Continuing Education

Ventilation Scintigraphy

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This is the fourth in a series of Continuing Education articles related to functional/quantitative imaging techniques. After studying this article, the reader should be able to: 1) identify the radiopharmaceuticals used for ventilation studies; 2) discuss the characteristics of various radiopharmaceuticals along with their advantages and limitations.

Ventilation scintigraphy is a well-established adjunct to perfusion lung imaging in the diagnosis of pulmonary thromboembolus (PE). Although PE may be diagnosed with a standard chest radiograph and perfusion scintigraphy, the findings may be largely nonspecific due to the many types of lung pathology that result in perfusion defects. The specificity of the perfusion (Q) study may be substantially increased with the addition of ventilation (V) scintigraphy, which allows one to differentiate perfusion defects due to PE (VQ mismatch) from those resulting from obstructive lung disease (VQ match). Ventilation scintigraphy is performed at most institutions with a radioactive gas, usually xenon-133 (^{133}Xe), xenon-127 (^{127}Xe), or krypton-81m (^{81m}Kr). More recently, however, radiolabeled aerosols have evolved as an accepted alternative to gas tracer techniques to evaluate regional ventilation. This article reviews the clinical uses, advantages, and disadvantages of gas and aerosol ventilation agents. A more in-depth discussion of aerosols is given due in part to the increasing use of this particular tracer to evaluate regional ventilation.

XENON-133 VENTILATION SCINTIGRAPHY

The most traditional imaging agent used to assess regional ventilation, ^{133}Xe was first introduced by Knipping et al. in 1955 *(1)*. It offers certain advantages over other gases, mainly its low cost, useful half-life (5.8 days), and ready availability. The use of ^{133}Xe also allows for the assessment of all phases of regional ventilation: instantaneous (single breath), wash-in (equilibrium), and wash-out. The single breath image represents instant ventilation to the lungs; wash-in images to equilibrium are proportional to aerated lung volume, and the

wash-out phase images show clearance of activity from the lungs, usually within a few minutes of wash-out. Regions of prolonged ^{133}Xe retention correspond to obstructive lung disease. Studies have shown that xenon wash-out images are the most sensitive part of the ventilation study for the detection of obstructive lung disease *(2)*.

Although it is the tracer most commonly used to assess ventilation, xenon has several disadvantages as an imaging agent. Imaging studies require a considerable amount of patient cooperation, especially for the single breath image. The patient must also be able to tolerate breathing on a closed spirometer system for several minutes in order to reach equilibrium. A rebreathing phase of at least 3–5 min is needed, as ^{133}Xe retention will not be detected in regions that exchange air slowly unless adequate time has been allowed for the tracer to enter those regions during the equilibrium phase *(3)*. Some patients with compromised lung function have considerable difficulty with this phase of the ventilation study. Wash-out images must also be carried out for a sufficient amount of time (> 5–6 min) in order to obtain maximum diagnostic information.

The physical characteristics of radioxenon, primarily its low gamma photon energy (80 keV), also present several imaging drawbacks. The 80-keV photons result in increased soft tissue absorption and decreased image resolution, thereby making single posterior projection images difficult to interpret. This may be overcome, however, with the addition of posterior oblique images during the wash-in and wash-out phases to better evaluate the anterior segments of both lungs (Fig. 1). In addition, the low energy necessitates that ^{133}Xe ventilation be performed prior to perfusion imaging. If ^{133}Xe ventilation is performed after perfusion, downscatter from the technetium-99m (^{99m}Tc) perfusion agent into the ^{133}Xe window degrades image quality.

The use of ^{133}Xe requires that special consideration be given to room design. Maintaining the camera room at a negative pressure relative to outside hallways and the use of a dedicated trap or exhaust vent to remove xenon gas is necessary in order to comply with regulatory policies. The use of a spirometer is also necessary to ensure that the xenon gas is properly delivered to the patient.

