

# Regional Ventilation Studies with Kr-81m and Xe-133: A Comparative Analysis

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***Krypton-81m and Xe-133 ventilation scintigrams, and particulate perfusion scintigrams with Tc-99m, were obtained on the same day in 41 patients. Of 14 studies demonstrating pulmonary embolism, Kr-81m complemented the perfusion study better than Xe-133 in seven and was judged essential for that diagnosis in two. Xenon-133 was better in none.***

***On the other hand, in 29 studies with obstructive or parenchymal lung disease, Kr-81m was essential for the diagnosis in only one of seven cases in which it was judged superior to Xe-133, whereas Xe-133 was essential in six of nine studies in which it was judged superior.***

***Ventilation scintigraphy with Kr-81m offers important advantages over Xe-133 in the diagnosis of embolic lung disease due to its improved spatial resolution and capacity to provide superimposable ventilation and perfusion images in multiple projections, so that defects can be accurately matched.***

***Obstructive pulmonary disease may be more easily diagnosed with Xe-133 ventilation images, because areas of gaseous retention, not visible with Kr-81m, can be seen on Xe-133 washout images.***

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Xenon-133 has been widely used for analysis of regional lung ventilation in patients with suspected pulmonary emboli or obstructive lung disease. However, its low photon energy (81 keV) results in reduced scintigraphic resolution. In addition, patient cooperation is necessary, multiple views are cumbersome, and its long half-life (5.27 days) might unnecessarily expose laboratory personnel. Krypton-81m with its 13-sec half-life and 190-keV emission is ideal for the imaging of regional ventilation by continuous tidal breathing, so that patient cooperation is not required and multiple views can readily be obtained, to be paired with corresponding perfusion views and thus providing precisely complementary ventilation/perfusion images (1,2). Its scintigraphic resolution compares with that of Tc-99m (140 keV), and there is little radiation exposure to personnel. However, clinical comparison of Kr-81m with Xe-133 ventilation studies has been lacking.

Accordingly, 44 patient studies employing both

Kr-81m and Xe-133 ventilation scintigraphy, performed on the same day, were reviewed retrospectively and the relative merits of each procedure evaluated.

## MATERIALS AND METHODS

Forty-four Kr-81m and Xe-133 ventilation studies performed in 41 patients on the same day were included for analysis.

All studies were separately reviewed by at least three of the authors, who were asked to judge the relative merits of each type of ventilation study in the detection of embolic and parenchymal/obstructive pulmonary disease. Matched defects or areas of abnormal ventilation, with normal perfusion, were

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ascribed to parenchymal/obstructive ventilatory causes. Regions that were better ventilated than perfused were considered to be embolic. Matched defects with Kr-81m, or areas of absent ventilation with Xe-133 in regions of radiographic abnormality, were considered indeterminate and were not evaluated in the study. In studies satisfying the criteria simultaneously for both embolic and parenchymal/obstructive ventilatory abnormalities, separate assessment was made for each diagnosis. Agreement by at least two observers was required for inclusion in the analysis. One study failed to meet these criteria and is not included.

Each patient first had a Xe-133 ventilation study performed, followed immediately by a Tc-99m perfusion study coupled directly with a Kr-81m ventilation study.

Xenon-133 ventilation studies were usually performed in the posterior projection. After maximal inspiration of 20 mCi of Xe-133, 2- to 4-min equilibrium views during tidal rebreathing were obtained, followed by 30-60 sec sequential washout images with the patient breathing room air.

The patients were subsequently injected supine with either Tc-99m macroaggregated albumin or Tc-99m-labeled microspheres (2-5 mCi). A standard disposable face mask was then placed over the patient's nose and mouth and ventilated with a continuous oxygen-air mixture at a rate of 3 l/min.

By means of a switch on the generator, Kr-81m was eluted from its cyclotron-produced parent (Rb-81,  $T_{1/2} = 4.7$  hr) by diverting the oxygen through the generator and into the patient's face mask. With the patient placed in front of the camera, ventilation imaging was begun some 45-60 sec after starting elution of the Kr-81m. During this short period of time, the concentration of regional lung radioactivity reaches a plateau that has been shown to be proportional to regional ventilation (2). Paired 200,000-count ventilation images and 200,000- to 500,000-count perfusion images, were then obtained by alternation of the 20% window settings between the 190-keV and 140-keV photopeaks of Kr-81m and Tc-99m. Elution of Kr-81m was halted while perfusion images were taken. Images were usually obtained in the anterior, posterior, and posterior oblique projections, with additional views added as necessary.

