thyroid gland is blocked with iodides prior to injection.

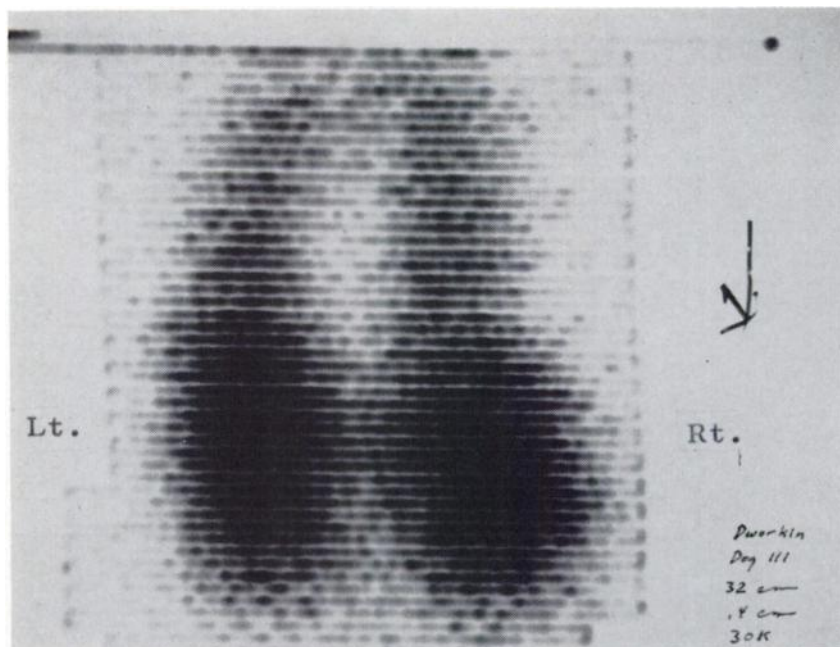


Fig. 3. Lung scan. Right middle lobe pulmonary artery ligation. Note small "pie" shaped cut in lateral border of right lung.

Tissue Counting

Tissue sample counts taken 10 minutes after injection of two dogs are recorded in Table I. The lung appears to have a minimum of 5-10 times the activity of any other tissue evaluated. Normal lung shows 10 or more times the activity of ligated lung.

Toxicity Studies

Toxicity studies have been completed on five dogs. Two of five dogs have tolerated up to two grams of colloidal human serum albumin without ill effect. Preliminary studies suggest that dyspnea and increased pulmonary arterial pressures occur when particle size approaches 250μ .

Pathological Examinations

No diffuse process has yet been noted microscopically that would be compatible with diffuse microembolism caused by the small colloidal albumin particles. No gross or microscopic changes secondary to ischemia were noted in a lobe for at least 24 hours following arterial occlusion.

DISCUSSION

The introduction of an inexpensive preparation which is cleared from the lungs rapidly after scanning and is readily excretable with a relatively short biologic half-life, makes feasible pulmonary scanning in the human subject.

Colloidal RISA has been used by others to estimate liver blood flow and reticuloendothelial phagocytic function (3,4) and for liver and spleen scanning (2). The colloidal aggregate size in these instances was well below 10 microns (estimated at 10-20 $m\mu$). These particles easily pass the pulmonary vascular bed on intravenous injection and were found primarily in the liver and spleen (5). No toxicity was reported in these studies in man or in any other

