# Gated Xenon Scans for Right Ventricular Function

William Martin, Ann C. Tweddel, Iain McGhie, and Ian Hutton

*Departments of Medical Cardiology and Cardiac Surgery, Royal Infirmary, Glasgow, Scotland*

The complex geometry of the right ventricle makes the use of radionuclides an attractive method for assessing right ventricular function. The use of the gated $^{133}$Xe technique for this purpose offers several advantages. A short i.v. infusion over 20 sec of $^{133}$Xe permits scans to be obtained, gated to the electrocardiogram at rest and during maximal exercise using a standard gamma camera. The method is both reproducible (3.5%) and repeatable (2.8%), and because of the short half-life within the patient with most of the radioisotope being excreted by the lungs, scans may be repeated within a few minutes and the radiation dose to the patient is small. Right ventricular ejection fraction obtained from gated xenon scans is shown to correlate well with measurements obtained from both standard gated technetium scans and first-pass studies.

**J Nucl Med 27:609–615, 1986**

Right ventricular function is of considerable clinical interest in a variety of conditions including myocardial infarction (MI), which may extend to involve the right ventricular wall (*1–2*), and chronic obstructive airways disease (*3–4*).

Contrast ventriculography is the accepted standard for the determination of left ventricular function and ejection fraction (*5–6*). However, due to the shape of the right ventricle, geometric assumptions used in the calculation of left ventricular ejection fraction (LVEF) are not tenable for right ventricular ejection fraction (RVEF). Various different geometric models have been employed, but none would appear to be ideal (*7*) and therefore there is no generally accepted standard reference for the measurement of RVEF.

Radionuclides provide a noninvasive method of evaluating LVEF, that correlates well with measurements obtained by contrast ventriculography (*8–9*). The determination of ejection fraction from radionuclide studies depends on the assumption that counts detected from within the ventricle are proportional to intraventricular volume. No further geometric assumptions are usually made, and the technique should thus be applicable to the determination of RVEF. Right ventricular function has been assessed in a number of studies using technetium ($^{99m}TcO_4^-$) (*10–13*), by either the first-pass technique or by electrocardiographically gated radionuclide ventriculography with $^{99m}$Tc-labeled red blood cells. Use of the first-pass technique requires a good bolus injection of tracer and assumes that adequate mixing of tracer occurs in the right ventricular blood pool. With relatively low counts within each cardiac cycle, statistical errors are increased and repeat studies require further injections of radiopharmaceutical. The electrocardiographically gated equilibrium technique allows better count statistics to be obtained over several minutes acquisition and enables sequential studies to be performed over several hours.

Another approach to evaluation of right ventricular function has been the use of inert noble gas tracers administered intravenously in saline. These are excreted by the lungs and thus allow the right heart to be visualized in isolation. Rapid lung clearance allows repeat studies within several minutes. Krypton-81m ($^{81m}$Kr) has been used in this manner (*14–16*), but because it has an ultrashort half-life (13 sec) it is both expensive and not readily available. A first-pass bolus technique with xenon-133 ($^{133}$Xe) has previously been used for assessing RVEF (*17*). We have evaluated $^{133}$Xe as a 20-sec infusion with acquisition gated to the electrocardiogram to assess right ventricular function. Theoretically, this approach should help overcome some of the methodological problems of first-pass studies and because of the absence of left heart activity, allows the use of a projection which reduces right atrial and right ventricular overlap. We report our initial results using $^{133}$Xe for the noninvasive assessment of right ventricular function.

Received May 9, 1985; revision accepted Dec. 11, 1985.

For reprints contact: William Martin, PhD, Dept. of Medical Cardiology, Royal Infirmary, 10 Alexandra Parade, Glasgow G31 2ER, Scotland.

## PATIENTS AND METHODS

### Study Population

A total of 55 subjects had resting ventricular function determined by gated $^{133}Xe$ scans. They were comprised of 15 male healthy volunteers, 12 male patients undergoing routine coronary angiography for the assessment of chest pain, 14 patients (ten male, four female) with acute inferior MI and 14 (12 male, two female) with chronic obstructive airways disease. In addition, RVEF was assessed at peak symptom limited supine exercise in ten of the normal volunteers and in the 14 patients with chronic obstructive airways disease.