#### RESULTS

Of 40 patients, 37 were referred with suspected pulmonary embolism and three for regional evaluation of obstructive lung disease. Nine studies showed entirely normal ventilation and perfusion, with complete agreement between Kr-81m and Xe-133. In 20 studies of patients with parenchymal/obstructive

lung disease detected scintigraphically, there was agreement in 11. Krypton-81m was judged better in four, usually due to improved resolution or multiple views. Xenon-133 was superior in five studies, all of which demonstrated subtle regional ventilatory abnormalities, not detectable with Kr-81m, that were seen on the Xe-133 washout images (Table 1).

In five studies that satisfied criteria for embolism without parenchymal/obstructive pulmonary disease, Xe-133 and Kr-81m agreed in three but Kr-81m was better in two, either due to multiple views or the absence of liver activity seen with Xe-133. In nine other studies of patients with combined embolic and nonembolic lung disease, separate assessment was made for each diagnosis. For embolic disease, Kr-81m was judged superior in five studies. In two of the five, Kr-81m was the sole indicator of scintigraphic mismatch, because there was a ventilatory abnormality, contiguous with the embolic (mismatched) region, which was not easily separable in

**TABLE 1. PATIENTS WITHOUT PULMONARY EMBOLISM**

Studies showing no scintigraphic abnormalities			
No. of studies	Kr-81m and Xe-133 agree	Kr-81m better	Xe-133 better
9	9	0	0
Studies showing parenchymal/obstructive lung disease			
No. of studies	Kr-81m and Xe-133 agree	Kr-81m better	Xe-133 better
20	11	4	5 (5)*

\* Alternative study missed diagnosis.

**TABLE 2. PATIENTS WITH PULMONARY EMBOLISM**

Studies showing embolic lung disease only			
No. of studies	Kr 81m and Xe-133 agree	Kr-81m better	Xe-133 better
5	3	2	0
Studies showing concurrent embolic and parenchymal/obstructive lung disease			
No. of studies	Kr-81m and Xe-133 agree	Kr-81m better	Xe-133 better
9	4	2	5 (2)*
	For PE	For OPD	For PE
	4	2	5 (2)*
	For PE	For OPD	For PE
	4	2	5 (2)*
	For PE	For OPD	For PE
	4	2	5 (2)*

\* Alternative study missed diagnosis.

PE = pulmonary embolism.

OPD = parenchymal/obstructive disease.

**TABLE 3. SUMMARY OF DATA**

Studies showing embolism with or without parenchymal/obstructive lung disease		
No. of studies	Kr-81m better	Xe-133 better
14	7 (2)*	0
Studies showing parenchymal/obstructive lung disease with or without emboli		
No. of studies	Kr-81m better	Xe-133 better
20	7 (1)*	9 (6)*

\* Alternative study missed diagnosis.

the posterior projection with Xe-133. For the diagnosis of nonembolic lung disease in these nine patient studies, Kr-81m was better in three and Xe-133 better in four. The alternative study missed the diagnosis in one case each (Table 2).

