

## PART VII: CONCISE BIBLIOGRAPHY

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strategies for imaging in the new health care climate. *Semin Nucl Med* 1994;24:188-207.

## PART VIII: LAST HOUSE OF DELEGATES APPROVAL DATE

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## PART IX: NEXT ANTICIPATED APPROVAL DATE

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# Procedure Guideline for Lung Scintigraphy: 1.0

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## PART I: PURPOSE

The purpose of this guideline is to assist nuclear medicine practitioners in recommending, performing, interpreting and reporting the results of lung scintigraphy for pulmonary embolism.

## PART II: BACKGROUND INFORMATION AND DEFINITIONS

- A. Aerosol Ventilation Scintigraphy  
A diagnostic imaging test that records the bronchopulmonary distribution of an inhaled radioactive aerosol within the lungs.
- B. Gas Ventilation Scintigraphy  
A diagnostic imaging test that records the pulmonary distribution of a radioactive gas during breathing maneuvers.
- C. Pulmonary Perfusion Scintigraphy  
A diagnostic imaging test that records the distribution of pulmonary arterial blood flow.
- D. Lung Scintigraphy for Pulmonary Embolism  
A diagnostic imaging test that assesses pulmonary perfusion and often includes ventilation scintigraphy.

## PART III: COMMON INDICATIONS

- A. The most common indication for lung scintigraphy is to determine the likelihood of pulmonary embolism.
- B. Less common indications (e.g., evaluation of lung transplantation, preoperative evaluation, right-to-left shunt evaluation) will be included in future versions of this guideline.

## PART IV: PROCEDURE

### A. Patient Preparation

1. A chest radiograph should be obtained before lung scintigraphy for pulmonary embolism. A routine chest radiograph obtained in both the posterior-anterior and lateral projections is preferred. A portable anterior-posterior chest radiograph is acceptable only if the patient cannot tolerate a routine chest radiographic examination. In patients who have no changes in signs or symptoms, a chest radiograph within 1 day of scintigraphy is adequate. A more recent chest radiograph (preferably within 1 hr) is necessary in patients whose signs and symptoms are changing.
2. Before intravenous administration of the pulmonary perfusion radiopharmaceutical, the patient should be instructed to cough and to take several deep breaths. The patient should be in the supine position during injection, or in the case of a patient with orthopnea, as close to supine as possible.

### B. Information Pertinent to Performing the Procedure

1. In women of childbearing age, pregnancy and lactation status should be noted and the procedure performed in a manner to minimize radiation exposure.
2. Pertinent clinical history includes, but is not limited to: (a) right-to-left shunt, (b) severe pulmonary hypertension, (c) chest pain, (d) dyspnea, (e) hemoptysis, (f) syncope, (g) symptoms of deep venous thrombosis, (h) oral contraceptive use, (i) recent surgery, (j) prior pulmonary embolism, (k) cancer, (l) congestive heart failure, (m) antecedent illness, (n) smoking and (o) intravenous drug abuse.
3. Pertinent findings on physical examination include, but are not limited to: (a) vital signs, (b) chest

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examination, (c) cardiac examination and (d) leg findings.

4. Review of prior lung scintigraphy.
5. Pertinent chest radiographic findings include, but are not limited to: (a) consolidation, (b) atelectasis, (c) effusions, (d) masses, (e) cardiomegaly and (f) decreased pulmonary vasculature. The chest radiograph may be normal in patients with pulmonary embolism.
6. Treatment with anticoagulant or thrombolytic therapy should be noted.
7. Results of tests for deep venous thrombosis, e.g., compression ultrasonography should be noted.
8. The referring physician's estimate of the prior probability of pulmonary embolism may be helpful.

#### C. Precautions

Reduced numbers of macroaggregated albumin (MAA) particles should be considered for patients with pulmonary hypertension or right-to-left shunting, and in infants and children. In adults, the number may be reduced to 100,000–200,000 particles without altering the quality of the images for detection of perfusion defects. Inhomogeneous distribution of activity may result from a reduction of the number of particles below 100,000 in adults.

#### D. Radiopharmaceuticals

Physical Characteristics of Radionuclides

Radionuclide	T1/2	keV	Decay
<sup>99m</sup> Tc	6 hr	140	IT
<sup>133</sup> Xe	5.2 days	81	Beta
<sup>81m</sup> Kr	13 sec	190	IT

IT = isomeric transition.

