Evaluation of the Accuracy of Steady-State Krypton-81m Method for Calculating Right Ventricular Ejection Fraction

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The accuracy of a steady-state ^{81m}Kr method for calculating the right ventricular ejection fraction (RVEF) has been examined in this study. Causes of errors using this method and their effects on the calculated RVEF were evaluated. The results suggested that mixing in the right ventricle during continuous infusion of ^{81m}Kr was homogenous, allowing for the calculation of ejection fraction using the count rate ratio. Lung activity was quite important and could not be neglected in computing RVEF, but the use of [^{99m}Tc]MAA lung perfusion scanning seemed to allow a correct subtraction of this background activity. The delineation of right ventricular regions of interest (ROIs) was complicated by the translation movements of the right ventricle during heart contraction. These ROIs should be drawn carefully on the count density distribution images and data shown by parametric images; such as first and second harmonic phase, amplitude images, and composite stroke volume image should be considered. Furthermore, this study demonstrates the superiority of the ^{81m}Kr technique compared with ^{99m}Tc methods for computing RVEF. In conclusion, even if the true accuracy of the ^{81m}Kr method for calculating RVEF cannot be proven due to the lack of reference methods, strong, suggestive evidence that the technique should be accurate is shown here.

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Despite widespread recognition of the interest in evaluating right ventricular ejection fraction (RVEF) in various clinical settings, relatively few works have been devoted to this subject (*1–7*). To some extent, the reason may be difficulties encountered by currently available techniques in assessing the right ventricular function. The right ventricle has a peculiar geometric configuration, which constitutes a major handicap for two-dimensional ultrasonic and radiographic methods (*8–11*). Radionuclides methods using technetium-99m (^{99m}Tc) do not require an a priori hypothesis on the right ventricular (RV) geometry but the methods are confronted by other difficulties. The equilibrium technique is hampered by the inextractable superimposition between the right ventricle and other heart chambers, while the low count rate and/or the availability of only a few heart beats constitute the limiting factors of the first-pass method (*12,13*).

The availability of krypton-81m (^{81m}Kr) in a suitable form for i.v. injection offers a new possibility (*14–17*). As it is an inert gas, almost all intravenously administered ^{81m}Kr is exhaled during transit through the lung, and the quantity of the tracer that returns to the left heart is negligible. The right ventricle can, therefore, be evaluated by placing the detector in such a way as to obtain the best separation between the right ventricle and the right atrium without being hampered by its superimposition with the left ventricle. Furthermore, the test can be performed during the steady state to collect statistically accurate count rate densities.

If, theoretically, the steady-state ^{81m}Kr method seems to be ideal for evaluating RVEF, its real accuracy still has to be evaluated. This is a difficult problem as there is no universally accepted standard method that can be used as a reference to validate this technique (*2,12,16*). For this reason, another approach was used in this study to assess the accuracy of the steady-state ^{81m}Kr method for calculating RVEF. It consisted of detecting all causes of error of the technique and to evaluate their effects on the calculated RVEF.

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The following factors were evaluated: (a) the mixing of the tracer in the right ventricle; (b) the importance of nonventricular activity and the accuracy of the correction that can be performed; and (c) the difficulty in delineating RV ROIs and the magnitude of variation of RVEF due to error in the ROI.

MATERIALS AND METHODS

Procedure of ECG-Gated ^{81m}Kr Study and Patient Data

The data acquired during a ECG-gated ^{81m}Kr study performed in 30 successive patients were used in this work. 15 children had cystic fibrosis, 13 adults had chronic obstructive lung disease, and two patients had myocardial infarction.

The ECG-gated ^{81m}Kr study procedure was as follows. The patient was placed in supine position and ^{81m}Kr in 5% glucose solution was continuously infused into the basilic vein of the right arm. The rubidium-81 (^{81}Rb) generator used had an activity of 15 mCi and the infusion rate was 15 ml/min. Due to the short half-life of ^{81m}Kr, steady-state activity in the entire cardiopulmonary system was reached in <1 min. During the steady-state, an ECG-gated study was performed in a 20° right anterior oblique (RAO) projection, for a preset count of 2,800k counts. This was obtained in ~5 to 10 min depending on the ^{81}Rb activity at the moment of the test. Sixteen frames per cardiac cycle were reconstructed.

After the gated study, 500 μCi of ^{99m}Tc-macroaggregate albumin (MAA) were administered and lung perfusion scintigraphy was obtained in exactly the same position as the gated study. These data were used for the correction of the background activity, which was performed for each frame on a pixel to pixel basis using the following procedure. An ROI (reference zone) was delineated at a well-perfused lung area. This ROI was carefully drawn to ensure that the area was not contaminated by the radioactivity in the superior vena cava, heart, or pulmonary artery. Corrected activity in the nth pixel of a given frame (A'n) was obtained by:

$$A'n = An - (An,\ Tc)(RKr/RTc), \qquad (1)$$

where An was the activity in the pixel on the uncorrected ^{81m}Kr image; An, Tc was activity in the pixel on the [^{99m}Tc]MAA image; RKr was the activity in the reference zone on ^{81m}Kr image; and RTc was the activity in the reference zone on [^{99m}Tc]MAA image.