### Data Acquisition

Patients were imaged supine using a mobile gamma camera* fitted with an ultra-high sensitivity parallel collimator. This has a factor of 2.6 in sensitivity over the standard low-energy, parallel hole, all-purpose collimator. The camera was interfaced to a mobile computer system (Link MAPS) and all data were acquired in listmode to allow accurate retrospective generation of a representative cardiac cycle. A 5–10° left anterior oblique (LAO) projection, with 6° caudal tilt was used, as our experience has shown this gives good separation of the right heart from the lung fields, and of the right atrium from the right ventricle. It also allows the camera to be placed close to the chest wall, thus obtaining the best resolution. One-hundred millicuries (400 MBq) of $^{133}Xe$ in 20 ml of saline were injected intravenously over 20–25 sec, data being acquired from the time of first visualization of the right ventricle until absence of activity. The average time of data acquisition was 24 sec. Using the R-wave and timing data stored on the listmode file, a representative cardiac cycle of 16 frames was then constructed for subsequent analysis cycles with R-R intervals falling more than 20% out of the running average being discarded. Exercise studies were obtained at symptom-limited maximal exercise using a supine bicycle ergometer and a standard exercise protocol. Acquisition commenced 20–30 sec prior to the end of the exercise test.

### Analysis

After a single spatial and temporal smooth of the 16 images, the end-diastolic (ED) and end-systolic (ES) frames were used to derive standard stroke volume and paradox images. These were used to define the tricuspid and pulmonary valve planes (Fig. 1). The right ventricular region of interest (ROI) was then extended from the valve planes to encompass the whole right ventricle, care being taken to include the apex of the ventricle. The ROI was confirmed by superimposition of a cine black and white display of the 16 frame representative cycle, and modified as necessary. A background ROI was drawn 3 pixels wide adjacent to the right ventricular ROI, carefully avoiding the right atrial and pulmonary artery region (Fig. 2). Activity/time curves were generated for both ROIs and RVEF calculated:

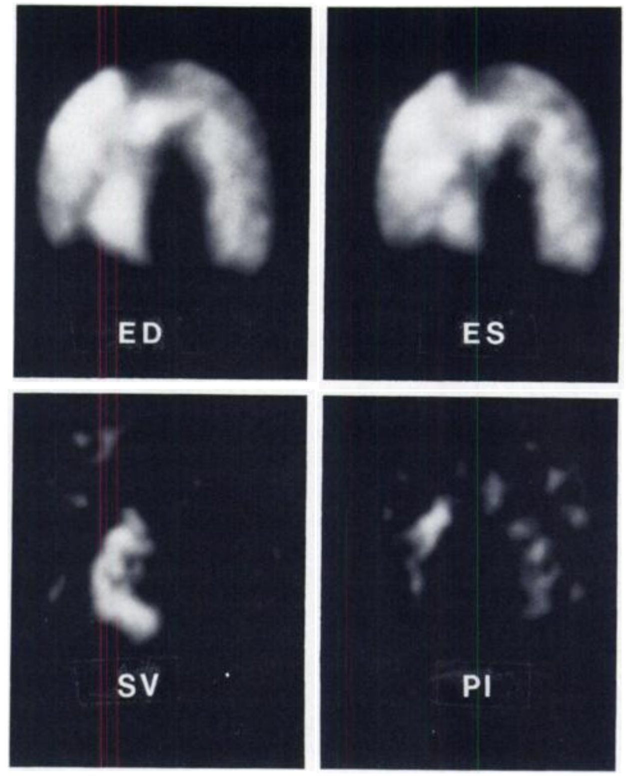


**FIGURE 1**
End-diastolic (ED), end-systolic (ES), stroke volume (SV) and paradox image (PI) from $^{133}Xe$ scan at peak exercise in normal volunteer. Note delineation of tricuspid and pulmonary valve planes. Images are temporally and spatially smoothed

$$RVEF = \frac{EDc - ESc}{EDc - B},$$

where EDc is end-diastolic counts;
ESc is end-systolic counts; and
B is background activity derived from the mean counts throughout the activity/time curve for the background ROI.