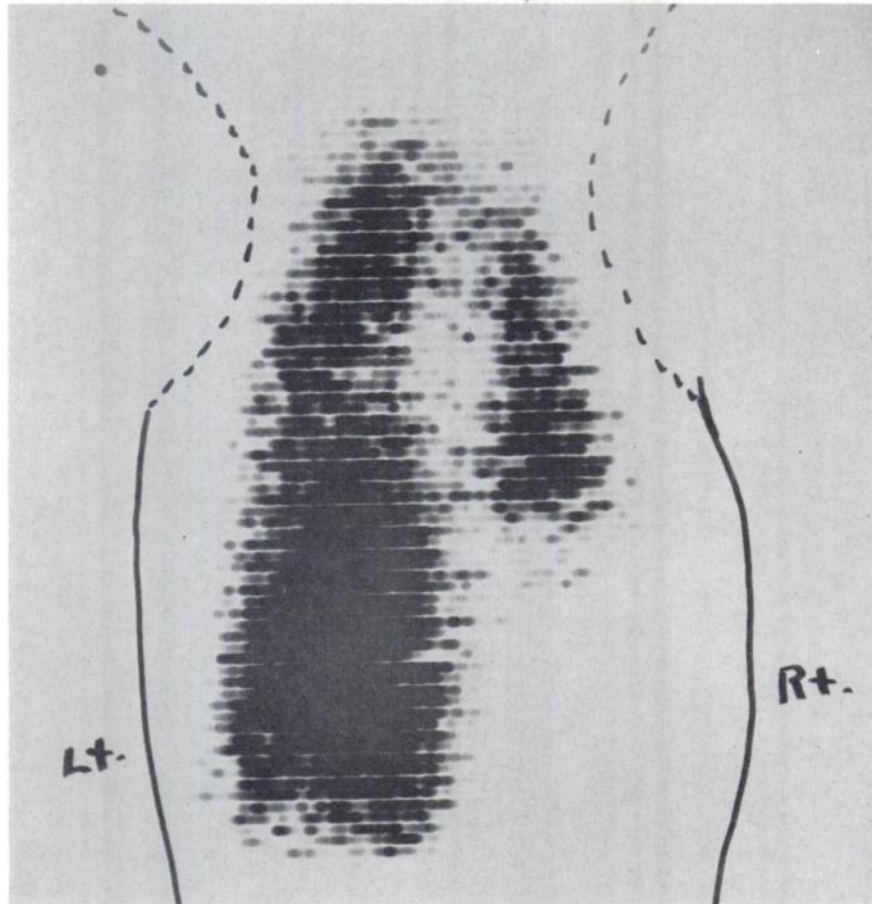


Fig. 4. Lung scan. Right lower lobe pulmonary artery ligation.

species tested using this particle size in doses varying from 1-10 mg albumin per kilogram body weight. Taplin (2) reports no anaphylactoid reactions after 1,000 intravenous injections in man, including 20 individuals who had multiple tests over periods varying from 3 weeks to 30 months.

Although we found no definite diffuse microembolic effect on the lung by 10-50 μ size particles, further evaluation will be necessary to determine the effects of these particles on an already partially compromised pulmonary system. Pathologic evidence may not parallel the disturbances in physiologic function.