The following images were then constructed: (a) first and second harmonic phase and amplitude images (*18–19*), and (b) a parametric image using time minimum as parameter. The time minimum of a given pixel is the time when the radioactivity in the pixel attained its minimum, and (c) composite stroke volume image (*20*).

Mixing in Right Ventricle

Two minutes after the gated study described above, ^{81m}Kr was infused again without moving the patient or the gamma camera. 300 frames of 100 msec were recorded from the beginning of the infusion in order to obtain the washin part of the RV time-activity curves. The purpose of the 2-min delay was to ensure that there was no residual ^{81m}Kr activity from the previous gated study. End-diastolic (ED) and end-systolic (ES) ROIs were delineated manually on ED and ES images obtained from the gated study, and the corresponding time-activity curves were obtained for the 300 frames (Fig. 1). ED and ES frames were then identified by the operator, their count rates were noted, and beat-to-beat RVEFs were calculated. This procedure was repeated three times in the same subject, at 2-min intervals.

In order to increase the statistical precision, a high-activity ^{81}Rb generator (40 mCi) was used for this study. This investigation was performed in five out of the 30 patients.

Background Activity

Importance of background activity. In the ECG-gated steady-state ^{81m}Kr study, the background activity was constituted by the radioactivity in the lung included in the RV ROIs. By assuming that the distribution of this radioactivity was equal to the distribution of [^{99m}Tc] MAA, the lung activity included in the ED ROI (Led) could be estimated.

$$Led = Ted\ (RKr/RTc), \qquad (2)$$

where Ted was the activity in the EDROI on [^{99m}Tc] MAA image, and RKr and RTc were the radioactivity in the reference zone on ^{81m}Kr and [^{99m}Tc]MAA images, respectively.

By comparing the results obtained with the total count rate in the ED ROI on ^{81m}Kr image, the impor-

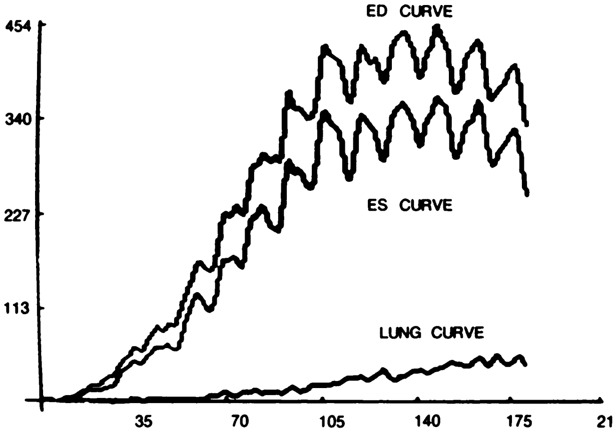

FIGURE 1
Time-activity curves in ED and ES ROIs as well as in lung ROI during washin of constant continuous infusion of ^{81m}Kr. ED and ES periods could easily be identified. During washin, lung activity was low and could, therefore, be neglected in calculating right ventricular EF

tance of the lung activity included in the ROI was appreciated.

Accuracy of background correction using [^{99m}Tc]MAA image. The accuracy of the background correction was evaluated by calculating the percentage of the lung activity that was corrected. This was performed in two ways described as follows.

1. Two additional ROIs were delineated at the lung area (test zones). These regions were also drawn very carefully to be sure not to include the radioactivity in the superior vena cava, heart, and pulmonary artery. The count rates in these test zones before and after correction were compared with evaluation of the accuracy of lung background correction. Separate analysis was performed depending on whether the test zone was located in a well-perfused or a markedly hypoperfused area.

2. By subtracting the corrected image from the original and then dividing the result by 1% of the original image, a new image was obtained. It showed the percentage of the subtracted activity on a pixel-to-pixel basis. The accuracy of the correction could, therefore, be assessed for each region of the lung. If the correction was accurate, the subtracted activity should be ~ 100% in all lung area. To allow for an easier evaluation, this image was presented using a color display in which each color corresponded to a specific value of the percentage of subtracted activity (Fig. 2).

