

RADIOAEROSOL INHALATION LUNG SCANNING: ITS ROLE IN SUSPECTED PULMONARY EMBOLISM

Toyoharu Isawa,* Michael Hayes, and George V. Taplin

*Harbor General Hospital, Torrance, California,
and the Laboratory of Nuclear Medicine and Radiation Biology,
University of California Los Angeles, Los Angeles, California*

Most lung scan requests are made either to exclude or verify the clinical diagnosis of pulmonary embolism. One of the most useful contributions of radioisotope lung scanning has been its capacity to detect regional pulmonary ischemia. It is now recognized that a diagnosis of pulmonary embolism cannot be made by perfusion scanning alone because other bronchopulmonary diseases may produce identical scan defects (1). Further information is needed to make a more definitive diagnosis. Radioaerosol inhalation scans have the capability of demonstrating the aerated space and the sites and extent of airway obstruction (2-4). The performance of perfusion and radioaerosol inhalation lung scans in rapid sequence is helpful in determining the relations of regional perfusion and aeration in bronchopulmonary disease.

This paper reports the use of these two types of lung scanning procedures in suspected pulmonary embolism. The results indicate their diagnostic value in clinical practice.

MATERIALS AND METHODS

Seventy-three patients (36 male and 37 female; ages 18-74) suspected of pulmonary embolism had initial perfusion lung scan findings compatible with such a diagnosis. Clinical suspicion of pulmonary embolism was primarily based on the classic symptomatology of sudden onset of chest pain, shortness of breath and/or hemoptysis with or without concomitant thrombophlebitis, congestive heart failure, history of surgery, or laboratory findings of suggestive serum enzyme levels. Most patients were studied 1-4 days after the onset of the symptoms. Their perfusion scans showed single or multiple areas of pulmonary ischemia which involved an entire lung, a lobe, a segment, or other less well-defined regions. They were then examined by radioaerosol inhalation lung scanning. Those patients with radiological evidence of lung consolidation or pleural effusion were excluded.

For inhalation lung scanning, solutions of ^{99m}Tc -tagged human serum albumin (^{99m}Tc -albumin) or ^{113m}In -tagged human serum albumin (^{113m}In -albumin) were converted to aerosols by a Mistogen ultrasonic nebulizer and inhaled during normal tidal volume breathing for 7-9 min. Radioaerosol inhalation was made with the patient in the sitting position, the same as for tracer injection for lung perfusion scanning.

When ^{99m}Tc -albumin aerosol is used for inhalation scanning following the initial perfusion scans with either ^{131}I - or ^{99m}Tc -tagged human serum albumin macroaggregates (^{131}I - or ^{99m}Tc -MAA), at least 24-hr delay is required for sufficient removal of radioactivity from the lungs. At this time, both types of lung scans are performed using ^{99m}Tc -albumin for inhalation and ^{131}I -MAA for perfusion studies. Currently, perfusion lung scanning is performed exclusively with ^{99m}Tc -MAA in the author's institution and is followed immediately by inhalation scanning with ^{113m}In -albumin aerosol when indicated (5).

Instruments used for lung imaging were a Picker Dynapix 10-probe rectilinear scanner, a Picker Dynacamera, and a Nuclear-Chicago Pho/Gamma III scintillation camera. Chest radiograms were obtained immediately after the scanning procedure.

RESULTS

Final diagnoses of the 73 patients based on clinical and scan findings are shown in Table 1. Twenty-eight of these had perfusion scans showing single or multiple areas of ischemia and aerosol inhalation scans indicating aeration in the nonperfused areas.

Received Nov. 13, 1970; revision accepted Feb. 24, 1971.

For reprints contact: George V. Taplin, Div. of Nuclear Medicine, Harbor General Hospital, 1000 W. Carson St., Torrance, Calif. 90509.

* Present address: The Research Institute for Tuberculosis, Leprosy and Cancer, Tohoku University, Sendai, Japan.

