

retention by the kidney. Thus the price to pay for adjusting sodium retention is hypertension. This hypothesis is in agreement with that of Dahl *et al.*⁴

We wish to thank Mr A. Krieglger for carrying out the radioimmunoassays and Dr J. P. van der Westhuyzen, Chief Medical Superintendent of Tygerberg Hospital, for permission to publish.

REFERENCES

1. Zaaiman J du T. Pre-eklampsie, die siekte van teorieë. *S Afr Med J* 1979; **56**: 121-122.
2. Beyers AD, Spruyt LL, Seifart HI, Krieglger A, Parkin DP, Van Jaarsveld PP. Digoxin immunoreactive substance in cord blood, neonates and placental extract of mothers not on digoxin therapy. *S Afr Med J* 1983; **64**: 42.
3. Dahl LK, Knudsen KD, Iwai J. Humoral transmission of hypertension: evidence from parabiosis. *Circ Res* 1969; suppl 1, 21-33.
4. De Wardener HE, MacGregor GA. Dahl's hypothesis that a saluretic substance may be responsible for a sustained rise in arterial pressure: its possible role in essential hypertension. *Kidney Int* 1980; **18**: 1-9.
5. MacGregor GA, Fenton S, Alaghband-Zadeh J, Markandu N, Roulson JE, De Wardener HE. Evidence for a raised concentration of a circulating sodium transport inhibitor in essential hypertension. *Br Med J* 1981; **283**: 1355-1357.
6. Kramer HJ. Natriuretic hormone — a circulating inhibitor of sodium- and potassium-activated adenosine triphosphate. *Klin Wochenschr* 1981; **59**: 1225-1230.
7. Haddy FJ. Humoral factors and the sodium-potassium pump in low renin hypertension. *Klin Wochenschr* 1982; **60**: 1254-1257.
8. La Bella FS. Is there an endogenous digitalis? *Trends Pharmacol Sci* 1982; **3**: 354-355.
9. Kuhnert BR, Kuhnert PM, Murray BA, Sokol RJ. Na/K- and Mg-ATPase activity in the placenta and in maternal and cord erythrocytes of pre-eclamptic patients. *Am J Obstet Gynecol* 1977; **127**: 56-60.
10. Valdes R, Brown BA. Endogenous substance in newborn infants causing false positive digoxin measurements. *J Pediatr* 1983; **102**: 947-950.
11. Gant NF, Worley RJ. *Hypertension in Pregnancy — Concepts and Management*. New York: Appleton-Century-Crofts, 1980.
12. Assali NS, Holm LW, Parker HR. Systemic and regional hemodynamic alterations in toxemia. *Circulation* 1964; **30**: suppl 2, 53-57.

First-pass determination of the right ventricular ejection fraction using two regions of interest and the right anterior oblique view

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Summary

The right ventricular ejection fraction (RVEF) was determined on the right anterior oblique view in 9 patients during the first pass of a bolus of technetium-99m employing a gamma camera with high count-rate capability. The RVEF was calculated by using: (i) a fixed end-diastolic region of interest (ROI); and (ii) an end-diastolic and end-systolic ROI.

Because of the movement of the tricuspid plane the first of these methods often gave low values, and agreement between the first two peaks was not as good as that when the second method was used. The mean for the second method was in agreement with that in a previous study using a gated first-pass technique and two ROIs but was somewhat higher than those reported by workers using either one ROI or the anterior view.

S Afr Med J 1984; **65**: 885-888.

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Evaluation of right ventricular performance in clinical medicine is often difficult. The clinical signs of lung disease characterized by hyperinflation overlap with those of failure and hypertrophy of the right ventricle. The presence of air between the heart and the thoracic wall makes echocardiographic evaluation of the heart impossible.¹ The ECG changes due to right ventricular overload are frequently subtle in chronic obstructive pulmonary disease, and the patterns of systolic overload or right ventricular hypertrophy are rarely seen.² The estimation of chamber size from chest radiographs is difficult in the presence of overinflation of the lungs.³

In view of this, radionuclide determination of the right ventricular ejection fraction (RVEF) has been examined and found useful. Marshall *et al.*⁴ studied 34 patients with chronic obstructive airway disease and found 17 with a reduced RVEF ($38 \pm 2\%$). In addition they found a clinical application, namely a significant increase in the RVEF in the presence of therapeutic blood levels of the bronchodilator aminophylline. Winzelberg⁵ has discussed the conditions in which a decreased RVEF may be observed.