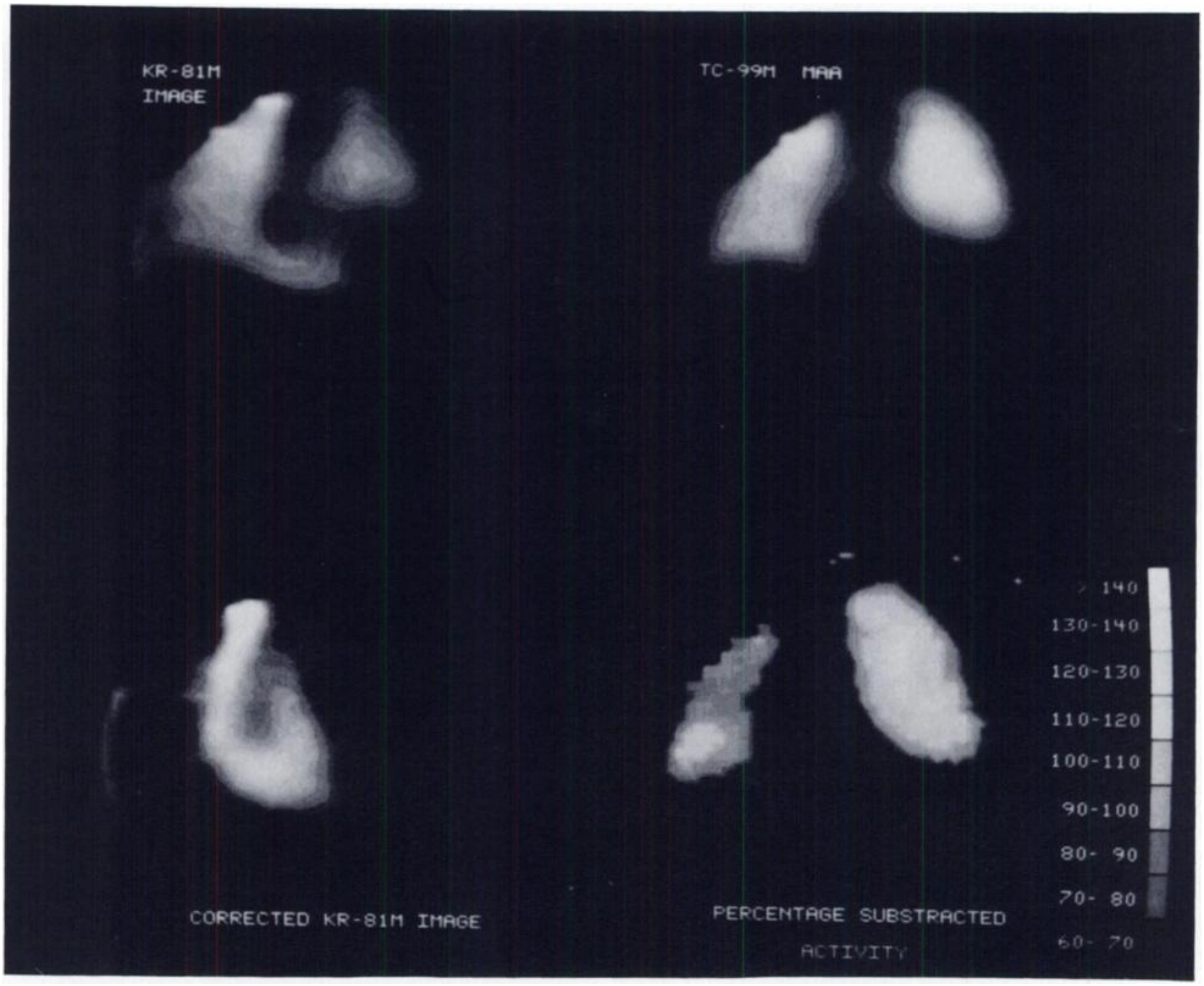

FIGURE 2
Upper panel shows ED frame obtained during ECG-gated ^{81m}Kr study and [^{99m}Tc]MAA lung scintigraphy obtained in exactly same position. One can see that lung activity was quite important and delineation of ED RV ROI on this image is not easy. ED frame after background correction (lower left) shows that lung activity was completely subtracted. This was confirmed by percentage subtracted image, which shows that outside heart and great vessels, correction of radioactivity was within 80 to 120% for each pixel in lung area. Originally this figure is presented using fix color scale in which each color corresponded to specific value of percentage of subtracted activity, allowing easy evaluation of quality of background subtraction. After subtraction of lung activity, limits between right atrium and right ventricle became more apparent

Accuracy in Delineating ED and ES ROIs and Its Effects on the Computation of RVEF

Effects of error in delineating ED and ES ROIs. Data obtained in the first ten patients were used for this study. At first, ED and ES ROIs were delineated. Then, the limits of these ROIs were modified, one pixel (3.3 mm) or two pixels larger or smaller, to simulate errors in ROIs delineation. The effects of these modifications on RVEF were then evaluated.

Three segments of the ROIs were studied separately: (a) free border of the right ventricle; (b) pulmonary valve plane; and (c) tricuspid valve plane.

Intra- and interobserver variability. To determine whether the information contained in the data was sufficient to allow a reliable and reproducible delineation of ED and ES ROIs, interobserver variabilities in delineating these ROIs were evaluated.

All data were available to observers: the dynamic series along with isocount lines projected in each count density frames, first and second harmonic phase and amplitude images, and T-minimum image and composite stroke volume image. No specific instruction, however, was given to the observers on how to delineate the ROIs.

Data Used to Locate RV Borders

For each patient, the observers were asked to determine which images were particularly helpful in delineating the ROIs and which images were not useful or even misleading. This information was used to establish the optimal data processing procedure.