Regional ventilation may also be assessed with xenon-127. It has photon energies of 172, 203, and 357 keV, and a half-life of 36.3 days. The higher photon energy makes it possible to perform perfusion scintigraphy first. If ventilation images are required, ^{127}Xe allows the patient to be ventilated in the same positions in which the perfusion defects are best demonstrated. The main disadvantage of ^{127}Xe is the fact that it is cyclotron-produced, resulting in a higher cost per milliCurie than ^{133}Xe. The most abundant gamma photopeaks of ^{127}Xe are at 172 and 203 keV, which may be imaged with a 25% window in order to encompass both peaks. The 357 keV gamma photon, however, precludes the use of a medium energy collimator (280 keV), making it necessary to image ^{127}Xe with a low resolution, high energy collimator (400 keV) (4). Additional shielding of the spirometer and the trapping mechanism must also be taken into consideration when using ^{127}Xe.

KRYPTON-81m VENTILATION SCINTIGRAPHY

Krypton-81m (^{81m}Kr) is a short-lived noble gas that was developed for clinical use by Fazio and Jones in 1975 (5). It became available commercially in 1980. It is a generator-produced gas with a half-life of 13 sec and a primary gamma photon energy of 190 keV. Krypton-81m is eluted from the generator by passing humidified oxygen over the generator column containing the parent nuclide rubidium-81 (^{81}Rb) (Fig. 2). The mixture of ^{81m}Kr and oxygen is then delivered to the
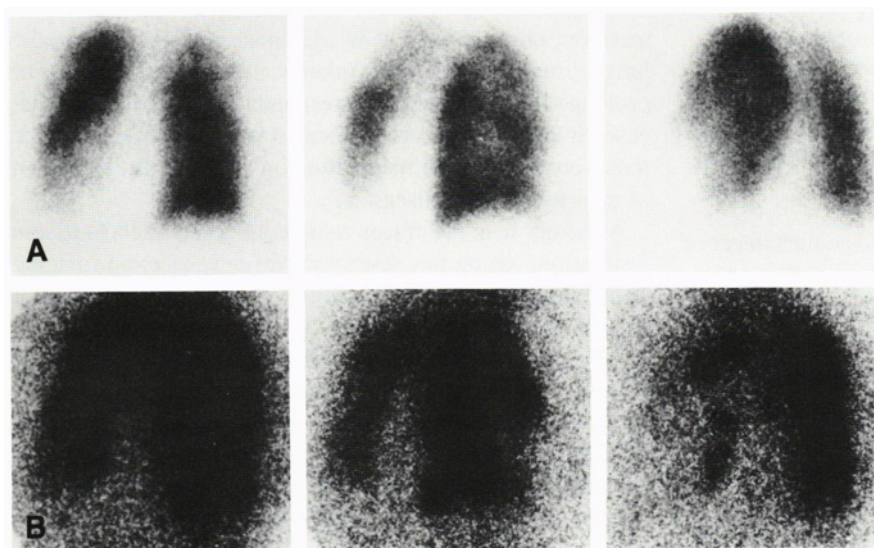