Although the ejection fraction is a well-accepted measure of ventricular function, right ventricular performance has been difficult to quantitate by conventional means.⁶ Calculation of right ventricular stroke volume on cine angiography depends on a geometrical approach and is difficult because of the complex geometry of this chamber.⁷ Since radionuclide techniques are much less dependent on geometrical factors, they represent an attractive way of determining the RVEF.^{5,8}

Although the RVEF could be obtained from a gated blood pool study at equilibrium,⁹ first-pass radionuclide cardiography is preferred by many because of temporal and

anatomical separation of radioactivity within each ventricle during the first transit.¹⁰

First-pass radionuclide studies of the right ventricle were performed by Steele *et al.*¹¹ and Tobinick *et al.*⁶ using the right anterior oblique (RAO) view with a single region of interest (ROI), while Berger *et al.*¹⁰ used the anterior view and a single ROI with a multicrystal camera. Maddahi *et al.*⁹ also used the anterior view for their first-pass study. They found it important to use separate ROIs for end-systolic and end-diastolic images because at end-systole, when the right atrium has maximal radioactivity, it is partially pulled into the end-diastolic right ventricular ROI on the anterior view.

However, the best separation between right atrium and right ventricle is obtained on the RAO view.⁶ The purpose of our study was to evaluate the influence of tricuspid movement in determining the RVEF with an end-systolic and end-diastolic ROI from the RAO view using a camera with high count-rate capability (the Elscint Apex 415 in 'fast' mode).

Methods

Nine patients who were scheduled for bone scans in the nuclear medicine clinic were studied. The 15 mCi technetium-99m (^{99m}Tc)-pyrophosphate dose for bone scanning was given as a bolus in the right medial cubital vein. The first-transit data were acquired in the RAO 15° view with a 20° caudal tilt and the patient in the supine position. This gave the best separation between the right atrium and right ventricle (Fig. 1). A super-high-sensitivity collimator (the Elscint APC 1) with a large-field-of-view camera employing a 20% window was used.

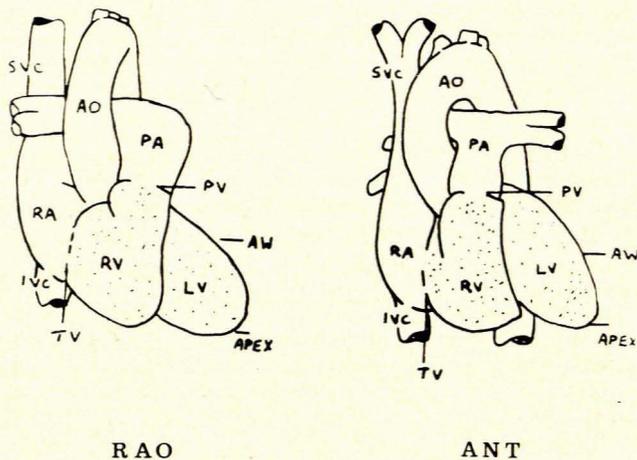


Fig. 1. Anatomical relationships between heart chambers on RAO and anterior (ANT) views.

In order to test the linearity of the camera at high count rates, samples containing known masses of pertechnetate were counted under the camera, and a curve of observed count rate against ^{99m}Tc activity was drawn.