RESULTS

Mixing in the Right Ventricle

An example of the beat-to-beat variation of the count rate in ED and ES ROIs during the washin phase is shown in Fig. 1. In all cases, the ED and ES periods were easily identified. During the first heart beats, the lung activity was very low. Its effect on the calculation of RVEF can, therefore, be neglected.

The beat-to-beat RVEFs obtained in the five investigated subjects are presented in Table 1. One can see that the RVEFs were quite similar from one beat to another and, most importantly, there was no tendency towards an inordinately higher or lower EF on the first beat as compared with subsequent beats.

Accuracy of Lung Background Correction

Importance of lung background. The ratio of background to ED count rate was calculated and showed that, during the steady state, the lung activity included in the RV ROI was not negligible. Moreover, this background activity varied from one patient to another. The mean value of background to ED count-rate ratio in the 30 patients was 0.51 (s.d. = 0.32, range 0.14–1.27).

TABLE 1

Beat-to-Beat Right Ventricle Ejection Fraction

Patient no.	RVEF			
	First beat	Second beat	Third beat	Fourth beat
1	39	34	43	37
	34	38	32	35
	31	37	39	39
2	26	22	25	23
	21	25	26	20
	23	24	27	21
3	31	35	38	34
	38	28	40	35
	34	31	32	35
4	30	30	21	25
	25	27	31	24
	24	29	25	23
5	28	34	34	33
	32	30	28	48
	32	29	35	34

Accuracy of background correction. The subtracted lung activities in the test zones are shown in Fig. 3. These results indicate that when the test zone was located in a well-perfused or slightly hypoperfused area, the correction was found to be acceptable. The subtracted lung activity was between 80 to 120%. When the test zone was located in a markedly hypoperfused area, however, the correction was often inaccurate, ranging from 35 to 160%.

Effects of Error in Delineating the ROIs

The variations of RVEF due to modifications of RV ROIs are shown in Table 2. As shown, errors in delineating the free border or the pulmonary artery have practically no effect on the EF. However, this was not true on the atrioventricular border. Two pixels variation in delineating ED and ES tricuspid valve plane induced errors as high as 4%, while a total of four pixels variation produced up to a 10% error on computed RVEF.

Interobservers Variabilities

In general, the interobserver variability was quite good (Table 3). However, in six patients (20% of the cases investigated), important variations (differences of >5%) of the calculated EF were observed.

Analysis of the ED and ES count rates employed for calculating RVEF showed that in these six cases, interobserver variabilities were observed in both ED and ES count rates suggesting that difficulty in delineating the ROI was true for ED ROI as well as ES ROI.

Images Used in Locating RV Borders

Images that helped the delineation of the ROIs varied from one patient to another and, also, depended on which border of the right ventricle was concerned. The first harmonic amplitude image, the composite stroke

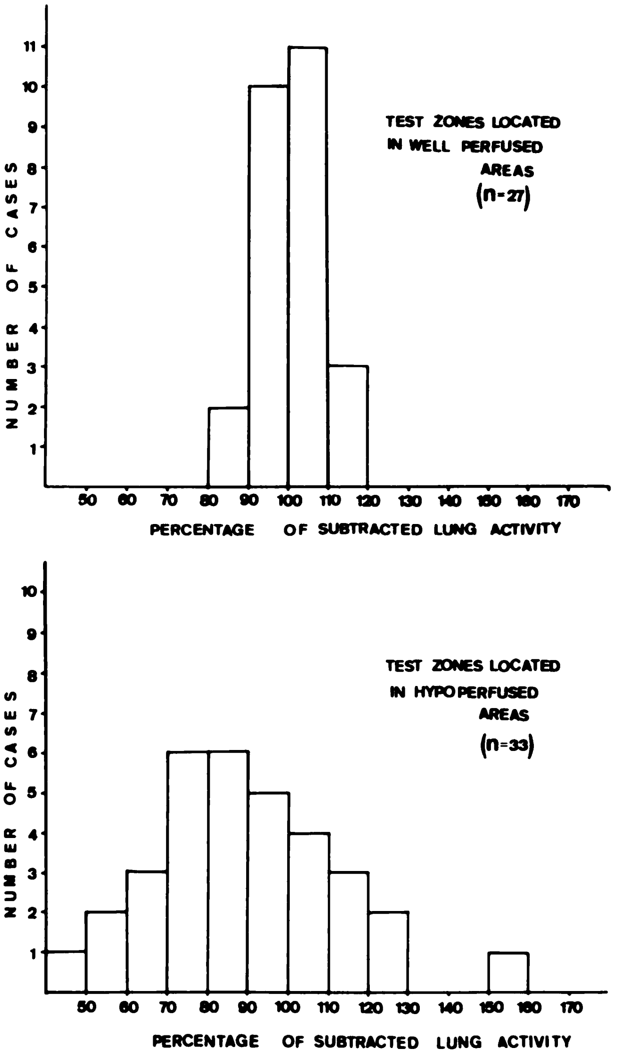

FIGURE 3
This figure shows percentage of subtracted activity in test zones. When these zones were located in well-perfused or slightly hypoperfused area, correction was quite accurate. It ranged betwene 80 to 120% (upper panel). When test zone was located in markedly hypoperfused area (lower panel), correction was less accurate. It ranged between 35 to 160%

volume image, and in some cases, the second harmonic phase and amplitude images were helpful in localizing the tricuspid valve plane on ED and ES frames. Another frequently useful indicator was the isocount line separating the right ventricle from the right atrium. The first harmonic phase image was useless in locating the tricuspidial valve plane.