TABLE 1. FINAL DIAGNOSIS IN 73 PATIENTS

Final diagnoses	Number of patients
Pulmonary embolism (without infarction)	28
Obstructive airways disease	43
Emphysematous	8
Bronchitic	12
Emphysematous and bronchitic	15
Asthma (bronchial and cardiac)	7
Bronchiectasis	1
Unilateral vascular anomalies	2
Pulmonary artery stenosis	1
Pulmonary artery hypoplasia	1
Total	73

They were diagnosed as pulmonary embolism by perfusion and aerosol inhalation lung scanning. Figure 1 illustrates lung scans of a patient with pulmonary embolism which show normal aeration in ischemic lung regions. Nine of these twenty-eight patients had radioaerosol scan evidence of associated obstructive airways disease. In these patients ischemia was present in well-aerated lung regions in addition to the areas with evident obstructive airway disease. Two embolic patients who had no evidence of obstructive airways disease showed slightly decreased aeration in the ischemic regions initially which returned to normal subsequently. Seven of the twenty-eight embolism patients underwent angiography which verified the diagnosis in each instance. One patient died 10 days after combined aerosol inhalation and perfusion scans and autopsy confirmed the diagnosis. The patients with pulmonary embolism were treated with heparin initially and later with coumadin in standard doses.

Repeated scans were helpful in evaluating the patients' response to treatment.

In the 43 patients, the aerosol scan patterns were abnormal in ischemic regions. Specifically, they resembled those observed previously in obstructive airways disease (4). For example, excessive deposition of radioaerosol in the major airways as found in emphysematous patients was seen in eight cases. Peripheral foci of increased radioactivity and/or irregular aerosol distribution, as seen in bronchitic patients, were observed in 12 patients. Figure 2 gives the findings in a patient with bronchitis who was suspected of having pulmonary embolism. Multiple perfusion defects were associated with nonaerated regions in the same locations. Fifteen patients had scan evidence of mixed emphysematous and bronchitic types of obstructive airways disease. Seven others were diagnosed clinically as bronchial or cardiac asthma on the basis of the history, scan findings, and response to treatment. One patient had well-documented bronchiectasis. Two other patients had unilateral pulmonary vascular anomalies, pulmonary artery stenosis, and pulmonary artery hypoplasia.

DISCUSSION

The procedure. Radioaerosol inhalation lung scanning is a relatively simple test of airway patency and regional aeration (2-4). The patient inhales radioaerosol during normal tidal volume breathing. Breath-holding is not required. The patient's position during inhalation is optional. However, the same position for perfusion scanning should be used when possible to permit comparison of the two procedures. Radio-