FIG. 1. Xenon-133 ventilation images. (A) Posterior, RPO, and LPO wash-in images demonstrate normal distribution in both lungs. (B) Posterior, RPO, and LPO wash-out images demonstrate diffuse retention of xenon.
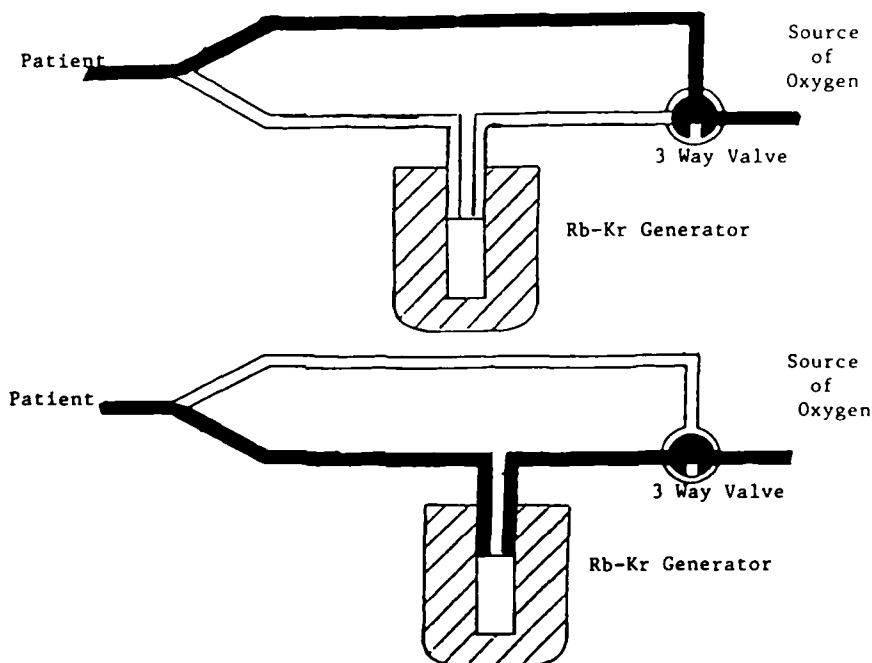

FIG. 2. Schematic representation of a krypton-81m generator. (A) Humidified oxygen flows through 3-way valve to the patient. (B) Humidified oxygen flows through 3-way valve to the krypton generator and is then inhaled by the patient.
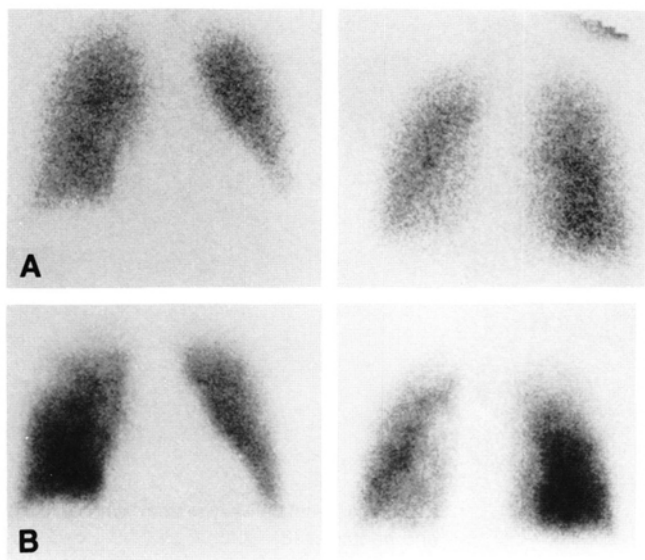
FIG. 3. (A) Normal anterior and posterior krypton ventilation images. (B) Corresponding normal anterior and posterior perfusion images.

patient via a nonrebreathing face mask. Because of its inherent physical characteristics, ^{81m}Kr has several advantages over xenon. The 190-keV photon of krypton is higher than that of ^{99m}Tc, therefore making it possible to perform the ventilation study concurrently with, or after the perfusion study (Fig. 3). Ventilation images are obtained from the generator system during continuous tidal breathing. The regional distribution of activity in the lungs observed during steady-state, tidal inhalation of this radionuclide is proportional to the regional ventilatory rate (6). Single breath and wash-out phase images are not possible with ^{81m}Kr because of its short half-life; however, as with ^{127}Xe, krypton images may be obtained in multiple projections that best profile perfusion defects. Krypton generator systems also offer the advantages of being able to be taken to intensive care units where ventilation studies may be performed on patients on mechanical ventilators. This is due largely to the fact that krypton, unlike xenon, does not need to be exhausted or trapped.

Unfortunately, ^{81m}Kr is extremely expensive and its availability is limited, making it somewhat impractical for routine clinical use. The main disadvantage stems from the short physical half-life (4.7 hr) of the parent nuclide, rubidium-81. A generator system contains only enough activity to be used for ventilation studies on the day it is delivered.