Data were acquired for 30 seconds at 20 frames per second in a 64 x 64 byte matrix using a zoom factor of 2. On replay the images were displayed 64 at a time on a monitor, and an end-diastolic and an end-systolic image were chosen visually (Fig. 2) or by examining a time-activity curve obtained from a preliminary ROI around the right ventricle. The images between these two frames were added together two by two to improve statistics, zoomed four times, and shown in cine format to give optimal identification of the tricuspid and pulmonary valve planes. The tricuspid valve plane was well visualized by its movement towards the apex during systole. The pulmonary valve plane could be seen as a constriction or the boundary between regions

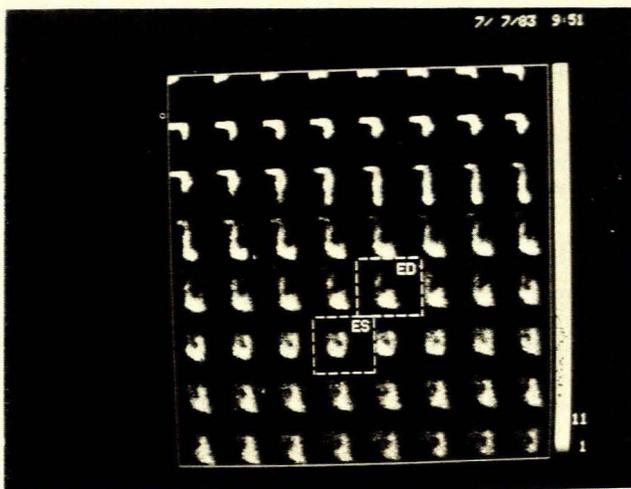


Fig. 2. First 64 images of a typical study. The framed images show an end-diastolic (ED) and an end-systolic (ES) image that could be used for drawing two ROIs. The images between these two frames may be summed two by two to yield better definition of the ventricle in the two phases.

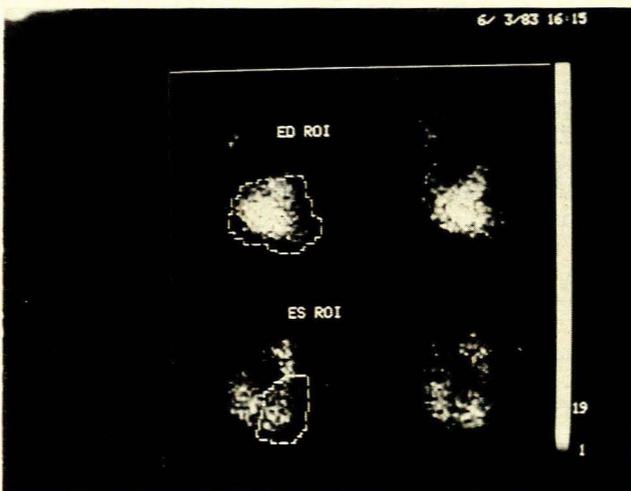


Fig. 3. End-diastolic image with an end-diastolic (ED) ROI and an end-systolic image with an end-systolic (ES) ROI.

of high activity in the pulmonary artery and regions of low activity in the right ventricle on the end-systolic image. End-diastolic and end-systolic ROIs were drawn around the right ventricle (Fig. 3). Smoothed time-activity curves of these two regions were generated from the original set of frames. The RVEF was calculated in two ways: (i) by using the maxima and subsequent minima on the end-diastolic ROI curve (i.e. a single ROI); and (ii) by using the maxima on the end-diastolic ROI curve and the subsequent minima on the end-systolic ROI curve (points X and Y in Fig. 4) (i.e. utilizing two ROIs).

Even if more than two peaks were present analysis was limited to the first and second peaks, since the third and later peaks were generally less well defined and identification of the end-diastolic and end-systolic points was not so accurate. Counts were also determined in a background area around the perimeter of the apex of the ventricle.