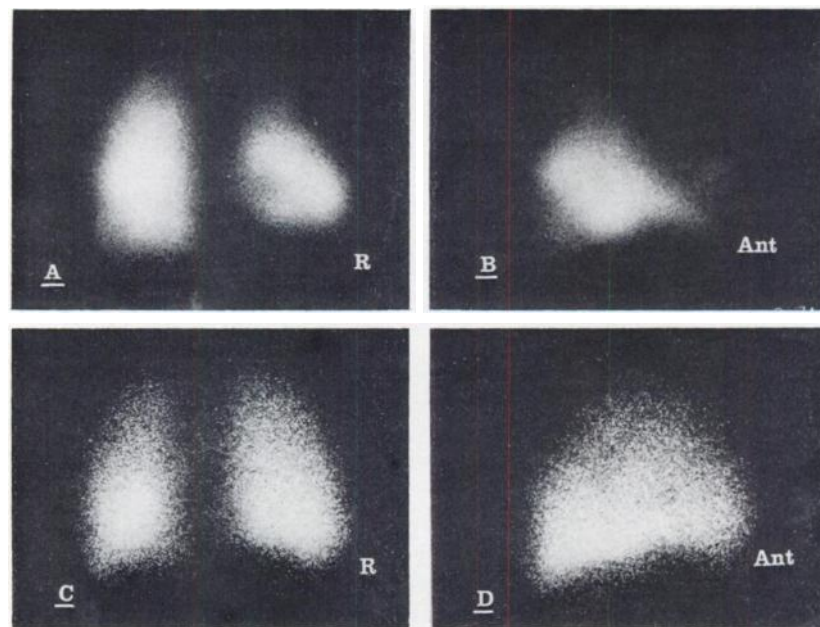


FIG. 1. Lung scans of 72-year-old female with suspected pulmonary embolism. A and B are perfusion lung scans (posterior and right lateral views) showing multiple large perfusion defects (^{99m}Tc -MAA; Dynacamera). C and D are radioaerosol inhalation lung scans (posterior and right lateral views) showing evidence of good aeration in ischemic areas (^{113m}In -albumin; Dynacamera). Diagnosis was of multiple pulmonary embolism.

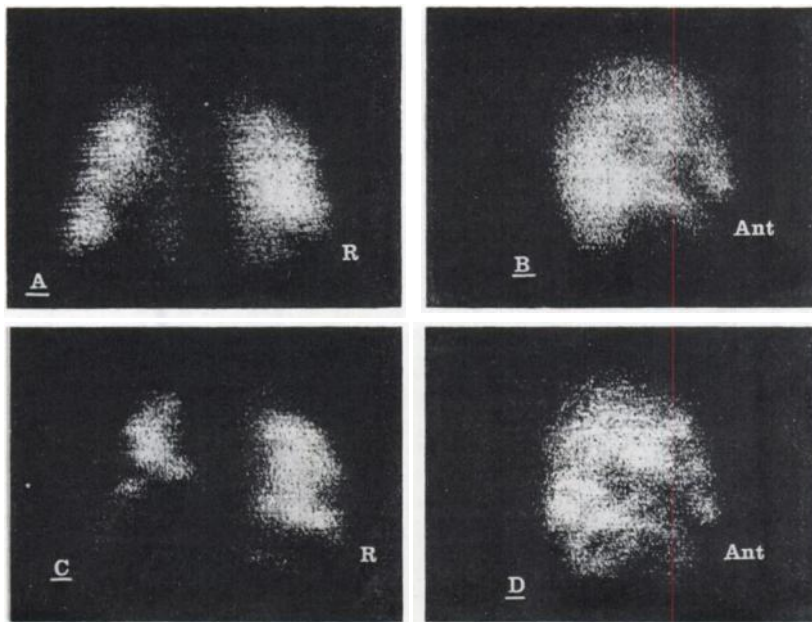


FIG. 2. Lung scans of 56-year-old male with suspected pulmonary embolism. A and B are perfusion lung scans (posterior and right lateral views) showing multiple perfusion defects (^{125}I -MAA; Dynapix). C and D are radioaerosol inhalation lung scans (posterior and right lateral views) showing evidence of poor aeration in ischemic areas ($^{99\text{m}}\text{Tc}$ -albumin; Dynapix). Diagnosis was of obstructive airways disease (bronchitic).

aerosol scans may be performed in most severely ill patients.

Interpretations. Since multiple views of the lungs are obtained by aerosol inhalation and perfusion lung scanning, comparison of aeration with perfusion on a regional basis is possible. As evident from the present results, the regions of pulmonary ischemia of embolic origin are well aerated in most cases. However, in patients with associated obstructive airways disease (nine of the 28) when there is normal or near normal aerosol deposition in ischemic areas, the ischemia is considered to be of vascular or embolic origin rather than due to primary airways disease. Two of the nine patients had pulmonary angiography which showed embolic occlusion as indicated by scans. Twenty-eight of the 73 patients were diagnosed as having pulmonary embolism based on the discrepancy between perfusion and aerosol deposition patterns. Pulmonary angiography in seven of these verified the diagnosis.