DTPA AEROSOL VENTILATION SCINTIGRAPHY

The use of radiolabeled aerosols to evaluate regional pulmonary ventilation was first introduced by Taplin and Poe in 1965 (7). Their initial technique, however, was hampered by several problems related to nonuniformity of the generated particles. Precipitation of large aerosol particles (greater than 2 μm) resulted in deposition of activity in the central airways, resulting in "hot spots" that made image interpretation difficult. Investigators in the 1970s made several attempts to im-

prove the production of submicron-sized, monodispersed particles that would better penetrate to the periphery of the lungs. These included the use of a heating chamber to reduce particle size by evaporation and the use of high frequency ultrasonic nebulizers. In 1979, Hayes et al. (8) introduced the use of a 3-liter reservoir bag into the delivery line to reduce particle size. Aerosol particles generated in the nebulizer would circulate in the bag before being breathed by the patient, while the larger particles would settle out. Studies since have shown that droplet size is the major determining factor of aerosol deposition in the lungs (9).

Commercially available, relatively inexpensive systems capable of producing uniform, submicron particles of acceptable size (< 0.5–1.0 μm) led to US Nuclear Regulatory Commission approval of ^{99m}Tc DTPA for ventilation studies in 1983. This suggested that the clinical utility of radiolabeled aerosols for routine ventilation scintigraphy should be reinvestigated. Several studies since have shown that aerosol ventilation images are diagnostically comparable with ventilation studies that employ ^{133}Xe or ^{81m}Kr (10,11).

The use of ^{99m}Tc DTPA aerosol for ventilation scintigraphy offers several advantages over other, more conventional agents. Technetium-99m is readily available in most nuclear medicine departments, and its 140 keV gamma photon provides high quality images. Very little patient cooperation is required since radiotracer deposition takes place during normal tidal breathing. Multiple projections may be obtained with a single 5-min administration of the aerosol. Since the delivery of the aerosol does not involve a spirometer or an exhaust vent, the patient may be ventilated in a room separate from the camera room. Aerosol studies may also be readily performed on patients undergoing mechanical ventilatory assistance.

Technetium-99m DTPA labeled aerosol also offers the advantage of being rapidly cleared from the lungs, thereby reducing radiation exposure. DTPA aerosol particles easily cross the alveolar–capillary membrane and enter the pulmonary circulation. Once in circulation, DTPA is rapidly cleared by the kidneys similar to intravenously administered DTPA.

The major disadvantage to ^{99m}Tc DTPA aerosols for ventilation scintigraphy is the fact that the aerosol generator systems are inefficient in delivering activity to the patient. Of the 30 mCi placed in the system's nebulizer, only 1–2 mCi are delivered to the patient for imaging. Unlike radioxenon ventilation studies, aerosol ventilation studies do not allow for single breath or wash-out phase images. This variance, however, between xenon and aerosol ventilation images does not affect the overall scintigraphic probability of pulmonary embolism. Lastly, aerosol particle hyperdeposition in the central airways still presents a problem in patients with obstructive pulmonary disease. This results in multiple "hot spots" throughout the lung fields corresponding to the regions of central airways turbulence where the aerosol particles cannot properly penetrate to the periphery of the lungs.