### Validation of Method

To assess intra-observer variation, RVEF was evaluated on two occasions for 30 scans. Interobserver variation of RVEF was determined on two occasions by two observers for 20 scans. Reproducibility was evaluated by repeating resting $^{133}Xe$ studies within 5–30 min in five patients and five normal volunteers had their scans repeated at ~3 mo.

For comparison, standard gated technetium blood-pool scans were performed in 20 patients immediately after completion of the resting $^{133}Xe$ study. Gated blood-pool scans were obtained in the modified LAO projection, that gave optimal septal separation and utilized in vivo labeling of the red cells with stannous

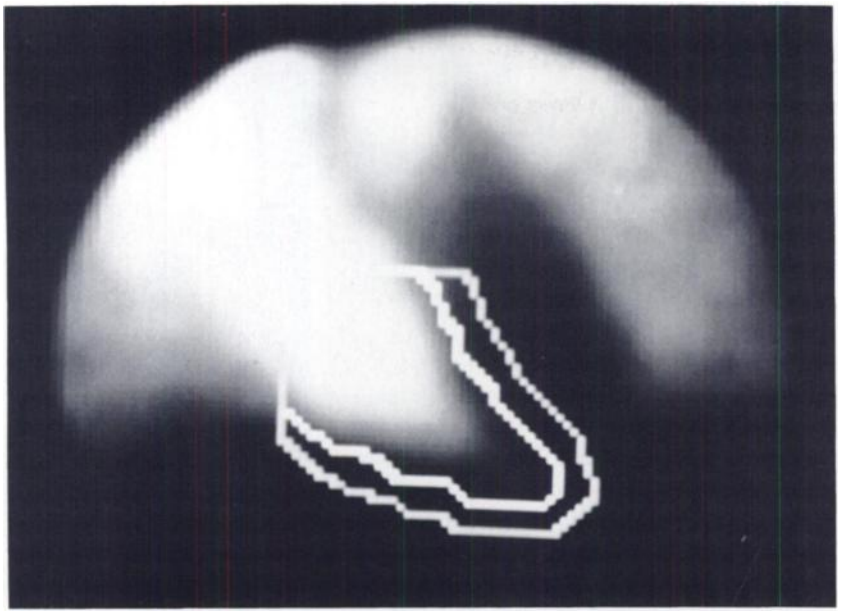

**FIGURE 2**
ED image showing selected right ventricular ROI and background ROI from which ventricular activity/time curves are derived

pyrophosphate with 20 mCi (800 MBq) of $^{99m}$Tc. List-mode data were acquired for 3 min using a high sensitivity parallel collimater. Data are acquired and analyzed in a manner similar in most respects to the xenon scan, with the background ROI drawn only around the free wall of the right ventricle. Again, the stroke volume and paradox images were used in assisting to delineate the right atrial to ventricular border.

In 13 patients, technetium first-pass studies were performed for comparison with xenon scans. These were acquired in the right anterior oblique (RAO) projection, and the representative cycles for the mean of five beats used to assess RVEF (*18*).

Statistical analysis was performed by the appropriate group or paired Wilcoxin test to obtain significance values.

## RESULTS

An activity/time curve derived from a gated $^{133}$Xe study in a volunteer is demonstrated in Fig. 3. In 20 studies, the average net ED counts were 3,620 ± 978 in 1/16 of a cardiac cycle (mean ± s.d.). The normal range of resting RVEF by this technique is shown in Fig. 4, with a mean value 43.2 ± 5.5%. In the 14 patients with acute inferior MI, significantly lower values of RVEF were obtained 19.9 ± 10.5 ($p < 0.001$). Figure 5 shows the stroke volume image from a normal volunteer and a patient with acute inferior MI, with associated right ventricular involvement confirmed clinically and hemodynamically. The arrow indicates the area of right ventricular akinesia. Similarly, the 14 patients with chronic obstructive airways disease had lower resting RVEF than normals – mean 28.1 ± 9.4% ($p < 0.002$). Twelve patients with chest pain, however, had resting ejection fraction similar to the volunteers 39.3 ± 4.9% (n.s.d.).

