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Left ventricular volume and ejection fraction determined by gated blood pool emission tomography

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SUMMARY Electrocardiogram gated single photon emission computed tomography of the intracardiac blood pools is a recent development that involves the acquisition of images in multiple projections after in vivo erythrocyte labelling with technetium-99m and reconstruction of these images into tomographic sections in any desired plane. The technique was used in 25 subjects to measure left ventricular volume, by summing the areas of the ventricle in each of the tomographic sections, and the results compared with those using a counts based (non-geometric) technique from planar radionuclide ventriculography. Endocardium was defined with the aid of a contour at 43% of maximum left ventricular counts, and this contour was validated for a left ventricular phantom. Correlation between tomographic and counts based left ventricular volume was close. Similarly, ejection fraction correlated well. The technique is therefore an accurate method for determining left ventricular volume and ejection fraction, avoiding the assumptions about shape made by other geometric methods.

The size of the cardiac shadow on a chest *x* ray film is one of the most commonly used indices of cardiac function since it reflects principally the volume of the cardiac chambers. Because of the complex geometry of the heart, however, it is difficult to determine these volumes accurately. The recent development of the technique of electrocardiogram gated blood pool single photon emission computed tomography provides a geometric method for determining left ventricular volume, making no assumptions about the shape of the ventricle, and therefore promises to provide an accurate, relatively non-invasive measurement of left ventricular volume. The purpose of this study was to establish the place of the technique by comparison with a counts based radionuclide method for volume determination.

Patients and methods

GATED BLOOD POOL EMISSION TOMOGRAPHY

After in vivo erythrocyte labelling with 740 MBq (20 mCi) of technetium-99m sodium pertechnetate, the intracardiac blood pools were imaged using an IGE 400 Autotune ZS rotating gammacamera and Star computer. Thirty two views were acquired rotating from right anterior oblique through left anterior oblique to left posterior oblique, and each view was acquired for one minute. Within each view two frames were acquired by electrocardiogram gating, at end diastole and at end systole, and each frame was 100 ms duration. The time of end systole was determined from a planar radionuclide ventriculogram as described below. The two sets of planar images were reconstructed into end diastolic and end systolic transaxial sections by back projection using a Ramp-Hamming filter with cutoff frequency 0·5,[1] and from these, oblique sections orthogonal to the long axis of the left ventricle were constructed. Figure 1 shows the planes of the oblique sections. This protocol typically acquired 3 million counts in the end diastolic planar images, of which 65 000 were in the left ventricle. Left ventricular volume was determined from those horizontal long axis sections that contained part of the ventricle (typically eight sections), and in these left ventricular endocardium was defined manually with the aid of a contour at 43% of maximum counts within the whole ventricle. The sum of the

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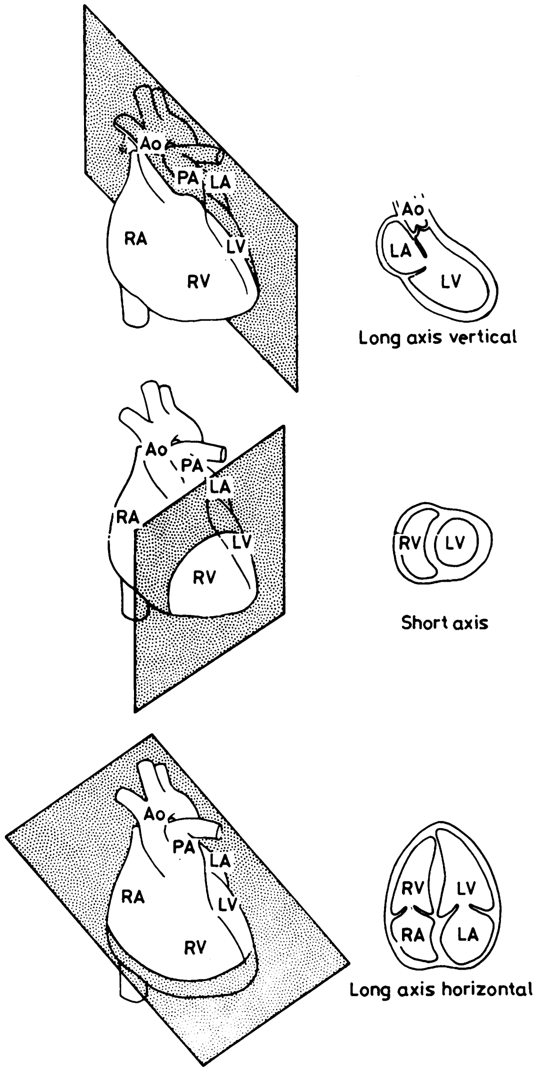

Fig. 1 *Diagram showing planes orthogonal to the long axis of the left ventricle used in the reconstruction of oblique blood pool sections.*