A time-activity curve was also drawn using a small ROI around the superior vena cava (SVC) in order to assess the quality of the bolus. The transit time of the bolus in the SVC was calculated by measuring the full width of the time-activity curve at the 0,369 level of the maximum.¹²

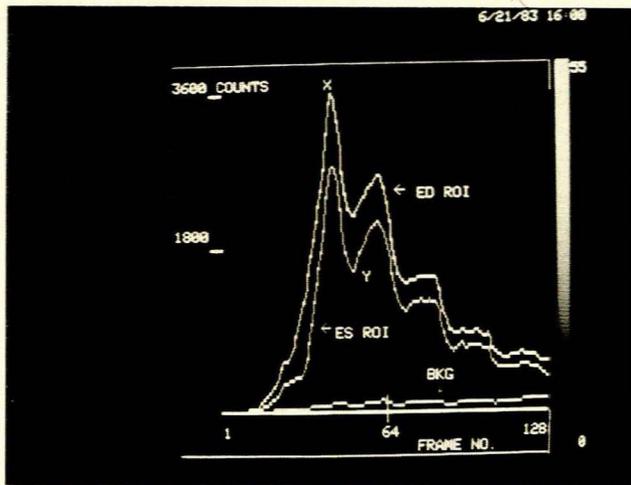


Fig. 4. Time-activity curves obtained from end-diastolic (ED) and end-systolic (ES) ROIs. The RVEF is calculated from points X and Y. Curve BKG indicates background from an area around the perimeter of the ventricular apex, normalized to end-diastolic area.

Results

The maximum count rate observed during acquisition in the field of view of the camera was typically 130 000 counts per second. At this count rate the camera showed a 15% loss of counts in the fast mode using a 20% window. The transit time of the bolus in the SVC was less than 1,7 seconds in all cases.

Ejection fractions calculated by the two methods are given in Table I for the first and second peaks on the time-activity curve. For each method the absolute percentage difference from the mean obtained from the first and second peaks is given. The mean ejection fraction (\pm SE) obtained using a single ROI was $34,1 \pm 2,5\%$ (range 22,9 - 51,2%), while the value obtained when both an end-diastolic and an end-systolic ROI were used was $63,9 \pm 1,84\%$ (range 54,1 - 72,0%).

Discussion

Count rates of the order of 130 000 counts per second over the full-field view were obtained using a super-high-sensitivity collimator giving on the average 3,7 K counts in the end-diastolic ROI at the first peak and 1,3 K counts at the subsequent minimum. This gives a typical standard error of 1,1 in the ejection fraction percentage. At 130 000 observed counts per second a 15% loss in counts is present. However, since the total counts in the field of view during the period of analysis were constant to within 12%, dead-time did not introduce any significant error.

The right ventricle is described by Strauss *et al.*¹³ as follows: 'The pyramidal shaped right ventricle has its base situated at the tricuspid valve plane. In a 70 kg adult, end-diastolic volume of the chamber is approximately 165 ml. During ventricular systole, the tricuspid valve plane moves towards the left ventricle while the apex of the right ventricle moves slightly towards the base of the right ventricle. The pulmonary outflow tract contracts in some patients.' The movement of the tricuspid valve plane is often seen in gated blood pool scans from the anterior view.

When one ROI is used, the right atrium is therefore drawn into this region at end-systole to a variable extent (Fig. 5). Accordingly the end-systolic counts become falsely high with a concomitant decrease in the ejection fraction,

$$EF = \left[1 - \frac{ES}{ED} \right] \times 100,$$

where EF = the ejection fraction, ES = end-systolic counts, and ED = end-diastolic counts.

It is possible that a portion of the right atrium is also included when the end-diastolic ROI is drawn; this would falsely elevate the ejection fraction. However, the right atrial contribution to the end-diastolic ROI would be much smaller than that to the end-systolic ROI.