Interobserver and intra-observer variation of the technique are shown in Fig. 6. In 20 studies the mean interobserver difference in repeat analysis was 2.8%, with a range of 0–9%. For intra-observer variation, assessed in 30 studies, a mean difference of 2.2%, with a range of 0–6% was obtained. The reproducibility of the technique with repeat acquisition of data was also assessed the mean difference was 3.5% with a range of

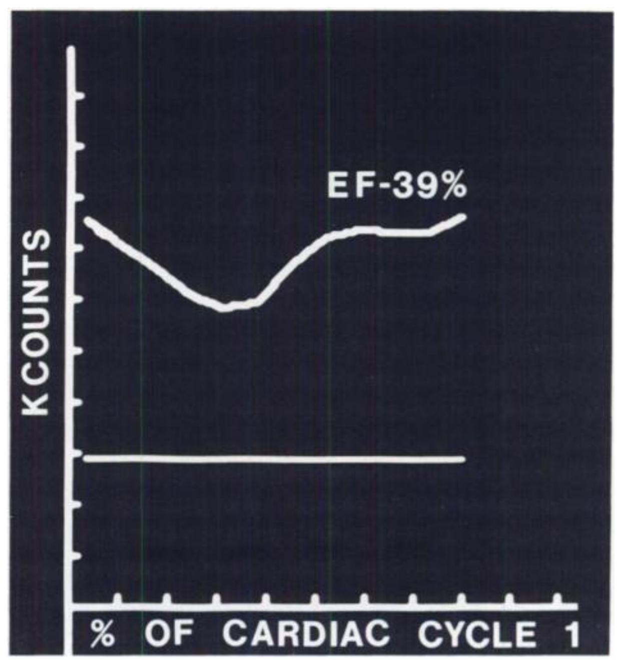


**FIGURE 3**
Right ventricular activity/time curve derived from $^{133}$Xe in normal volunteer with good right ventricular function

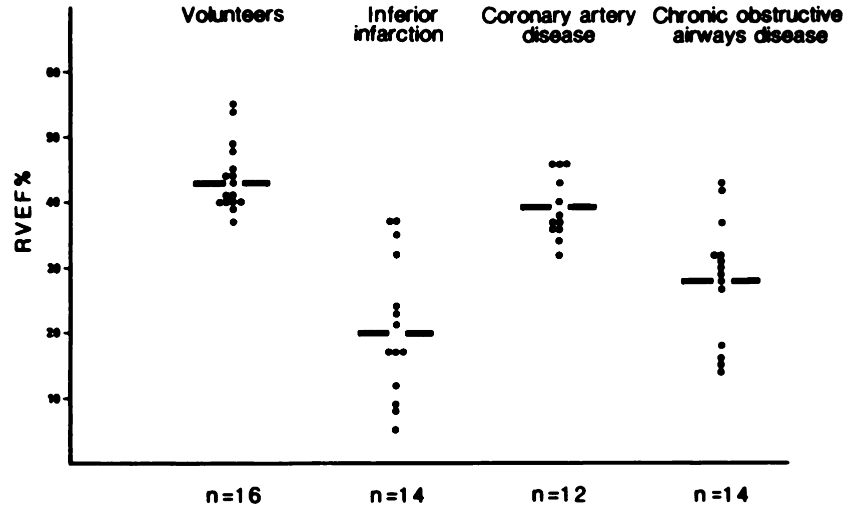


**FIGURE 4**
Resting RVEF in volunteers (43.2 ± 5.5%; mean ± s.d.), patients with acute inferior MI (19.9 ± 10.5%; $p < 0.001$), patients with chest pain due to obstructive coronary artery disease (39.3 ± 4.9%; n.s.d.) and patients with chronic obstructive airways disease (28.1 ± 9.4%; $p < 0.002$)

1–14% for five scans repeated at intervals from 10 min to 1 hr and five scans repeated at 3 mo.

Figure 7 graphs the values of RVEF at rest for the xenon technique against those obtained from the technetium gated blood-pool study. There was a highly significant correlation with a correlation coefficient $r = 0.92$ ($p < 0.001$). The line of best fit did not differ significantly from the line of identity for the two measurements. Similarly, there was good correlation between the ejection fraction values obtained by the xenon technique and the RAO first-pass technetium as shown in Fig. 7, with a correlation coefficient of $r = 0.80$ ($p < 0.001$). In this case, there is a significant difference between the line of best fit and the line of identity, suggesting a systematic error in one or both techniques; however, they are both reproducible.