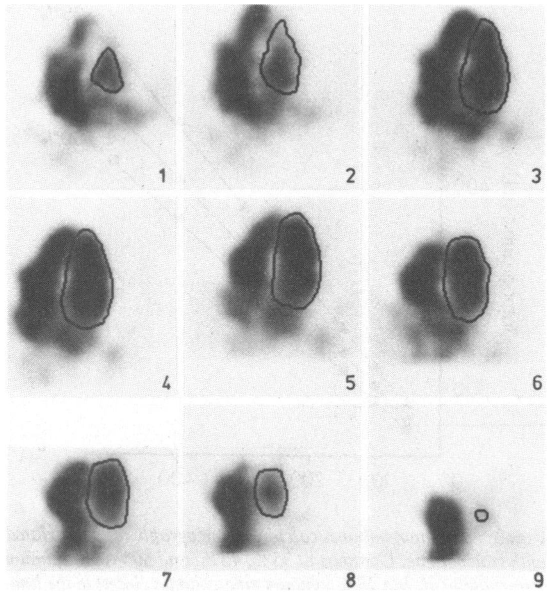

Fig. 2 *Nine horizontal long axis sections at end diastole cutting the left ventricle from inferior (1) to anterior (9) walls. The contours drawn define the left ventricular cavity, and volume is calculated from the sum of these areas (in this case 168 ml).*

areas of these left ventricular sections was taken to be the left ventricular volume, having corrected for the known voxel size of the imaging system (0·26 cm^3). A typical case is seen in Fig. 2, in which there are nine sections containing parts of the ventricle, and volume is calculated from the sum of the regions of interest shown.

PLANAR RADIONUCLIDE VENTRICULOGRAPHY

Planar equilibrium radionuclide ventriculography was performed in the left anterior oblique projection that best visualised the interventricular septum, and in addition 20° of caudal tilt were applied to minimise overlap between the left atrium and ventricle. Twenty four frames per cardiac cycle were acquired with electrocardiogram gating, and acquisition was for five minutes, providing approximately the same number of counts within the left ventricle at end diastole as for the tomographic study. Left ventricular volume was determined by an adaptation of the method of Links *et al*[2] as follows. Immediately after the acquisition a skin marker was placed over the centre of the left ventricular image, and another image was acquired at right angles (left posterior oblique) in order to measure the depth of the left ventricle. A 10 ml sample of blood was also taken and counted under the camera to determine the specific activity of the blood. After smoothing and background subtraction, left ventricular volume could be determined from the number of counts within the left ventricle using the specific activity of the blood and the depth of the left ventricle and assuming a linear attenuation coefficient of 0·10 cm^{-1}.[3]

PHANTOM STUDIES

To assess the accuracy of the different methods of volume determination, a phantom was used which consisted of a pear shaped balloon filled with a known volume of normal saline with a specific activity of 0·15 MBq/ml and suspended at a depth of 10 cm within a tank of elliptical cross section. The tank was filled

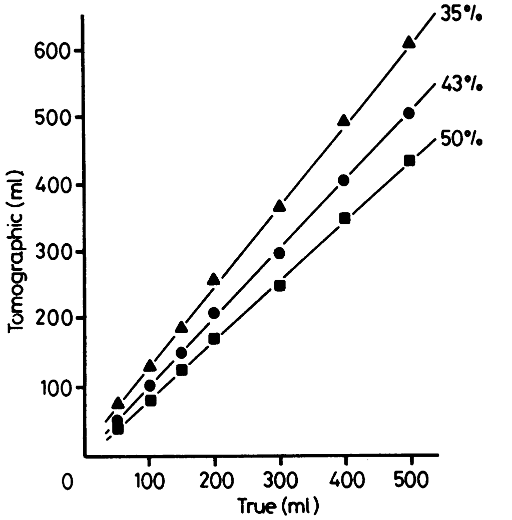

Fig. 3 *Phantom volumes calculated tomographically correlated with true volume. Contours at 35%, 43%, and 50% of maximum counts are used, but 43% contours give volumes closest to the line of identity. The linear regression equations are: 50% contour, y=1·9x+12, r=1·000: 43% contour, y=1·01x+0, r=1·000: 35% contour, y=0·88x−9, r=0·999.*

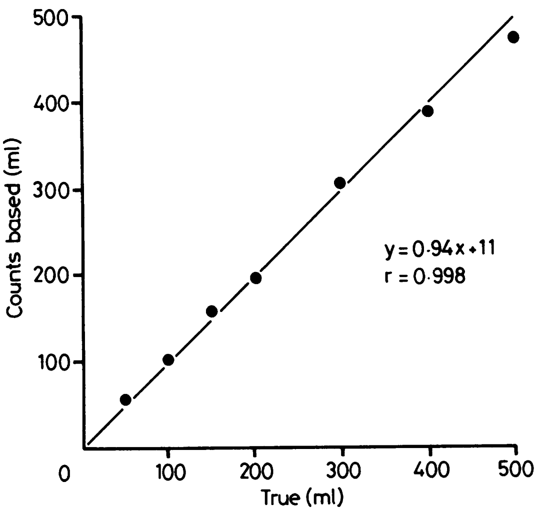

Fig. 4 *Phantom volumes calculated by a counts based method from a planar image.*

with saline of specific activity 0·015 MBq/ml, and the design was intended to mimic a labelled left ventricular cavity within the thorax surrounded by background activity. The volume of the phantom was determined either by summing the areas of the tomographic sections or from the number of counts within a single planar image after correction for background activity and for attenuation.