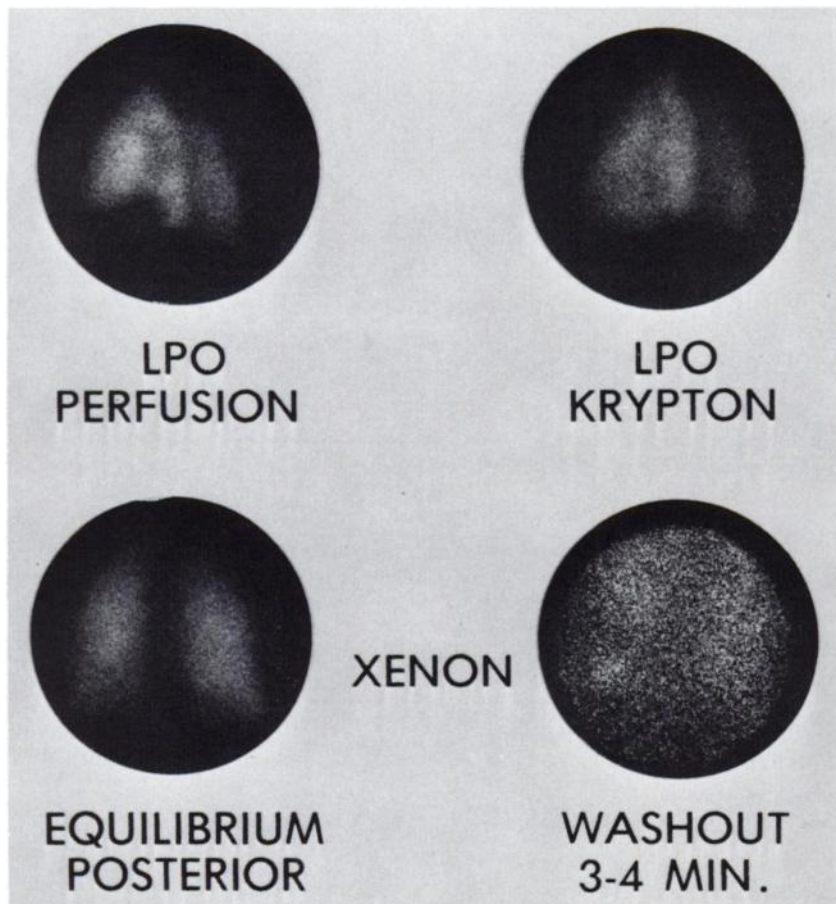
A summary of the data is shown in Table 3. Of 14 studies of patients with pulmonary embolism, Kr-81m was significantly better for detection of embolism in seven and Xe-133 better in none ( $p <$

0.02). In patients with parenchymal/obstructive lung disease detectable scintigraphically, Kr-81m was better in seven and Xe-133 in nine. However, ventilatory abnormalities were detected by Xe-133 only in six cases, compared with one case by Kr-81m. Although not significant at the 0.05 level of confidence, these data suggest that Xe-133 may be better for the detection of obstructive lung disease.

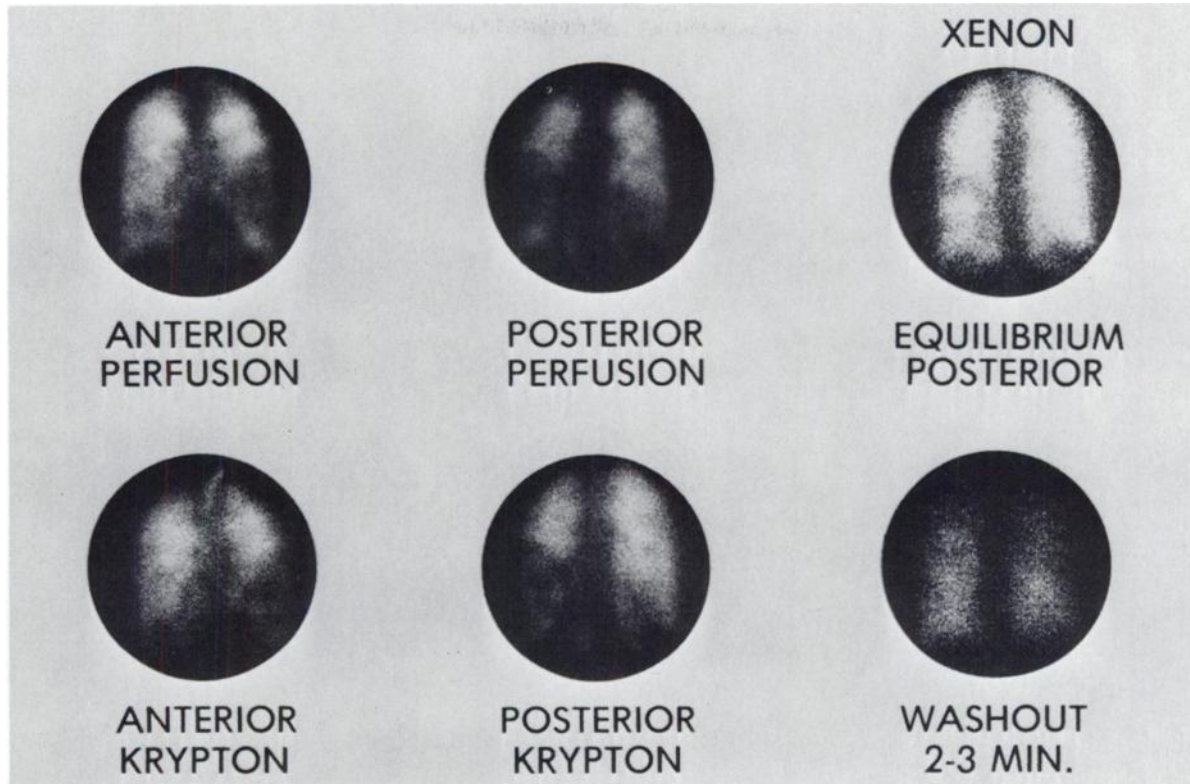
Angiographic data were available for only two patients, both without emboli. Pulmonary function studies were done in 12 patients at various time intervals from the date of scintigraphic study. Generally there was excellent agreement when obstructive pulmonary disease was diagnosed. Three patients with restrictive lung disease had normal ventilation/perfusion studies.