The values obtained for rest and peak supine exercise RVEF in ten volunteers and 14 patients with chronic obstructive airways disease are shown in Fig. 8. In the volunteers, ejection fraction increases from a mean of 41.5 ± 4.6% at rest to 51.7 ± 6.2% ($p < 0.001$) on exercise. In contrast, in patients with chronic obstructive airways disease, RVEF falls from a mean of 28.1 ± 9.4% to 25.9 ± 11.2% (n.s.d.), although there was considerable individual variation.

## DISCUSSION

The use of inert tracers in solution that are excreted by the lungs has considerable advantages in the assessment of right ventricular function. The lack of left heart activity permits a much shallower LAO projection to be used than is possible with gated blood-pool studies, enabling better separation of the right ventricle and right atrium. Spatial separation of right heart and right atrial activity is probably obtained optimally from an RAO projection, as is normally employed for first-pass technetium studies. However, the use of the RAO projection with gated xenon scans results in the superimposition of right heart and lung activity and also increases the patient to collimator distance, degrading resolution.

Krypton-81m has been used for evaluation of right ventricular function (*14–16*). The higher energy emissions, 191 kev for $^{81m}$Kr compared with 80 keV for $^{133}$Xe are attractive due to the better resolution, decreased patient absorption of gamma rays, and lower scatter improving image quality. The very short half-life of $^{81m}$Kr (13 sec) and the nature of the cyclotron production process, however, limits its use to a few centers on certain production days. Xenon-127, with

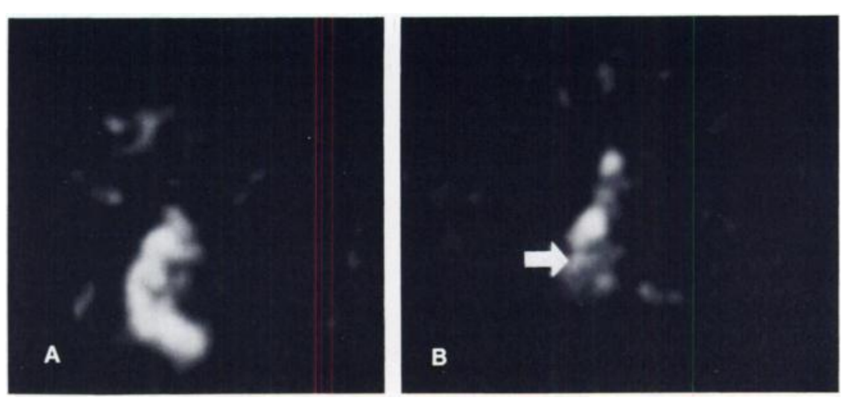


**FIGURE 5**
Stroke volume image from normal volunteer (A) and patient with hemodynamically significant right ventricular involvement from inferior MI (B). Area of akinesis is indicated by arrow. Note ventricular enlargement