#### 1. Aerosols

- a. Technetium-99m-diethylenetriamine-pentaacetic acid (DTPA) is the preferred radiopharmaceutical.
- b. The usual administered activity of <sup>99m</sup>Tc-DTPA is 900–1300 MBq (25–35 mCi) in the nebulizer from which the patient receives approximately 20–40 MBq (0.5–1.0 mCi) to the lungs.
- c. Aerosol imaging is usually performed before perfusion imaging because it is more difficult to deliver a larger dose of the <sup>99m</sup>Tc aerosol than it is to deliver a larger dose of <sup>99m</sup>Tc-macroaggregated albumin (MAA). Because both agents are labeled with <sup>99m</sup>Tc, it is extremely important that the count rate of the second study is at least four times the count rate of the first study.

#### 2. Xenon-133

The usual administered activity is 200–750 MBq (5–20 mCi). The usual dose for children is 10–12 MBq/kg (0.3 mCi/kg) with a minimum of 100–120 MBq (3 mCi).

#### 3. Krypton-81m

- a. Krypton-81m is obtained from a <sup>81</sup>Rb/<sup>81m</sup>Kr generator.
- b. The usual administered activity of <sup>81m</sup>Kr is 40–400 MBq (1–10 mCi).

#### 4. Perfusion

- a. The radiopharmaceutical used most commonly for perfusion imaging is <sup>99m</sup>Tc-MAA.
- b. The biological half-life of the macroaggregated albumin in the lungs varies (usually 1.5 to 3 hr).

- c. The usual adult administered activity is 40–150 MBq (1–4 mCi). The usual pediatric administered activity is 0.5–2.0 MBq/kg (20–80 μCi/kg) with a minimum of 7–8 MBq (200 μCi). See dosimetry tables below.
- d. The number of particles should be in the range of 200,000–700,000. For children, the number of particles is a function of age (see Table 11.2, Treves, ST. *Pediatric Nuclear Medicine*, 2nd ed. New York, NY: Springer-Verlag; 1995:168).
- e. Labeled MAA particles will settle in the vial with time. Vials should be agitated prior to withdrawing a dose, and the syringe should be inverted prior to injection.

Radiation Dosimetry in Adults

Radiopharmaceutical	Administered activity MBq (mCi)	Organ receiving the largest radiation dose* mGy (rad)	Effective dose* mSv (rem)
<sup>99m</sup> Tc-MAA†	40–150	0.067	0.012
	(1–4)	(0.248)	(0.044)
<sup>99m</sup> Tc-DTPA‡	20–40	0.047	0.007
	(0.5–1.0)	(0.174)	(0.026)
<sup>133</sup> Xe§	200–750	0.0011	0.0008
	(5–20)	(0.004)	(0.003)
<sup>81m</sup> Kr¶	40–400	0.0068	0.0007
	(1–10)	(0.025)	(0.0026)

\*per MBq (per mCi).

†ICRP 53, page 224

‡ICRP 53, page 218

§ICRP 53, page 218.

¶ICRP 53, page 345, rebreathing for 5 min.

‡Package insert (MediPhysics, Inc., October 1990), rebreathing for 1 min; ICRP 53, page 160.

Radiation Dosimetry in Children (5 yr old)

Radiopharmaceutical	Administered activity MBq/kg (mCi/kg)	Organ receiving the largest radiation dose* mGy (rad)	Effective dose* mSv (rem)
<sup>99m</sup> Tc-MAA†	0.5–2	0.21	0.038
	(0.02–0.08)	(0.777)	(0.14)
<sup>99m</sup> Tc-DTPA‡	0.4–0.6	0.12	0.02
	(0.01–0.03)	(0.444)	(0.074)
<sup>133</sup> Xe§	10–12	0.0037	0.0027
	(0.2–0.3)	(0.014)	(0.01)
<sup>81m</sup> Kr¶	0.5–5	0.022	0.0023
	(0.015–0.15)	(0.081)	(0.0085)

\*per MBq (per mCi).

†ICRP 53, page 224.

‡ICRP 53, page 345, rebreathing for 5 min.

‡Package insert (MediPhysics, Inc., October 1990), rebreathing for 1 min; ICRP 53, page 160.