DISCUSSION

The potential advantages of performing regional ventilation studies with Kr-81m in patients suspected of having pulmonary embolism have been enumerated previously (1). The 190-keV photopeak of Kr-81m allows improved spatial resolution compared with Xe-133, due to improved scatter rejection.



**FIG. 1.** False-negative xenon study for pulmonary embolism. Paired perfusion and Kr-81m ventilation images in left posterior oblique projection show unequivocal mismatch in lateral and anterior basal segments of left lower lobe, consistent with embolism. Xenon-133 equilibrium and washout views show retention in contiguous region not easily separable in posterior projection, which could lead to erroneous diagnosis of obstructive, rather than embolic, lung disease.



**FIG. 2.** Diffuse obstructive pulmonary disease. Xenon-133 equilibrium and washout views (far right) show diffuse retention in lower lungs bilaterally, more prominent on left. Paired perfusion and Kr-81m ventilation images (upper and lower panels) allow improved diagnostic accuracy in analysis of multiple perfusion defects in this patient with severe obstructive pulmonary disease.

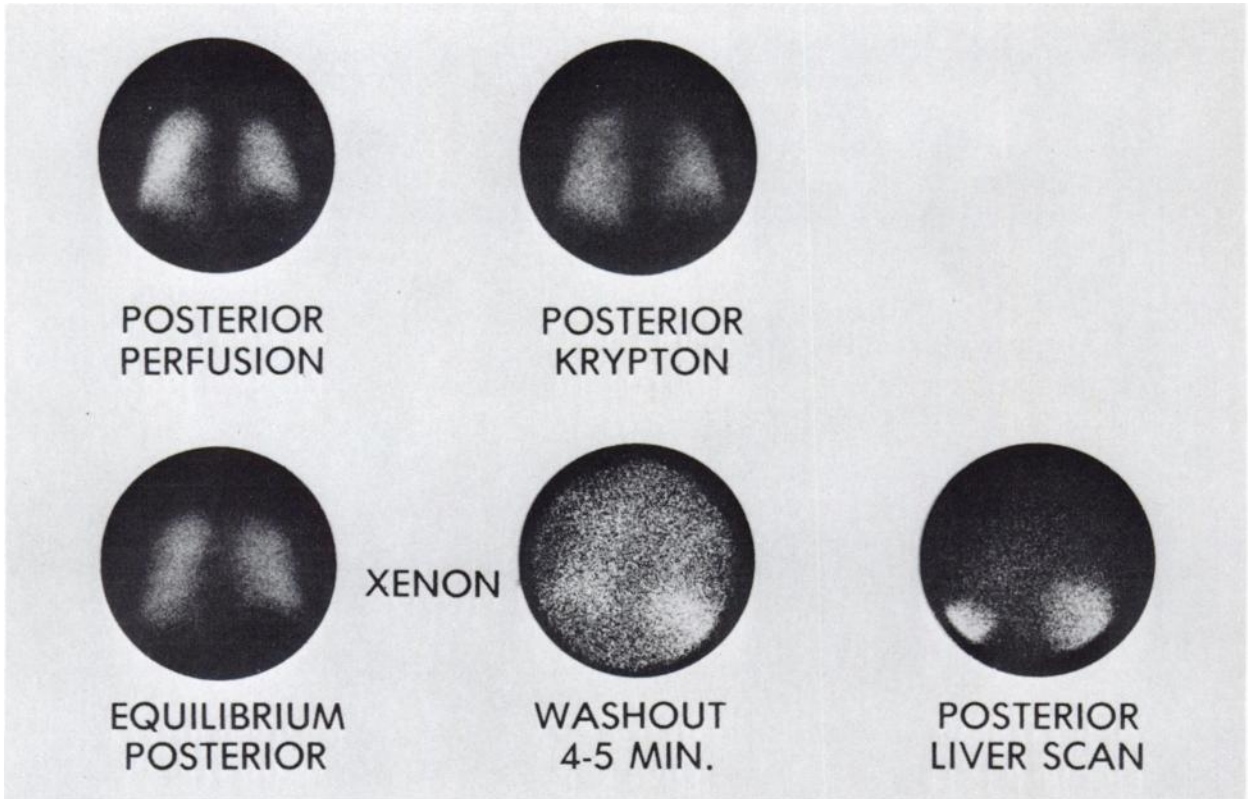
tion, higher tissue penetration, and greater energy transfer to the sodium iodide crystal. Because the gamma energy of Kr-81m is higher than that of Tc-99m, the ventilation study may be performed concurrently with or following the perfusion study, thus obviating the need for ventilation studies in patients with normal perfusion lung images.