Our clinical experience with ^{99m}Tc DTPA aerosol ventilation scintigraphy has been primarily with the Ultravent* aerosol delivery system (Fig. 4). The system consists of the main components: a nebulizer and a yoke. The nebulizer is fitted with a venturi tube and a port to connect an oxygen line from
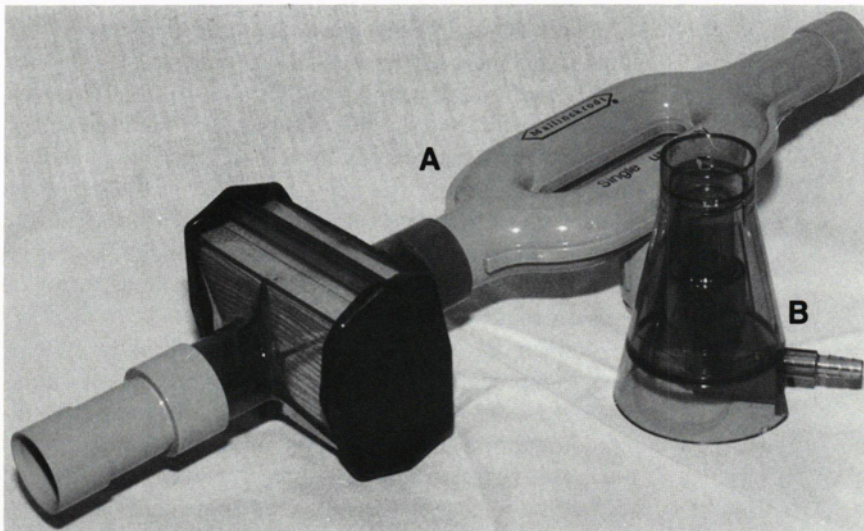
FIG. 4. Aerosol delivery system* with yoke (A) and nebulizer (B).

a source of compressed oxygen. Liquids placed in the nebulizer are raised in the venturi tube and sheared by a jet of compressed oxygen to generate the aerosol (11). The yoke, which snaps on top of the nebulizer, is fitted with a flexible length of tube at one end for the patient to breathe through and a bacterial filter at the other end to trap any aerosol particles that are exhaled. The nebulizer and yoke assembly are placed within a shielded box provided by the manufacturer (Fig. 5).

Technetium-99m DTPA is prepared from a commercially available kit†. The vial contents are reconstituted with 60 mCi of sodium pertechnetate in a total volume of 4 ml. Thirty milliCuries of ^{99m}Tc DTPA in a volume of 2 ml is injected into the nebulizer. Oxygen tubing is connected to the nebulizer's side port and the yoke is attached to the top of the nebulizer. The oxygen flow rate, if obtained from wall-supplied oxygen, should be calibrated with a flow meter prior to beginning the ventilation study. The suggested flow rate for this particular system is 9.0 L/min. A mouthpiece with a nose clip or a face mask is then used to administer the aerosol. For patients on ventilators the system is connected to the patient's endotracheal tube. The patient is allowed to breathe at tidal volume for 5 min in the supine position in order to reduce the effects of gravity on aerosol deposition in the bases of the lungs. Imaging commences immediately after the patient finishes breathing the aerosol. Aerosol ventilation images may be acquired on a scintillation camera that is peaked for ^{99m}Tc and fitted with a low energy collimator. Normal aerosol ventilation images demonstrate symmetric aerosol deposition from apex to base in both lung fields. Areas of lung that are not ventilated are seen as regions of decreased or absent aerosol activity (Fig. 6).

The initial image is the posterior view, which is taken for a total of 200,000 counts or 3 min, whichever occurs first. Imaging should be done in the erect position whenever possible. When aerosol ventilation studies are performed on patients on mechanical ventilators, or who are restricted to bed rest, the posterior image is obtained with the patient in a lateral decubitus position. The remaining views include both posterior

obliques, anterior, and both laterals. After the completion of the aerosol ventilation study a perfusion study is performed using 5 mCi of ^{99m}Tc macroaggregated albumin administered intravenously. The same six views are obtained for the perfusion study. The posterior perfusion is acquired first for a total of 600,000 counts. The remaining images are then acquired for the same amount of time as the posterior image.