It was surprising to find that in over 50% of the 73 patients with suspected pulmonary embolism, perfusion changes could be explained on the basis of obstructive airways disease such as pulmonary emphysema, acute and chronic bronchitis, or bronchial asthma. Small pulmonary emboli could not be excluded completely in this group of patients, but strong scan evidence for obstructive airways disease was useful in making the initial treatment decision. Without radioaerosol inhalation scanning, the majority of the patients could have been misdiagnosed as having pulmonary embolism and treated as such. Serial lung scans helped guide the patients' subsequent management by demonstrating the validity or

errors in the initial working diagnoses. For instance, in emphysematous patients, perfusion scan patterns remained unchanged, but in reversible airways disorders such as bronchial asthma or bronchitis, their perfusion abnormalities returned toward normal. As reported previously (4), aerosol inhalation scans are sensitive indicators of airway obstruction. Local ischemia occurs promptly after regionally diminished airflow as demonstrated in unilateral experimental airway occlusion (6) or alveolar hypoxia (7). These physiologic vascular responses are considered to play an important role in the changing perfusion patterns in obstructive airways disease. Moreover, anatomical displacement or attenuation of blood vessels is also known to decrease perfusion in emphysematous lungs (8).

Abnormal ventilation in acute pulmonary embolism. It has been observed clinically and demonstrated experimentally that regional decreases in pulmonary perfusion may cause regional decreases in ventilation due to bronchoconstriction (9-11). The two patients who showed evidence of hypoventilation in ischemic areas initially could have fallen into this category, but the bronchoconstriction in pulmonary embolism seems to be a very early transient phenomenon. After recovery from this phenomenon in several hours in dogs, normal ventilation can persist in embolic areas unless complications such as pulmonary congestion, alveolar hemorrhage, or infarction develop (12). By the time patients are examined by lung scanning, this physiological phenomenon can well have disappeared, and aerosol inhalation scans show normal ventilation in ischemic regions if complications do not coexist. No shift of ventilation away

from regions with reduced perfusion is described in patients whose pulmonary embolism is of 2 days or longer in duration (13). Therefore, from a practical clinical standpoint, the presence of bronchoconstriction in pulmonary embolism should not hinder the application of perfusion-inhalation lung scans in the diagnosis of pulmonary embolism.

Optimal scanning sequence. Perfusion lung scanning should be done first for screening purposes. Until recently, it was necessary to wait 24 hr after the initial perfusion scan either with ^{131}I - or $^{99\text{m}}\text{Tc}$ -MAA to perform the inhalation study with $^{99\text{m}}\text{Tc}$ -albumin aerosol. Currently, both procedures are done during the same visit when indicated. The perfusion scans are made first with $^{99\text{m}}\text{Tc}$ -MAA and, if positive, the inhalation study is done immediately afterwards using the higher-energy $^{113\text{m}}\text{In}$ -albumin aerosol. This perfusion-inhalation procedure can be completed within 1 hr or less with a scintillation camera. It has definitely facilitated the earlier diagnosis and initial management of patients with suspected pulmonary embolism.

Radioxenon inhalation procedures. Radioactive xenon (^{133}Xe) gas has also been used for the purpose of diagnosing pulmonary embolism (14). However, in our experience with both inhalation procedures in over 60 suspected pulmonary embolism patients, the aerosol method is preferred for several reasons; breath-holding is not required; normal tidal volume breathing makes the procedure acceptable and applicable in nearly all suspected patients; multiple views of the lungs are possible; the lung images have high and uniform radioactivity levels with better resolution; the procedure does not require a camera, and a rectilinear scanner as well as scintillation cameras may be used. Most importantly, in pulmonary embolism the aerosol inhalation scans not only detect ventilation in ischemic regions, but also disclose evidence of bronchitis and emphysema as described in this paper and elsewhere (4).