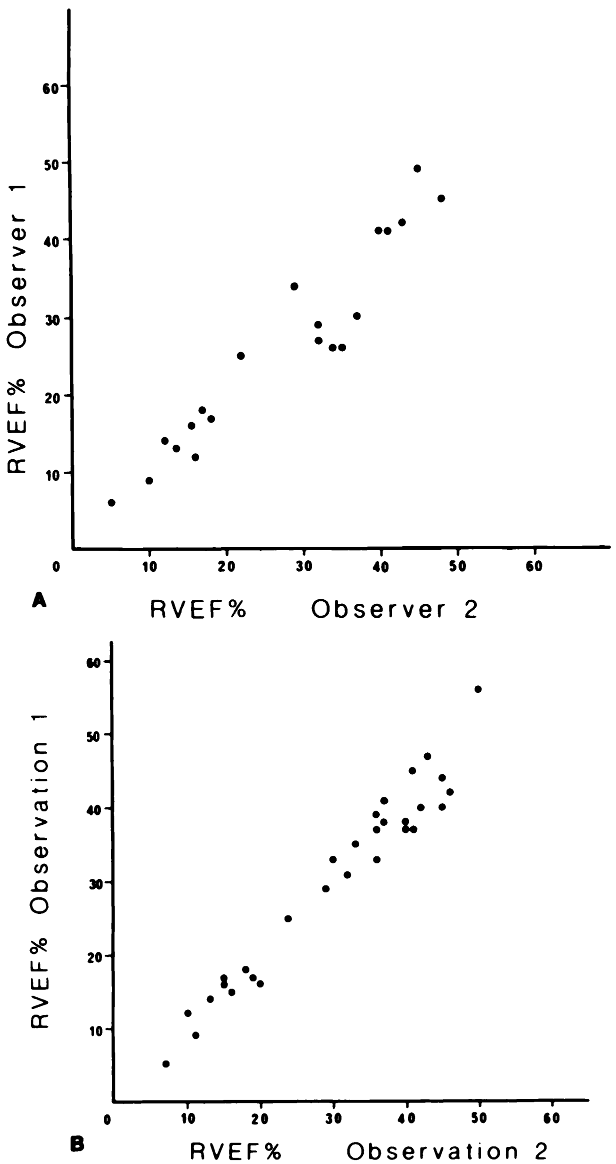


**FIGURE 6**
A: Plot of RVEF obtained by two independent observers in 20 patients (n = 20; r = 0.96) with mean interobserver difference of 2.75%, ranging from 0 to 9%. B: Plot of repeat analysis of RVEF by one observer in 30 patients (n = 30), with mean difference of 2.2%, ranging from 0 to 6%

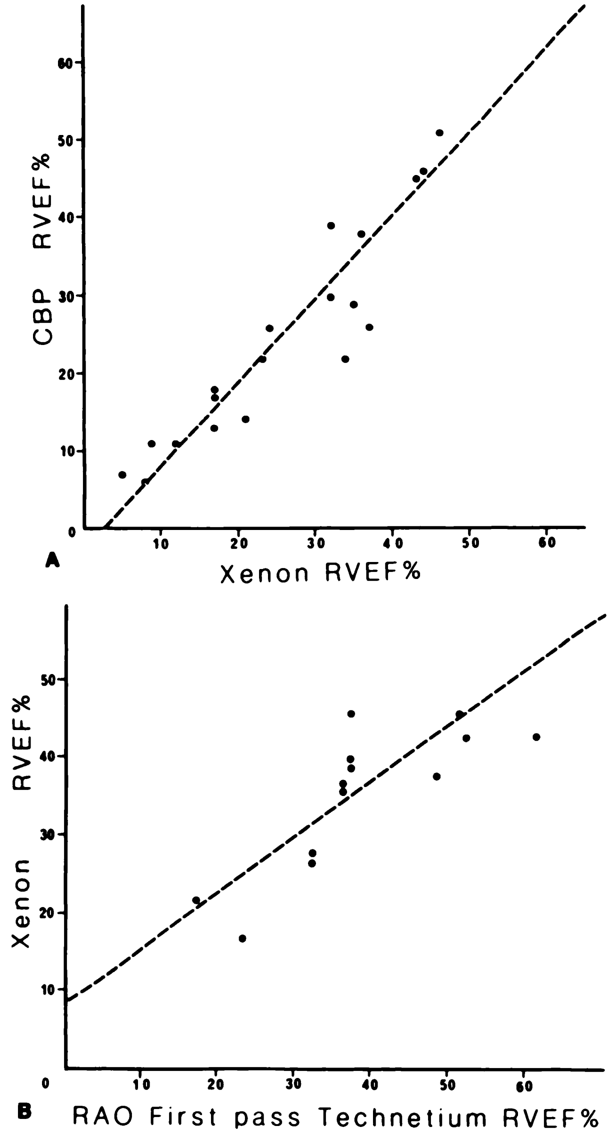


**FIGURE 7**
A: Correlation between gated blood-pool and $^{133}$Xe methods of assessing right ventricular function, with correlation coefficient of 0.92, $p < 0.001$ in 19 patients (n = 19). B: Correlation between $^{133}$Xe and RAO first-pass evaluation of RVEF, with correlation coefficient of 0.80, $p < 0.001$ in 13 patients (n = 13)