Xenon-133 studies, on the other hand, must generally be performed before or a day after perfusion imaging. Although single-breath ventilation studies with Xe-133, following perfusion studies, have been successfully obtained (3), this method is limited only to cooperative patients or to those with relatively large defects; in McNeil's study, 34% of patients could not be evaluated (4). Moreover, many patients with documented obstructive lung disease have normal first-breath images and abnormal washout views, which further limits the diagnostic sensitivity of the technique.

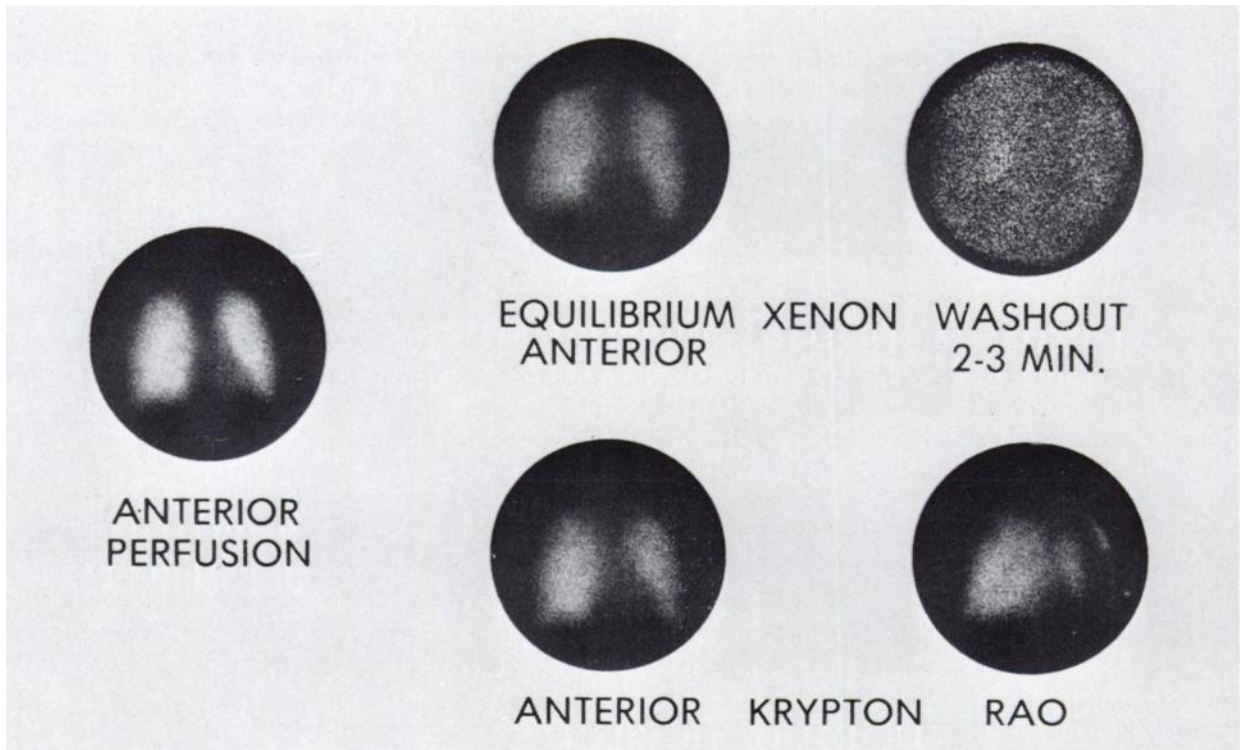
The most notable advantage observed of Kr-81m over Xe-133 was the ability to provide superimposable ventilation and perfusion images in multiple projections. This was particularly useful for proper evaluation of studies with perfusion defects confined to lung segments better seen in anterior or oblique projections. It was essential in two instances, in