## E. Image Acquisition

### 1. Sequence of Imaging

- a. A chest radiograph should be obtained and reviewed before lung scintigraphy.
- b. Ventilation scintigraphy using  $^{133}\text{Xe}$  is usually performed before perfusion scintigraphy using  $^{99\text{m}}\text{Tc}$ . Alternately, perfusion scintigraphy can be performed first and ventilation scintigraphy omitted if not needed.
- c. The disadvantages of performing perfusion imaging first are:
  1. With  $^{133}\text{Xe}$  gas or  $^{99\text{m}}\text{Tc}$  aerosol imaging, the perfusion image contributes background activity to the ventilation image.
  2. A decision to perform or not to perform the ventilation study must be made in a timely manner.
- d. The advantages of performing perfusion imaging first are:
  1. If the perfusion study is normal or matches the chest radiographic findings, the ventilation study can be omitted.
  2. For single-projection ventilation studies, the projection that best shows the defect can be obtained.
- e. Because of the higher energy of the gamma emissions and the short half-life of  $^{81\text{m}}\text{Kr}$ , images obtained with this gas can be alternated with those obtained with  $^{99\text{m}}\text{Tc}$ -MAA.
- f. When  $^{99\text{m}}\text{Tc}$ -labeled aerosol imaging is performed before  $^{99\text{m}}\text{Tc}$ -MAA perfusion imaging, smaller amounts (40 MBq [1.0 mCi]) of activity should be administered to the lungs.

### 2. Aerosol Ventilation Imaging

- a. The aerosol is administered through a mouth-piece with the nose occluded and the patient performing tidal breathing.
- b. An advantage of aerosol imaging is that images can be obtained in multiple projections to match those obtained for perfusion imaging.
- c. It is preferable to have the patient inhale the aerosol in the upright position, but the supine position can be used if necessary.
- d. Aerosol ventilation imaging can be performed at the bedside.
- e. A disadvantage of aerosol imaging is that aerosol deposition is altered by turbulent flow, and central deposition can result in a suboptimal study.

### 3. Xenon-133 Ventilation Imaging

- a. An advantage of  $^{133}\text{Xe}$  ventilation is that single-breath, equilibrium and washout images can be obtained, which provide a more complete characterization of ventilation and a more sensitive test for obstructive airway disease. Physiologic information about ventilation can best be obtained from  $^{133}\text{Xe}$  imaging.
- b. The imaging room should be at negative pressure with appropriate exhaust for radioactive gas. Regulations for safe handling of radioactive gas should be followed.
- c. The patient is positioned upright in front of the scintillation camera. If necessary, the patient can be positioned supine.

d. The projection that best shows the defect(s) on perfusion scintigraphy is used for ventilation scintigraphy if performed after perfusion scintigraphy. Otherwise, the posterior projection is generally used. When possible, posterior oblique images should be obtained during washout.

e. If ventilation scintigraphy is performed after perfusion scintigraphy, a  $^{99\text{m}}\text{Tc}$  background image should be obtained using the Xe-133 window.

f. A face mask or mouth piece (with nose clip) should be connected via a bacterial filter to the xenon delivery system.

g. Single-breath, equilibrium and washout images are obtained.

h. Equilibrium is obtained by breathing in a closed xenon delivery system for 3–6 min as tolerated by the patient.

### 4. Krypton-81m Imaging

a. The advantage of  $^{81\text{m}}\text{Kr}$  is that images can be obtained in all views without interference from prior perfusion imaging. Alternating  $^{99\text{m}}\text{Tc}$ -MAA and  $^{81\text{m}}\text{Kr}$  imaging allows ventilation and perfusion images to be obtained without patient repositioning between paired MAA and  $^{81\text{m}}\text{Kr}$  views.

b. The patient breathes continuously from the  $^{81}\text{Rb}/^{81\text{m}}\text{Kr}$  generator. Due to the short half-life of  $^{81\text{m}}\text{Kr}$ , the distribution of radioactivity approximates single-breath gas distribution.

c. A medium-energy collimator is preferred to image the 190-keV photopeak of  $^{81\text{m}}\text{Kr}$ .

d. The disadvantage of  $^{81\text{m}}\text{Kr}$  is that the short half-life of the generator decreases availability and increases cost.