All observers used the first harmonic phase and amplitude images or the composite stroke volume image for delineating the pulmonary valve plane. The count density images and the isocount lines were not helpful at all in locating the pulmonary valve plane, but they were essential in determining the inferior and lateral borders of the right ventricle.

TABLE 2
Variations of Ejection Fraction Due to Variation of ROIs

	Error on RVEF*	
Error in delineating	Error on 2 pixels On ROI	Error of 4 pixels on ROI
Free border	1%	2%
Pulmonary valve plane	0%	2%
Tricuspid valve plane	4%	10%

* Presented in absolute values.

DISCUSSION

Many factors may influence the accuracy of radionuclide techniques in calculating ventricular ejection fraction. Some of these factors are independent of the nature of the radionuclide employed. The linearity of the detector, the frame rate of the irregularity of heart beats, and the photon absorption, for example, influence the accuracy of the ^{81m}Kr method and ^{99m}Tc methods in exactly the same way. These factors, their effects on the calculation of EF, and methods to minimize some of these effects have been investigated by other authors (*21–28*).

There are, however, three factors that are specific to the ^{81m}Kr ECG gated study: (a) the mixing of the tracer in the right ventricle, (b) background activity, and (c) the delineation of the ROIs. These factors are also present in the ^{99m}Tc methods, but under different conditions. The analysis of these factors would produce a clearer assessment of the accuracy of the ^{81m}Kr method and would provide a comparison to the ^{99m}Tc techniques.

The calculation of EF using the count density ratio method is only valid if the tracer is distributed homogeneously in the ventricle. This condition exists during

TABLE 3
Interobservers Variability

RVEF
(n = 30)

Patient no.	Observer 1	2	3	Patient no.	Observer 1	2	3	Patient no.	Observer 1	2	3
1	34	31	29	11	38	39	39	21	49	50	45
2	43	39	39	12	37	37	40	22	56	54	56
3	59	50	51	13	48	31	43	23	39	38	35
4	33	32	27	14	61	51	43	24	68	47	64
5	52	50	48	15	36	37	36	25	54	53	50
6	49	51	51	16	38	37	36	26	56	52	53
7	37	34	35	17	34	33	33	27	42	43	41
8	39	35	34	18	50	49	50	28	48	48	48
9	49	50	50	19	45	45	47	29	50	25	31
10	42	39	44	20	34	37	34	30	41	42	41

the steady state of a relatively long-lived radionuclide such as ^{99m}Tc. Using an ultra-short, half-lived radiotracer such as ^{81m}Kr, the homogeneity of the distribution of the tracer in the right ventricle during the steady state is not evident. Indeed, several investigators (*29–30*) have shown that a tracer introduced directly into the right ventricle did not mix homogenously in the whole ventricular volume. Therefore, there is a theoretical possibility that during the steady state, decay of the tracer results in distribution that is still not homogenous (*31*).

To evaluate the degree of mixing of ^{81m}Kr during the steady state, we calculated beat-to-beat RVEF during the washin phase of a continuous infusion of the tracer. During this period, an inhomogenous mixing should produce an inordinately high or low first-beat RVEF that would tend to decrease or increase regularly in the subsequent beats, until a plateau was reached.

Our results showed, however, that the RVEF of the first beat was not different from those of the subsequent ones, suggesting that the mixing in the right ventricle was already homogenous when the first-beat RVEF was calculated. This is probably because in this study, the tracer was introduced from a peripheral vein in the form of a continuous infusion with a relatively low infusion rate. This contrasts with the direct intraventricular administration referred to above (*29–30*) or with the very short bolus employed in the first-pass method (*12*). It is evident that the 100 msec framing rate is not optimal for calculating EF (*21*). It does not, however, constitute a bias in this particular work as we are mainly interested in comparing the results of beat-to-beat RVEF rather than the exact value of this parameter.

Another factor should be considered in discussing the mixing of ^{81m}Kr in the right ventricle. The steady-state distribution of a tracer in a system does not depend on the absolute value of its half-life, but on its relative value as compared with the mean transit time of the system (*32*). In the case of ^{81m}Kr, the half-life is relatively long as compared with the exchange rate in the right ventricle. A slight heterogeneity of ^{81m}Kr distribution during the washin period is, therefore, not critical because the difference between the real half-life of the tracer and the exchange rate of the right ventricle will contribute to a better mixing during the steady state.