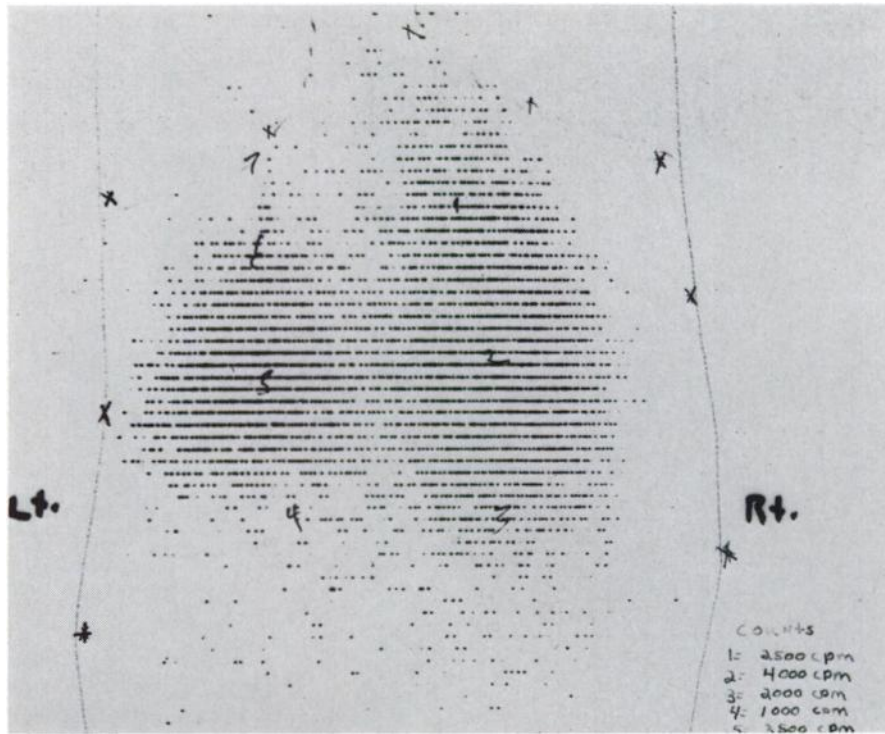


Fig. 5. Lung scan. Left upper lobe pulmonary artery ligation. (Dot scan).

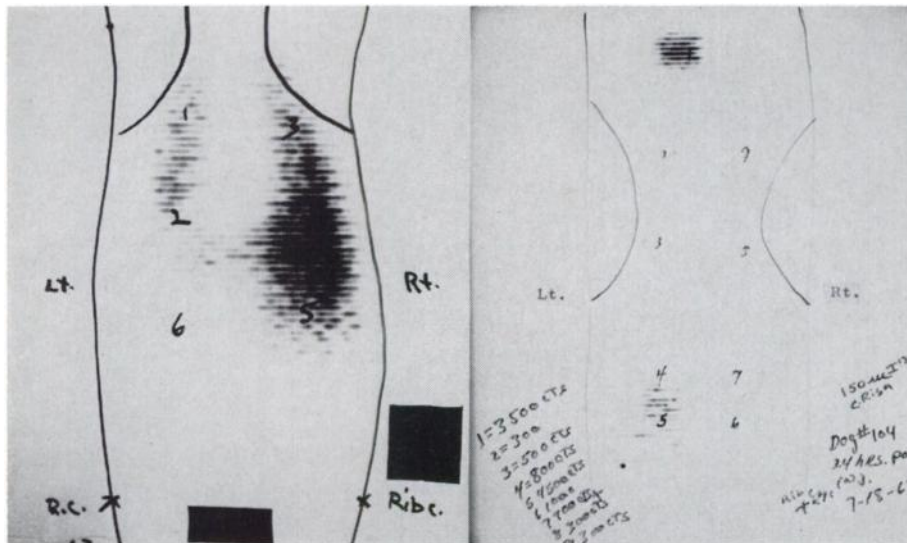


Fig. 6

Fig. 7

Fig. 6. Lung scan. Left lower lobe pulmonary artery ligation.

Fig. 7. Whole body scan. Twenty-four hours after injection. No ligation of lung arteries. Radioactivity has apparently cleared from the lung and is seen in the liver, spleen and thyroid gland (not blocked with I).

The biologic half-life of $1\frac{1}{2}$ to 2 days is in keeping with that found for smaller diameter colloidal particles in man (3). The calculated whole-body exposure to the dogs in this series based on a 2 day biologic half-life is approximately 41 m rad/75 μ c (6) which is within permissible limits for diagnostic tests.