which perfusion defects were in areas with contiguous ventilatory abnormalities not easily separable with Xe-133 images in the posterior projection (Fig. 1). Another patient had scintigraphic findings of both embolic and obstructive lung disease in two Kr-Xe ventilation and perfusion studies, but an intervening perfusion and ventilation study with Xe-133 failed to detect a ventilation-perfusion mismatch in an anterior basal segment of the left lower lobe, principally because the perfusion defect in that segment was not readily appreciated. The subsequent Kr-81m ventilation and perfusion images in the oblique and lateral projections were unequivocal in demonstrating a mismatch.

Evaluation of patients with diffuse retention of Xe-133 and multiple perfusion defects can be difficult (5). Krypton-81m, however, offers distinct advantages due to improved spatial resolution and the ability to compare superimposable ventilation and perfusion images (Fig. 2). With xenon, moreover, underlying activity in the liver may obscure the ventilatory dynamics of the right lower lung. Xenon-133 activity in the liver was noted in 21% of our studies, a value somewhat lower than that previously reported (6). With Kr-81m, this disadvantage is avoided (Fig. 3).



**FIG. 3.** With xenon, liver activity obscures right lower lobe's ventilatory dynamics. Retention of xenon-133 within liver on washout images (lower panel) is identified by its location below right hemidiaphragm and by comparison with simultaneous liver scan (lower right). Krypton-81 ventilation image in posterior projection (upper panel, right) allows accurate assessment of this region. Note retention of xenon-133 in left lower lobe, not discernible in Kr-81m study.



**FIG. 4.** False-negative Kr-81m study for obstructive pulmonary disease. Xenon washout image (upper right) shows obvious retention in right middle lobe. Perfusion and Kr-81m ventilation images (lower panel) are normal.

Xenon-133 provides a highly sensitive test for obstructive lung disease, even when compared with tests sensitive for small-airways disease (7,8). In our study, Xe-133 washout images were considerably more sensitive than Kr-81m in the detection of regional ventilatory abnormalities. This sensitivity was due primarily to improved capacity of Xe-133 to discern areas of retention in a region of low radioactivity, rather than areas of diminished ventilatory activity in regions of high count density with Kr-81m (Fig. 4).

Potentially false-positive diagnosis of pulmonary embolism with normal Kr-81m images (when Xe-133 was abnormal) was not a problem, since those abnormalities discernible only with Xe-133 were usually in regions of normal perfusion.

Regional ventilation scintigraphy with Kr-81m offers refinement in the diagnosis of pulmonary embolism because of improved spatial resolution and the capacity to provide multiple superimposable views. Note, however, that in 40 patient studies performed for suspected pulmonary embolism, Kr-81m was essential for the diagnosis in only two. Because the generator is cyclotron-produced and must be supplied daily, other factors such as cost and availability may be major determinants in the ultimate role of Kr-81m for our diagnostic use. For the evaluation of parenchymal/obstructive pulmonary disease, Xe-133 scintigraphy (including washout views) appears superior, especially when the ventilatory abnormalities are subtle.

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