The situation is different in cases with severe wall motion abnormalities, such as those with important dyskinesia. In these cases, because the local exchange rate is slow, the distribution of ^{81m}Kr during the steady state could remain heterogenous.

Concerning the method for background subtraction, it is evident that, theoretically, the distribution of [^{99m}Tc]MAA differs from that of ^{81m}Kr; the former determined solely by regional blood flow while the latter reflects the balance between regional blood flow and alveolar ventilation.

Our data agree with data reported by Ciofetta et al. (*33*), showing that the difference between ^{81m}Kr and [^{99m}Tc]MAA distribution varied depending on the state of the perfusion of the areas evaluated. This difference was small for well-perfused areas and significantly higher in areas with perfusion defects. This means that, depending on the state of the perfusion of the lung area included in the RV ROI, the background correction could be accurate or totally inaccurate. However, influence of suboptimal background correction on the calculated RVEF depends not only on the degree of the accuracy of this correction, but also on the ratio of background to true ventricular activities. An important relative error on a low background might introduce a smaller error on EF as compared with that introduced by a smaller relative error on a high background.

For this reason, we choose a well-perfused area as reference zone. If the lung activity included in the RV ROI is also well perfused, the correction will be accurate. If this zone is markedly hypoperfused, the relative error in the background correction of the EF will be low.

A background correction that is accurate at a range between 80% and 120% is quite good considering that the correction is performed using a two-dimensional presentation of three-dimensional data. Furthermore, the [^{99m}Tc]MAA method allows the "percentage subtracted image" to be obtained. This can be used for evaluating quality of the background subtraction before the computation of the EF. If this image shows inaccurate correction in lung areas outside the reference zone, a suboptimal correction of lung activity included in the RV ROIs can be suspected. In this case, the reference zone can be modified before computing the EF.

The calculation of several values of EF using various reference zones for background correction also allows estimation of the range of possible error in the calculated EF.

The method using [^{99m}Tc]MAA lung scintigraphy for background correction has been preferred for the following reasons. Krypton-81m lung ventilation can be used instead of [^{99m}Tc]MAA perfusion scintigraphy. This method is hampered, however, by the practical difficulty in having a ^{81}Rb generator that can be used simultaneously for perfusion and ventilation, and by a theoretical handicap of the tendency towards greater error in the presence of V-P inequalities.

Another alternative is the use of a right ventricular washout curve (*34*). This method is based on a solid theoretical basis, but needs a very high count rate to obtain an accurate lung washout curve.

The classic method of background correction usually employed in ECG gated blood-pool study can also be used in the ^{81m}Kr study. This approach uses a periventricular area as the reference zone and the ratio of area as correcting factor. The method assumes, however, that the average value of lung activity in this area is equal to that included in the RV ROI. This assumption is certainly not valid in the presence of regional lung perfusion or ventilation abnormalities. It is, therefore, unlikely that this method would be more accurate than the [^{99m}Tc]MAA method that offers the possibility of choosing the best reference zone, and that uses the physiologic distribution of lung perfusion as a correcting factor.

Background activity correction constitutes the most important source of error in the calculation of EF using equilibrium ^{99m}Tc methods. This study demonstrates that using the steady-state ^{81m}Kr method results in a much more favorable situation. A nonempirical method is available, which allows minimization of the effect of nonventricular activity on the calculation of RVEF.

Another potential cause of an important error in calculating RVEF was the delineation of the ROIs. The simulated study showed that the error in delineating the free border of the right ventricle or the pulmonary valve plane produced only a minimal variation on the RVEF. This was probably because the count rates in these regions were relatively low as the lung activity had been correctly subtracted. The demonstrated variation in delineating the tricuspid valve plane, however, was critical because it induced an important fluctuation in the calculated RVEF.

Unfortunately, a correct delineation of ED and ES RV ROIs is quite difficult. This is because on RAO projection, an important and complex movement of the right ventricle occurs during the heart contraction (*35*). The tricuspid valve plane moves downward toward the apex, while a combined upright and lateral movement is often observed in the inferior border. A displacement to the right might occur in the ventricular lateral wall and the infundibulum. All these movements could be expected to influence the parametric images that are usually employed for delineating ventricular ROI. Nevertheless, by taking into account all the available data, an acceptable interobserver variability was obtained in most of the cases.

In this study, no specific instruction was given to the observers on how to delineate the ROIs. Therefore, the low interobserver variability means that the information contained in these data were sufficient to allow a reliable and reproducible delineation of ROIs. The data that helped in delineating the ROI varied, however, from one patient to another and, also, depended on the right ventricular border concerned.

The isocount lines were very helpful in determining the free borders of the right ventricle. This was not surprising since after background correction, there was no significant activity outside these borders. The isocount lines were, however, useless for locating the pulmonary valve plane as the count rate observed in the infundibulum was often quite similar to that observed in the pulmonary artery. Fortunately, this valve plane could easily be located by using the first harmonic phase and amplitude images because the pulmonary artery and the infundibulum had different phase and amplitude values.