SUMMARY

Radioisotope perfusion lung scanning is useful in the diagnosis and management of pulmonary embolism. However, scan findings are often misleading in patients with underlying obstructive airways disease. Fortunately, radioaerosol inhalation scans demonstrate whether the ischemic regions are aerated in addition to showing other evidence of obstructive airways disease. Seventy-three suspected pulmonary embolism patients were examined with both perfusion and radioaerosol inhalation scans on the same visit. Twenty-eight with aerated ischemic regions were diagnosed and treated for pulmonary embolism. Forty-three with nonaerated ischemic regions showed

scan evidence of obstructive airways disease. Most of these could have been misdiagnosed and improperly treated for pulmonary embolism without the radioaerosol scan information. Although concurrent small emboli could not be excluded in this group, aerosol scan evidence for or against airways disease was helpful in the differential diagnosis of pulmonary embolism.

ACKNOWLEDGMENTS

The authors are grateful to John Mullins, Mrs. Ethel Plummer, and Shirley Cash for their technical help; to Gordon Lindenbladh of the Mallinckrodt Radiopharmaceutical Development Division for a grant-in-aid and for furnishing supplies of ^{133}Xe and $^{99\text{m}}\text{Tc}$ used in these studies; and to Mrs. Ann Lubahn for her clerical assistance.

This work was partly supported by a grant from the American Cancer Society, California Division (D-137) and Contract AT(04-1) GEN 12 between the USAEC and the University of California at Los Angeles.

REFERENCES

- POTCHEN EJ: Lung scintiscanning. *JAMA* 204: 907-912, 1968
- TAPLIN GV, POE ND, DORE EK, et al: Bronchial patency and aerated space assessment by scintiscanning. *Lahey Clin Found Bull* 16: 297-312, 1967
- TAPLIN GV, POE ND, DORE EK, et al: Scintiscanning and roentgenographic procedures in managing pulmonary disorders. In *Medical Radioisotope Scintigraphy*, vol 2, Vienna, IAEA, 1969, pp 111-124
- ISAWA T, WASSERMAN K, TAPLIN GV: Lung scintigraphy and pulmonary function studies in obstructive airway disease. *Amer Rev Resp Dis* 102: 161-172, 1970
- ISAWA T, HAYES M, TAPLIN GV: Preparation of $^{113\text{m}}\text{In}$ -albumin solution. *J Nucl Med* 12: 138, 1971
- ISAWA T, BENFIELD JR, JOHNSON DE, et al: Pulmonary perfusion changes after experimental unilateral bronchial occlusion and their clinical implications. *Radiology* 99: 355-360, 1971
- ISAWA T, SHIRAISHI K, YASUDA T, et al: Effect of oxygen concentration in inspired gas upon pulmonary arterial blood flow. *Amer Rev Resp Dis* 96: 1199-1208, 1967
- LOPEZ-MAJANO V, TOW DE, WAGNER HN: Regional distribution of pulmonary arterial blood flow in emphysema. *JAMA* 197: 81-84, 1966
- GUREWICH V, THOMAS D, STEIN M, et al: Bronchoconstriction in the presence of pulmonary embolism. *Circulation* 27: 339-345, 1963
- SEVERINGHAUS JW, SWENSON EW, FINLEY TN, et al: Unilateral hypoventilation produced in dogs by occluding one pulmonary artery. *J Appl Physiol* 16: 53-60, 1961
- NADEL JA, COLEBATCH HJH, OLSEN CR: Location and mechanism of airway constriction after barium sulfate microembolism. *J Appl Physiol* 19: 387-394, 1964
- ISAWA T, CRILEY JM, BEAZELL J, et al: Immediate and prolonged effect of pulmonary artery occlusion on regional ventilation, presented at the Annual Meeting of American Thoracic Society, Los Angeles, May 17-19, 1971
- BASS H, HECKSCHER T, ANTHONISEN NR: Regional pulmonary gas exchange in patients with pulmonary embolism. *Clin Sci* 33: 355-364, 1967
- DE NARDO GL, GOODWIN DA, RAVASINI R, et al: The ventilatory lung scan in the diagnosis of pulmonary embolism. *New Eng J Med* 282: 1334-1336, 1970