its emissions at 172 keV and 203 keV also has some attraction as a radioisotope for right heart studies. It does, however, require the use of a medium energy collimator, again degrading resolution and, in addition, is more expensive and less readily available than $^{133}$Xe. The short biologic half-life of $^{133}$Xe due to its lung excretion results in a low radiation dose to the patient (10 mCi (400 MBq) xenon giving a total lung dose 1/6 of that with 20 mCi (800 MBq) technetium-99m used in blood-pool studies), and allows repeat studies with low residual lung activity within several minutes. A further potential advantage of gated $^{133}$Xe scans with the lack of left heart activity, is the assessment of regional wall motion, especially of the right ventricular septum. First-pass data is particularly unsuited to study wall motion due to poor mixing, especially where there is ventricular dysfunction. In addition, interventricular septal wall motion may be more difficult to assess from standard gated equilibrium studies, since the rotational motion of the heart during systole may produce overlap of counts from the right and left ventricular pool and background activity is high.

To obtain gated xenon scans, we used a relatively short infusion period of 20–25 sec, that we found by experience to yield reliable results. A short infusion was

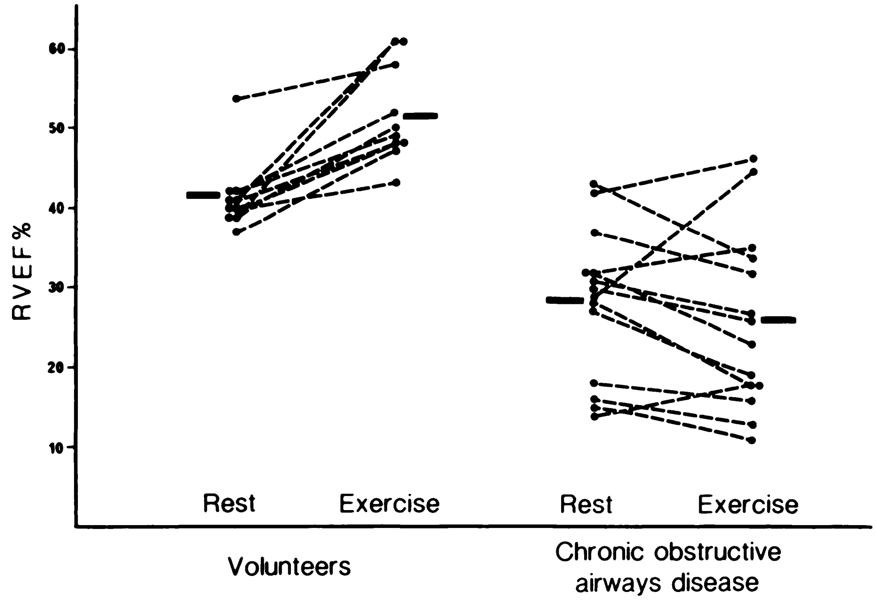


**FIGURE 8**
Plot of rest and peak supine exercise RVEF in ten normal volunteers and 14 patients with chronic obstructive airways disease. All volunteers increased their ejection fraction on exercise, from 41.5 ± 4.6% at rest to 51.7 ± 6.2% at peak exercise ($p < 0.001$). In patients with chronic obstructive airways disease there was diverse response, mean value falling from 28.1 ± 9.4% to 25.9 ± 11.2% at peak excercise

chosen in preference to a first-pass technique for the following reasons. First, first-pass methods require a good bolus injection and rely on the assumption that rapid and adequate mixing occurs within the right ventricle. This may be the case in a normal right ventricle, but where there is right ventricular dysfunction, inadequate delivery of tracer to the apex of the ventricle becomes apparent. A gated technique is independent of bolus flow and allows more time for mixing to occur. Count statistics are adequate, with an average of 3.62k counts within the ED right ventricular ROI. One major advantage of xenon is that infusion over 20–25 sec makes exercise studies attractive, since data may be acquired at peak exercise and motion artifacts are minimized. In this respect, $^{133}Xe$ is also superior to $^{81m}Kr$ which is produced in generators at low specific activity and thus requires longer acquisition times (5–20 min).

The results we have obtained for resting RVEF are similar to those reported in the literature using a variety of methods (*4,14,16*). The lower values for ejection fraction found in some patients with acute MI confirm the right ventricular involvement which may be found in patients with inferior MI.