The observers agreed that the delineation of the ED and ES tricuspidial border of the right ventricle constituted the most difficult problem. This is because the tricuspid valve plane anatomically constitutes a thin structure, far beyond the resolution of the gamma camera. Furthermore, there is a significant displacement of this valve plane during heart contraction. In some cases, the isocount lines indicated the location of this valve plane, but in others, this technique was not helpful because the difference of count rate in the right atrium and the right ventricle was sometimes quite low.

The first harmonic phase image also could not be used because the tricuspidial border of the area having ventricular phase values indicated the middle of the tricuspidial displacement area and not the ED and ES tricuspidial border of the right ventricle. The first harmonic amplitude image, however, was very useful. As a matter of fact, the amplitude of count rate variation in the tricuspidial displacement area was low because the reduction of radioactivity due to ventricular contraction was compensated by the increase of the radioactivity due to the entry of the atrium. For this reason, this area was systematically shown as a hypoamplitude zone. The ED tricuspidial border of the RV was therefore, indicated by the left border of this hypoamplitude area and the ES border was indicated by the right border of this hypoamplitude area.

Composite stroke volume image was often useful in locating the tricuspidial valve plane. This was expected because the information contained in this image was basically the same as that given by the first harmonic amplitude image.

The second harmonic phase and amplitude image sometimes aided in locating the tricuspidial valve plane during ED and ES. Indeed, due to atrioventricular displacement during the heart contraction, the shape of the time-activity curves in the tricuspidial area has a double period which can be recognized by the second harmonic temporal Fourier transform. In some cases, however, the second harmonic phase and amplitude images were not helpful as the noise contained in the data influenced the precision of the calculation of these parameters.

It should be noted, however, that even if the observers agreed in delineating the RV contour, the accuracy of this optimal contour cannot be evaluated because the true contour is unknown.

There is another factor that may influence the accuracy of the calculated EF. The count density ratio method assumes that the count rate observed in the ROI corresponds to the activity in the ventricle, and that the activity inside the atrium that is eventually included is negligible. For this reason, a 20° or 30° RAO projection is employed that generally separates, correctly, the right atrium from the right ventricle. In an individual case, however, the projection used might be suboptimal and a certain degree of superimposition between these two chambers remains. In some pathologic cases, especially in patients with chronic obstructive lung disease with emphysema, this superimposition is unavoidable. It is well documented that in these cases, a compression and a rotation of the right ventricle do occur, producing an inextractable superimposition no matter what projection is employed. The same problem may also occur in patients with congenital heart malformations. The five cases in whom important inter-observers variabilities were observed were cases with evident overlap between the right atrium and the right ventricle. The count density images gave no indication concerning the border of these two cavities. This explains why a slight variation in the ROIs produced an important variation in the calculated EF.

Even if the superimposition factor still constitutes a problem with the ^{81m}Kr study, it should be stressed that it is present on a much smaller scale as compared with that observed in the equilibrium ^{99m}Tc methods. In the ^{81m}Kr study, the superimposition on the left heart can be neglected and the detector can be placed in such a way as to get the best separation between the right atrium and right ventricle. During the equilibrium ^{99m}Tc study, the right atrium and the right ventricle are totally superimposed, precluding a correct separation of these two sources of radioactivity (*12*). In the first-pass ^{99m}Tc method, the problem of right atrium—right ventricular overlap is present in exactly the same way as in ^{81m}Kr study. Using the first-pass method, however, the delineation of atrioventricular borders has to be performed on lower count rate activity distribution images.

In conclusion, this study strongly suggests evidence that the ECG-gated steady-state ^{81m}Kr method is an accurate technique for calculating the RVEF. It shows that in most of the cases, important causes of error of the method can be handled properly, and the degree of the accuracy of the technique can be estimated on an individual basis. Furthermore, this study indicates the superiority of the ^{81m}Kr method as compared with the equilibrium or first-pass ^{99m}Tc techniques for evaluating RVEF.