### 5. Perfusion Imaging

a. After having the patient cough and take several deep breaths,  $^{99\text{m}}\text{Tc}$ -MAA is injected slowly during 3–5 respiratory cycles with the patient in the supine position.

b. A well-flushed indwelling line can be used if venous access is difficult. Do not administer in the distal port of a Swan-Ganz catheter or any indwelling line or port that contains a filter, e.g., chemotherapy line.

c. Imaging is preferably performed in the upright position to increase chest cavity size and to minimize diaphragmatic motion. If necessary, images can be obtained in the supine or decubitus position.

d. Planar images should be obtained in multiple projections, including anterior, posterior, both posterior oblique, both anterior oblique and both lateral projections. The anterior oblique or the lateral projections can be omitted. It may be possible to obtain only limited views in some patients.

## F. Interventions

1. In patients with acute obstructive lung disease, the use of bronchodilator therapy before lung scintigraphy may decrease ventilatory defects and improve the accuracy of the study. Because perfusion defects often change as acute obstruction resolves,

patients are best imaged when bronchospasm has resolved.

2. In patients with congestive heart failure, improved specificity will be obtained if imaging can be delayed until therapy for heart failure has been instituted.

#### G. Processing

None

#### H. Interpretation/Reporting

1. Modified PLOPED criteria: The following modifications of the PLOPED criteria were derived from a retrospective analysis (2) of the PLOPED database (1). The criteria were prospectively tested and shown to be more accurate than the original PLOPED criteria (3).

- a. High Probability ( $\geq 80\%$ , in the absence of conditions known to mimic pulmonary embolism)

1.  $\geq 2$  large mismatched segmental perfusion defects or the arithmetic equivalent in moderate or large and moderate defects. (A large segmental defect,  $>75\%$  of a segment, equals 1 segmental equivalent; a moderate defect,  $25\text{--}75\%$  of a segment, equals 0.5 segmental equivalents; a small defect,  $<25\%$  of a segment, is not counted.)
2. Two large mismatched segmental perfusion defects or the arithmetic mean are borderline for "high probability." Individual readers may correctly interpret individual images with this pattern as "high probability." In general, it is recommended that more than this degree of mismatch be present for the "high probability" category.

- b. Intermediate Probability (20%–79%)

1. One moderate to two large mismatched perfusion defects or the arithmetic equivalent in moderate or large and moderate defects.
2. Single-matched ventilation-perfusion defect with clear chest radiograph. Very extensive matched defects can be categorized as "low probability."
3. Single ventilation-perfusion matches are borderline for "low probability" and thus should be categorized as "intermediate" in most circumstances by most readers, although individual readers may correctly interpret individual scintigrams with this pattern as "low probability."
4. Difficult to categorize as low or high or not described as low or high.

- c. Low Probability ( $\leq 19\%$ )

1. Nonsegmental perfusion defects (e.g., cardiomegaly, enlarged aorta, enlarged hila, elevated diaphragm).
2. Any perfusion defect with a substantially larger chest radiographic abnormality.
3. Perfusion defects matched by ventilation abnormality (see IV.H.1.b.2) provided that there are: (a) clear chest radiograph and (b) some areas of normal perfusion in the lungs.
4. Any number of small perfusion defects with a normal chest radiograph.

- d. Normal

1. No perfusion defects or perfusion exactly

outlines the shape of the lungs seen on the chest radiograph (note that hilar and aortic impressions may be seen and the chest radiograph and/or ventilation study may be abnormal).

2. Gestalt interpretation: The experienced nuclear medicine physician may be able to provide a more accurate interpretation of the ventilation-perfusion study than is provided by the criteria alone; however, his/her opinion is usually informed by detailed knowledge of the various lung image interpretive criteria (3).

#### 3. Further Interpretive Considerations

- a. Ventilation-perfusion mismatch can result from any cause of pulmonary arterial blood flow obstruction. Although there is a very long differential diagnosis for ventilation-perfusion mismatch, there are few common causes: (a) acute pulmonary embolism, (b) old pulmonary embolism, (c) obstruction of an artery by tumor and (d) radiation therapy.
- b. On perfusion scintigraphy, extrapulmonary activity (which may be seen at the edges of lung images in the thyroid or kidneys) may be due to either right-to-left shunt, to free  $^{99m}\text{Tc}$ -pertechnetate or reduced technetium compounds, or to a recent nuclear medicine procedure. An image of the head can be used to differentiate free pertechnetate reduced technetium from shunt.
- c. Some authors have found that neural network evaluation of lung scintigrams findings assists the interpretive process.
- d. The stripe sign (activity at the periphery of a perfusion defect) lowers the chance of pulmonary embolism (6) in the zone of the perfusion defect that shows the stripe.