When two ROIs were used the mean RVEF was therefore significantly higher and showed less fluctuation between the two values obtained from the first two peaks. Although the use of two ROIs has been mentioned in the literature,^{9,14} its importance is

TABLE I. RIGHT VENTRICULAR EJECTION FRACTIONS

Patient	RVEF from ED ROI only			RVEF from both ED and ES ROIs		
	1st peak	2nd peak	Absolute difference (%)	1st peak	2nd peak	Absolute difference (%)
1	32,0	43,8	31,0	57,0	58,4	2,4
2	27,7	37,7	30,6	59,2	65,3	9,8
3	51,2	48,9	4,6	65,0	61,7	5,2
4	26,0	41,0	44,8	68,8	66,6	3,2
5	30,7	29,8	3,0	67,5	66,6	1,3
6	22,9	29,7	25,9	68,8	67,7	1,6
7	30,1	32,9	8,9	54,1	51,5	4,9
8	36,7	33,9	7,9	67,4	63,7	5,6
9	26,0	32,7	22,8	72,0	68,8	4,5
Mean RVEF (\pm SE)	34,1 \pm 2,5%			63,9 \pm 1,84%		
Mean absolute difference between peaks	19,9%			4,3%		

ED = end diastolic; ES = end-systolic.

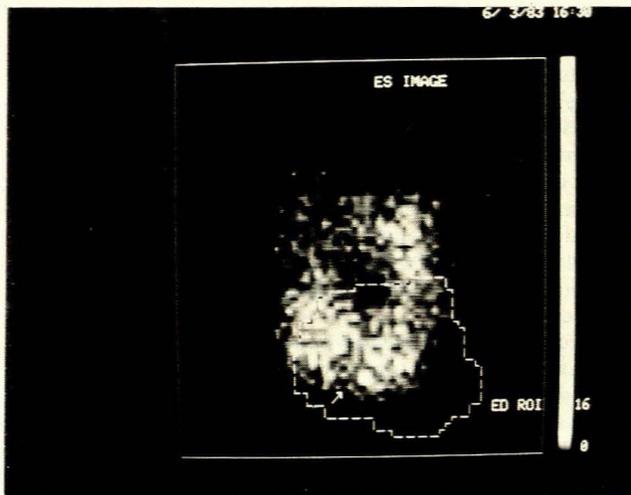


Fig. 5. End-systolic image with end-diastolic (ED) ROI superimposed. The arrow marks the tricuspid plane. A large portion of the right atrium is included in the end-diastolic ROI.

often not realized. For example, in a recent publication¹⁵ a protocol for calculating the RVEF using only a single ROI was recommended.

When two ROIs were used, we believe that the first peak gave the most reliable values since it had the highest counts, was generally well defined, and was free of any significant background contribution. Background subtraction made no significant difference to the ejection fraction obtained from the first peak, as might be expected. Although the average ejection fraction derived from the second peak was not significantly different from that derived from the first, in 2 patients background subtraction yielded values which differed significantly from the first, suggesting that in these cases the background ROI was not truly representative of the right ventricle. On the other hand, in 4 patients the third peak yielded ejection fraction values significantly different from the first two, with or without background subtraction. This is due to the fact that the third peak is not as well defined as the first, so that the end-diastolic and end-systolic points are not so easily identified.

Accordingly, in this study determination of the RVEF was limited to the first two cycles on the time-activity curve without background correction, since during this time background activity makes a negligible contribution. Using a camera with high count-rate capability this is preferable to applying a background correction, since adequate statistics can be obtained using only two cycles and the possibility of obtaining false values due to choice of an unrepresentative background area is avoided.

Mena *et al.*¹² reported that a transit time of more than 4 seconds resulted in inability to process first-pass cardiac studies in 85% of cases. However, this included processing of left ventricle data, in which case more stringent requirements are placed on the bolus quality owing to lengthening of the bolus time in the lungs. Although the transit times in the present series were less than 1.7 seconds, in patients with severely depressed right ventricular function or tricuspid incompetence it may be difficult to obtain an adequate bolus. For determination of the RVEF the requirements are that enough counts are obtained in the first two peaks used for analysis to yield adequate statistics

and that no appreciable activity should appear in the lungs or left ventricle during this time. Although these requirements were fulfilled in the present study, the extent to which they are met by an increased bolus time should be investigated.