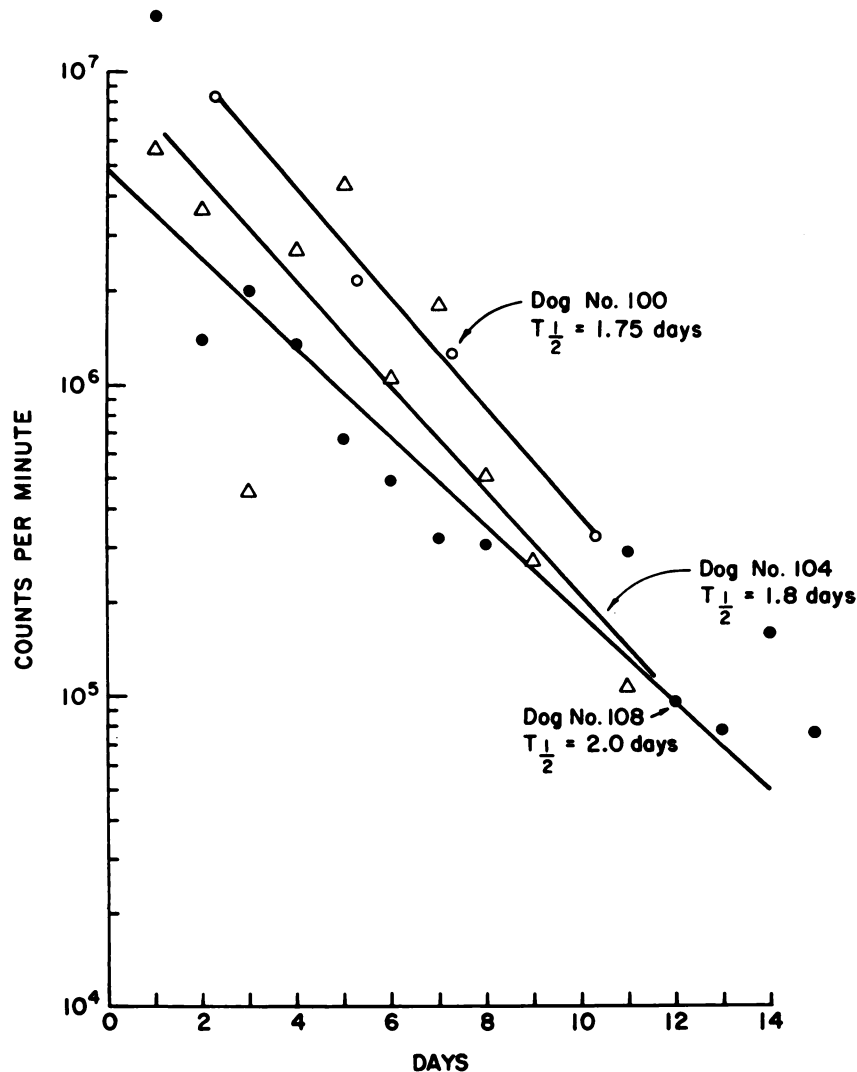


Fig. 8. Biologic half-life of colloidal RISA in dogs. Dog #108 received Lugol's solution prior to colloidal RISA injection; #100 and #104 did not.

Further excreta studies are needed to determine a more accurate biological half-life, since another much longer half-life may become evident beyond 12 days.

With lobar artery occlusions, no difficulty was encountered in perceiving the "cold" area. As pointed out by Haynie *et al* (1), a 3 cm diameter lesion may not be observed due to the limits of resolution, however, position of such a cold area

relative to nearby activity will also prove to be a limiting factor. Thus, certain segmental arterial occlusions may offer difficulty in detection by this technique, but multipositional views might aid in the detection of smaller lesions.

TABLE I
TISSUE COUNTS

<i>Tissue</i>	<i>Dog #116 cpm/gram</i>	<i>Dog #117 cpm/gram</i>
Normal Lung		
RU Lobe	—*	195,224
RM Lobe	—	437,960
RL Lobe	—	875,400
LU Lobe	219,733	108,050
LL Lobe	516,914	745,625
Ligated Lung*		
RU Lobe	3,165	—
RM Lobe	2,970	—
RL Lobe	8,342	—
LU Lobe, segment	—	10,321*
Heart	966	1,541
Spleen	5,006	2,925
R Kidney	2,293	4,305
L Kidney	3,562	4,047
Liver	7,440	4,861
Blood	4,178	—

*The pulmonary artery to the entire right lung of Dog 116 was ligated. Only a small artery to a segment of the left upper lobe of Dog 117 was ligated.

Table I. Activity per gram of tissue ten minutes after injection of colloidal RISA in two dogs. The activity in lower lobes is less than that in the upper lobes. Note the markedly diminished activity in the ligated portions of the lung.

SUMMARY AND CONCLUSIONS

The use of colloidal RISA injected intravenously in a particle size of 10-50 microns followed by lung photoscanning offers a practical, atraumatic method of visualizing pulmonary artery occlusions in the dog. The fact that the particles have a relatively short biological half-life appears to decrease the radiation dose delivered and the duration of occlusion of pulmonary capillaries as compared to ceramic microspheres. Work is in progress to apply this technique to the study of pulmonary artery occlusion in the human.

ACKNOWLEDGMENT

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