In conclusion, the use of $^{133}Xe$ for measuring ventricular function offers several practical advantages over other techniques. The isotope is readily available and the rapid lung clearance allows repeat studies after a few minutes with a low lung radiation dose. The analysis routine outlined is simple and reproducible, and it would therefore appear that gated $^{133}Xe$ scanning is suitable as a noninvasive assessment of right ventricular function.

## FOOTNOTE

* General Electric, Milwaukee, WI (GE porta camera II).

## REFERENCES


1. Tobinick E, Schelbert HR, Henning H, et al: Right ventricular ejection fraction in patients with acute anterior and inferior myocardial infarction assessed by radionuclide angiography *Circulation* 57:1078–1084, 1978
2. Nemerovski M, Shah PK, Pichler M, et al: Radionuclide assessment of sequential changes in left and right ventricular function following first acute transmural myocardial infarction. *Am Heart J* 104:709–717, 1982
3. Brent BN, Berger HJ, Matthay RA, et al: Physiologic correlates of right ventricular ejection fraction in chronic obstructive pulmonary disease: A combined radionuclide and haemodynamic study. *Am J Cardiol* 50:255–262, 1982
4. Korr KS, Gandsman EJ, Winkler ML, et al: Hemodynamic correlates of right ventricular ejection fraction measured with gated radionuclide angiography. *Am J Cardiol* 49:71–77, 1982
5. Dodge HT, Sandler H, Ballew EW, et al: The use of biplane angiocardiography for the measurement of left ventricular volume in man. *Am Heart J* 60:762–776, 1960
6. Sandler H, Dodge HT: The use of single-plane angiocardiograms for the calculation of left ventricular volume in man. *Am Heart J* 75:325–334, 1968
7. Slutsky R, Bhargava V, Dittrich H, et al: Comparison of single-plane and biplane contrast analyses of right ventricular function and size. *Am Heart J* 104:100–104, 1982
8. Marshall RC, Berger HJ, Costin JC, et al: Assessment of cardiac performance with quantitative radionuclide angiography: Sequential left ventricular ejection fraction, normalised left ventricular ejection rate, and regional wall motion. *Circulation* 56:820–829, 1977
9. Burow RD, Strauss HW, Singleton R, et al: Analysis of left ventricular function with multiple gated acquisition cardiac blood pool imaging: Comparison to contrast angiography. *Circulation* 56:1024–1028, 1977
10. Berger HF, Matthay RA, Pytlik L, et al: First-pass radionuclide assessment of right and left ventricular

performance in patients with cardiac and pulmonary disease. *Semin Nucl Med* 9:275–295, 1979
11. Maddahi J, Berman DS, Matsuoka DT, et al: A new technique for assessing right ventricular ejection fraction using rapid multiple-gated equilibrium cardiac blood pool scintigraphy. *Circulation* 60:581–589, 1979
12. Slutsky R, Hooper W, Gerber K, et al: Assessment of right ventricular function at rest and during exercise in patients with coronary heart disease: A new approach using equilibrium radionuclide angiography. *Am J Cardiol* 45:63–71, 1980
13. Legrand V, Chevigne M, Foulon J, et al: Evaluation of right ventricular function by gated blood-pool scintigraphy. *J Nucl Med* 24:886–893, 1983
14. Knapp WH, Helus F, Lambrecht RM, et al: Kr-81m for determination of right ventricular ejection fraction (RVEF). *Eur J Nucl Med* 5:487–492, 1980
15. Ham HR, Piepsz A, Vandevivere J, et al: The evaluation of right ventricular performance using krypton-81m. *Clin Nucl Med* 8:257–260, 1983
16. Horn M, Witztum K, Neveu C, et al: Krypton-81m imaging of the right ventricle. *J Nucl Med* 26:33–36, 1985
17. Dahlstrom JA: Radionuclide assessment of right ventricular ejection fraction: A comparison of first pass studies with 133-Xe and 99m-Tc. *Clin Physiol* 2:205–214, 1982
18. Berger HJ, Matthay RA, Loke J, et al: Assessment of cardiac performance with quantitative radionuclide angiography: Right ventricular ejection fraction with reference to findings in chronic obstructive pulmonary disease. *Am J Cardiol* 41:897–905, 1978