#### 4. Reporting

- a. The report should include a description of the lung scintigraphic findings, diagnostic category and an overall assessment of the likelihood of pulmonary embolism based on the scintigraphic findings. Terms referring to test outcome, e.g. "likelihood ratio," are preferred over terms referring to posterior probability, e.g. "probability of pulmonary embolism."
- b. The report should include an assessment of the post-test probability of pulmonary embolism based on the result of lung scintigraphy and an estimate of the prior probability of disease.

#### I. Quality Control

Radiochemical purity and particle size determination of  $^{99m}\text{Tc}$ -MAA should be performed. Reconstituted MAA should be stored in a refrigerator and used before expiration.

#### J. Sources of Error

1. Perfusion images can show "hot spots" in the lung if clotting of blood occurs in the syringe during the injection or if the injection is made through an indwelling catheter that is not well flushed.
2. Ventilation scintigraphy is obtained at a different point in time than the perfusion scintigraphy. In the intervening time, there can be changes in ventilation and perfusion. Similarly, ventilation scintigraphy may be obtained in an upright position and perfusion scintigraphy injected in the supine position. These changes in

position may also affect the comparability of the two scintigrams.

3. Injection of  $^{99m}\text{Tc}$ -MAA through a central line can result in inadequate mixing of activity in the pulmonary artery. This inadequate distribution of activity is especially true if the activity is injected through a pulmonary artery line.
4. A decubitus or oblique patient position can markedly affect the distribution of ventilation and perfusion. If the injection for perfusion scintigraphy or if ventilation scintigraphy is performed in the decubitus or oblique position, mismatched patterns can result. Accordingly, any nonstandard patient positioning should be recorded and considered during subsequent interpretation.

#### **PART V: DISCLAIMER**

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different than the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may greatly vary from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

#### **PART VI: ISSUES REQUIRING FURTHER CLARIFICATION**

None

#### **PART VII: CONCISE BIBLIOGRAPHY**

1. PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism: Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). *JAMA* 1990;263:2753-2759.

The PIOPED criteria for interpretation of lung scintigraphy (see IV.H.1) were tested prospectively.

2. Gottschalk A, Sostman HD, Coleman RE, et al. Ventilation-perfusion scintigraphy in the PIOPED study. Part II. Evaluation of the scintigraphic criteria and interpretations. *J Nucl Med* 1993;34:1119-1126.

The PIOPED database was reviewed retrospectively and modified PIOPED criteria were developed.

3. Sostman HD, Coleman RE, DeLong DM, et al. Evaluation of revised criteria for ventilation-perfusion scintigraphy in patients with suspected pulmonary embolism. *Radiology* 1994;193:103-107.

The revised PIOPED criteria were tested prospectively. The gestalt interpretation of lung scintigraphy by experienced observers outperformed both the PIOPED and modified PIOPED criteria.

4. Lee ME, Biello DR, Kumar B, et al. "Low-probability" ventilation perfusion scintigrams: clinical outcomes in 99 patients. *Radiology* 1985;156:497-500.

Smith R, Maher JM, Miller RI, et al. Clinical outcomes of patients with suspected pulmonary embolism and low-probability aerosol-perfusion scintigrams. *Radiology* 1987;164:731-733.

Kahn D, Bushnell DL, Dean R, et al. Clinical outcome of patients with a "low probability" of pulmonary embolism on ventilation-perfusion lung scan. *Arch Intern Med* 1989;149:377-379.

Patients without documented thromboembolic disease who have low likelihood results from their lung scintigraphy have little thromboembolic disease in follow-up.

5. Tourassi GD, Floyd CE, Sostman HD, et al. Acute pulmonary embolism: Artificial neural network approach for diagnosis. *Radiology* 1993;189:555-558.

Neural network analysis of reader derived parameters outperformed readers in diagnosis of pulmonary embolism.

6. Worsley DF, Alavi A. Comprehensive analysis of the results of the PIOPED study. *J Nucl Med* 1995;36:2380-2387.

Other findings such as the "stripe sign" may assist in the diagnosis in some patients.

#### **PART VIII: LAST HOUSE OF DELEGATES APPROVAL DATE**

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#### **PART IX: NEXT ANTICIPATED APPROVAL DATE**

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