REFERENCES

1. Steele P, Kirch D, LeFree M, et al: Measurements of right and left ventricular ejection fraction in patients with coronary artery disease. *Chest* 70:51–56, 1976
2. 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
3. Tobinick E, Schelbert HR, Henning H: Right ventricular ejection fraction in patients with acute anterior and inferior myocardial infarction assessed by radionuclide angiography. *Circulation* 57:1078–1084, 1978
4. 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. Description, validation and findings in chronic coronary artery disease. *Circulation* 60:581–589, 1979
5. Matthay RA, Berger HJ, Like J, et al: Right and left ventricular performance in ambulatory young adults with cystic fibrosis. *Br Heart J* 43:474–480, 1980
6. 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
7. 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
8. Dotter CT, Steinberg I: The normal angiogram. In *Angiography*, Dotter, Steinberg, eds. New York, Harber and Brother, 1953, p 50
9. Arcilla RA, Tsai P, Thilenius O, et al: Angiographic method for volume estimation of right and left ventricle. *Chest* 60:446–454, 1971
10. Gentzler R, Briselli M, Gault J: Angiographic estimation of right ventricular volume in man. *Circulation* 50:324–330, 1974
11. Jaffe CC, Ellis K: Angiographic quantitation of ventricular volume, shape and mass. *Curr Probl Radiol* 4:1–55, 1974
12. Berger HJ, Matthay RA: Noninvasive radiographic assessment of cardiovascular function in acute and chronic respiratory failure. *Am J Cardiol* 47:950–962, 1981
13. Botvinick EH, Engelstad BL, Glazer HB, et al: Blood pool scintigraphy of the heart: Current status. In *Nuclear Medicine Annual*, Freeman LM, Weismann HS, eds. New York, Raven Press, 1982, pp 1–34
14. Knapp WH, Helus F, Lambrecht RM, et al: Kr-81m for determination of right ventricular ejection fraction. *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-81 m. *Clin Nucl Med* 8:257–260, 1983
16. Sugrue DD, Kamal S, Deanfield JE, et al: Assessment of right ventricular function and anatomy using peripheral vein infusion of krypton-81m. *Br J Radiol* 56:657–663, 1983
17. Horn M, Witzum K, Neveu C, et al: Krypton-81m imaging of the right ventricle. *J Nucl Med* 26:33–36, 1985
18. Botvinick E, Dunn R, Frais M, et al: The phase image: its relationship to patterns of contraction and conduction. *Circulation* 65:551–560, 1962
19. Geffers H, Adams WE, Bitter, et al: Data processing and functional imaging in radionuclide ventriculography. *Proceedings of the Fifth International Conference of Information Processing in Medical Imaging,*

Brill AB, Price RR, McLain WJ, et al., eds. ORTN/BCTIC-2, Nashville, 1977, pp. 322-332

20. Rigo P. Alderson PO, Roberson RM, et al: Measurement of aortic and mitral regurgitation by gated blood pool scans. *Circulation* 60:306-312, 1979
21. Bacharach, Green MV, Borer JS, et al: Left-ventricular peak ejection rate, filling rate, and ejection fraction: Frame rate requirements at rest and exercise: Concise communication. *J Nucl Med* 20:189-193, 1979
22. Bacharach SL, Green MV, Borer JS, et al: Beat by beat validation of ECG gating. *J Nucl Med* 21:307-313, 1980
23. Bacharach SL, Green MV, Bonow RO, et al: Measurements of ventricular fucntion by ECG-gating during atrial fibrillation. *J Nucl Med* 22:226-231, 1981
24. Brash HM, Wraith PK, Hannan WJ, et al: The influence of ectopic heart beats in gated ventricular blood-pool studies. *J Nucl Med* 21:391-393, 1980
25. Green MV, Ostrow HG, Douglas MA, et al: High temporal resolution ECG-gated scintigraphic angiocardiography. *J Nucl Med* 16:95-98, 1975
26. Green MV, Bacharach SL, Douglas MA, et al: Sources of virtual background in multi-image blood-pool studies. In *Nuclear Cardiology: Selected Computer Aspects*, New York, The Society of Nuclear Medicine, 1978, pp 99-106
27. Schneider RM, Jaszczak RJ, Coleman RE, et al: Disproportionate effects of regional hypokinesis on radionuclide ejection fraction: Compensation using attenuation-corrected ventricular volumes. *J Nucl Med* 25:747-754, 1984
28. Yeh EL, Yeh YS: Theoretical error in radionuclide ejection fraction study due to photon attenuation. *Eur J Nucl Med* 6:69-71, 1981
29. Swan HJC, Beck W: Ventricular non-mixing as a source of error in the estimation of ventricular volume by the indicator-dilution technique. *Circ Res* 8:989, 1960
30. Maseri A, Enson Y: Mixing in the right ventricle and pulmonary artery in man: evaluation of ventricular volume measurements from indicator wash-out curves. *J Clin Invest* 47:848-859, 1968
31. Knesaurek K: Dependence of distribution of short-lived tracers on decay. A non-compartimental approach. (lett) *J Nucl Med* 24:4543, 1983
32. Knesaurek K, Spaventi S: A stochastic approach to tracer kinetics. *Nuklearmedizin* 23;15-18, 1984
33. Ciofetta G, Pratt TA, Hughes JMB: Regional pulmonary perfusion assessed with continuous intravenous infusion of krypton-81m: A comparison with Tc-99m macroaggregates. *J Nucl Med* 19:1126-1130, 1978
34. Ham HR, Vandevivere J, Sergeysels R, et al: Assessment of right ventricular performance using krypton-81m: Comparison of first pass and continuous infusion method. *Proceedings of the Third World Congress of Nuclear Medicine and Biology*, Raynaud C, ed. Pergamon Press, 1982, pp 1411-1414
35. Rushmer R: Functional anatomy and control of the heart. In *Cardiovascular Dynamics, 4th ed*, Rushmer R, ed. Philadelphia, W.B. Saunders, 1976, pp 89-98