The mean RVEF in this study ($63.9 \pm 1.8\%$) is in agreement with a value quoted previously,^{14,16} viz. $60 \pm 7\%$; these workers also used two ROIs on the RAO view but employed a gated first-pass technique. It is, however, somewhat higher than reported by most other workers,^{6,9,11} who either used one ROI^{6,11} or used the anterior view.⁹ The contribution of the right atrium in the anterior view is probably higher than on the RAO view since the latter gives a better separation between the right atrium and the right ventricle. The RVEF will therefore be higher in the latter case because of a smaller contribution during end-systole. As shown above, using a single ROI also yields a lower RVEF.

The identification of the pulmonary and tricuspid valve planes is dependent on the operator to a certain extent. Since the main purpose of this project was to investigate the effect of using two ROIs as opposed to a single ROI on the RAO view, rigorous inter- and intra-observer variability studies were not performed. Such studies may be performed on a further series of patients with suspected abnormalities of the right side of the heart in order to validate the technique in patients with normal and abnormal right ventricular function. In such a series one could justifiably use a larger dose and employ a higher resolution collimator. This should improve identification of the pulmonary and tricuspid valve planes.

REFERENCES

- Ball WC, Summer WR. Clinical manifestations and diagnosis of pulmonary diseases. In: Harvey A McG, Richard JJ, McKusick VA, Owens AH, Ross RS, eds. *The Principles and Practice of Medicine*. 20th ed. New York: Appleton-Century-Crofts, 1976: 359-396.
- Schaeffer JW, Pryor R. Pseudo left axis deviation and the $S_1S_2S_3$ syndrome in chronic airway obstruction. *Chest* 1977; **71**: 453-455.
- Murphy ML, Boger J, Adamson JS *et al.* Evaluation of cardiac size and pulmonary emphysema. *Chest* 1977; **71**: 712-717.
- Marshall RC, Harvey MD, Berger J *et al.* Quantitative radionuclide angiography for assessment of left and right ventricular performance. In: Lieberman DE, ed. *Computer Methods: The Fundamentals of Nuclear Medicine*. St Louis: CV Mosby, 1977: 162-175.
- Winzelberg GG. Diminished right ventricular ejection fraction on radionuclide cardiography. *Semin Nucl Med* 1982; **12**: 304-305.
- Tobinck 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* 1978; **57**: 1078-1084.
- Arcilla RA, Tsai P, Thilenius O, Ranniger K. Angiographic method for volume estimation of right and left ventricles. *Chest* 1971; **60**: 446-454.
- Strauss HW, Pitt B. Evaluation of cardiac function and structure with radioactive tracer techniques. *Circulation* 1978; **57**: 645-654.
- 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* 1979; **60**: 581-589.
- Berger HJ, Zaret BL. Use of radionuclides to evaluate myocardial structure and function. In: Stollerman GH, ed. *Advances in Internal Medicine*. Chicago: Year Book Medical Publishers, 1980: 239-275.
- Steele P, Kirch D, LeFree M, Battock D. Measurement of right and left ventricular ejection fraction by radionuclide angiography in coronary artery disease. *Chest* 1976; **70**: 51-56.
- Mena I, Oren V, Bennett LR, Uszler JM. First-pass radionuclide ventriculography performed with the Anger camera at rest and during exercise. In: *Medical Radionuclide Imaging 1980*, vol. II. Vienna: International Atomic Energy Agency, 1981: 219-229.
- Strauss HW, McKusick KA, Boucher CA, Bingham JB, Pohost GM. Of lines and laces — the eighth anniversary of the gated blood pool scan. *Semin Nucl Med* 1979; **9**: 296-309.
- McKusick KA, Bingham JB, Pohost GM, Strauss HW. The gated first pass radionuclide angiogram: a method for measurement of right ventricular ejection fraction (Abstract). *Circulation* 1978; **58**: suppl II, 130.
- Klipper SA, Dillon W, Ashburn W. First pass radionuclide angiography. *Software* 1982; **9**: 3rd quarter, 2-8.
- Liberthson RR, Boucher CA, Strauss HW, Dinsmore RE, McKusick KA, Pohost GM. Right ventricular function in adult atrial septal defect. *Am J Cardiol* 1981; **47**: 56-60.