We have encountered certain technical difficulties at various times when performing aerosol ventilation studies. Most of them were caused by improper assembly of the aerosol device itself, resulting in incomplete aerosolization of the ^{99m}Tc
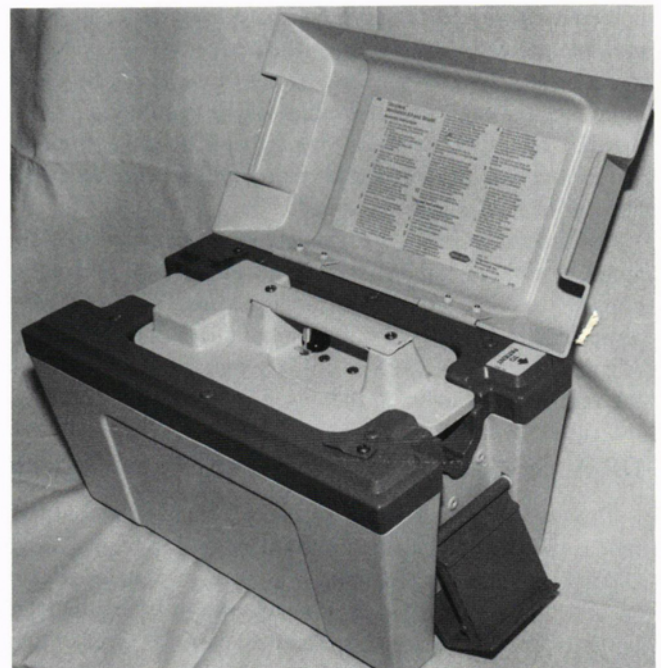

FIG. 5. Shielded box within which is placed the aerosol delivery system.
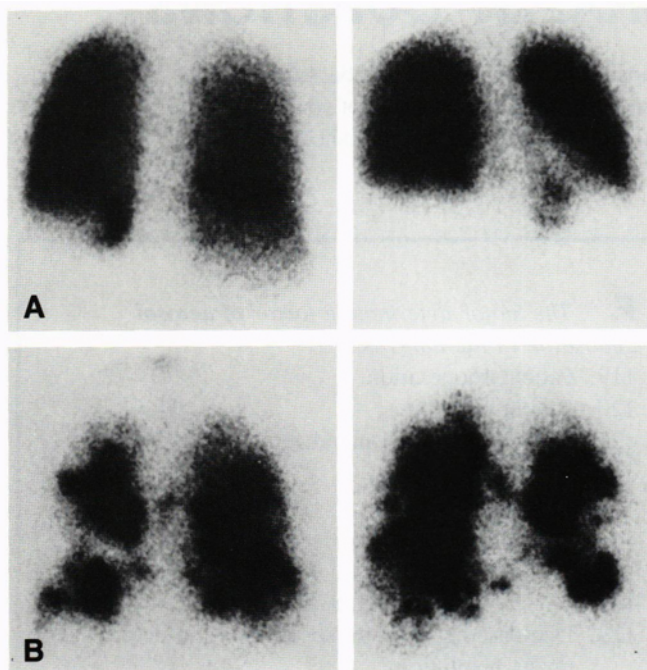
FIG. 6. (A) Normal DTPA aerosol ventilation images in the posterior and anterior projections. (B) Posterior and anterior DTPA aerosol ventilation images demonstrating regions of decreased ventilation in both lungs.

DTPA. Proper attention must also be given to obtaining the correct oxygen flow rate of 9 L/min through the nebulizer. The oxygen should be turned on slowly in order to avoid having the oxygen tubing "pop" off the side port of the nebulizer. We have also found it necessary for patients who are intubated to have a nurse or respiratory therapist check that the cuff around the endotracheal tube is fully inflated and to suction the patient before administering the aerosol. The patient may also require resuctioning after the administration of the aerosol if there is hyperdeposition of activity in the endotracheal tube.

Summary

Ventilation scintigraphy has been shown to increase the sensitivity of perfusion lung imaging in the diagnosis of pulmonary embolus. Regional pulmonary ventilation can be assessed with several different tracers each with its own inherent advantages and disadvantages. The use of ^{133}Xe gas is still the most common approach to evaluating regional ventilation; however, the use of DTPA radiolabeled aerosol has become an acceptable alternative to gas tracer technique. Technetium-labeled DTPA aerosol ventilation studies are easy to perform from a technical standpoint, are relatively inexpensive, and are diagnostically equivalent to gas ventilation scintigraphy.

NOTES

ACKNOWLEDGMENTS

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