STUDY POPULATION

A total of 25 patients was studied, of whom six had no demonstrable cardiac abnormality, 16 coronary artery disease (10 with previous infarction), one valvar heart disease, and two congestive cardiomyopathy.

Results

PHANTOM EXPERIMENTS

Figure 3 shows the results of the tomographic method for determining volume, and it can be seen that there is an excellent linear correlation over a wide range of volumes. The value obtained is highly dependant upon the contour used to define the edge of each section, but a contour at 43% of maximum counts within the phantom gives a regression line closest to the line of identity. For this reason a 43% contour was used in the subsequent determination of left ventricular volume. For the sake of brevity the detailed results are not shown here, but the effect of different filters in the reconstruction of the transaxial sections was studied, and as expected filters with heavier smoothing gave higher volumes and vice versa. For instance, filtering with a cutoff frequency of 0·25 increased calculated volumes by 3% and with a cutoff frequency of 0·75 decreased volumes by 3%.

Figure 4 shows the results of the planar counts based method, and again there is an excellent linear correlation.

LEFT VENTRICULAR VOLUMES

Figure 5 shows typical mid-cavity blood pool sections in one of the normal subjects to illustrate the quality of the images that was consistently obtained.

Figure 6 correlates the tomographic and the counts based methods for the determination of left ventricular volume, and both end diastolic and end systolic volumes are included. The individual regression equations for each set of points are shown, and since the difference between these is not statistically significant ($t=0·14$, $p>0·1$) a single regression line has been drawn through all the points. Standard errors of the slope and intercept are 0·0032 and 6·7 respectively, giving 95% confidence limits of 0·76 to 0·96 for the slope and of 12 to 34 for the intercept. The line of identity lies only just outside these limits. From visual inspection of the data, it appears that the slope is less than 1 either because low volumes are overestimated slightly by the tomographic method or because they are underestimated by the counts based method. This is discussed below.

Given both end diastolic and end systolic volumes, it is possible to calculate ejection fraction, and Figure 7 correlates tomographic ejection fraction with that from the planar study. Again a good correlation is obtained, with a regression line not significantly dif-

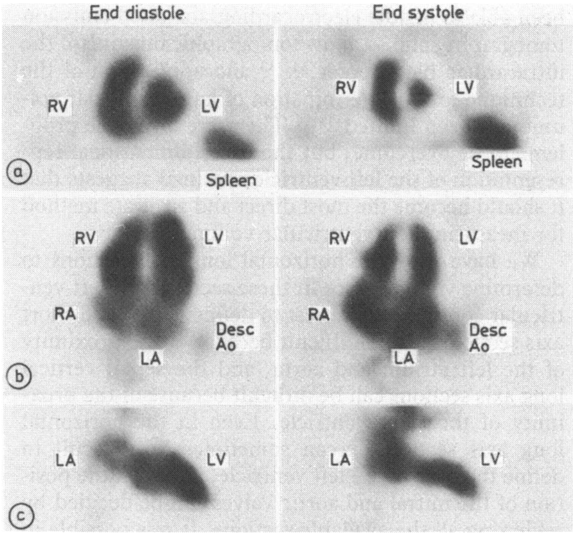

Fig. 5 *(a) Short axis, (b) horizontal long axis, and (c) vertical long axis electrocardiogram gated blood pool sections in a normal subject. RA, right atrium; LA, left atrium; RV, right ventricle; LV, left ventricle; Desc Ao, descending aorta.*

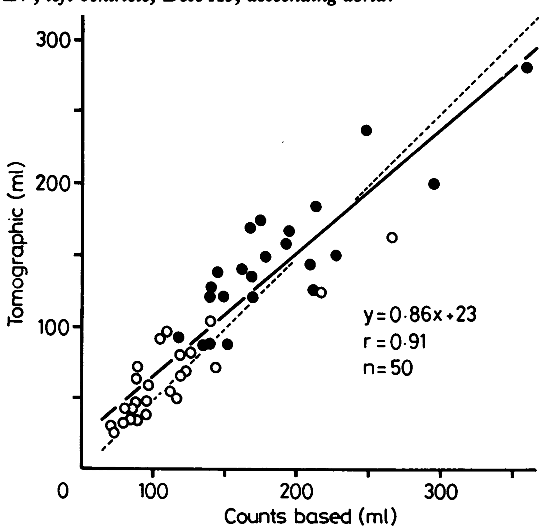

Fig. 6 *Left ventricular volumes calculated tomographically correlated with counts based volumes from a planar radionuclide ventriculogram. (●) end diastolic volumes, (○) end systolic volumes. The dashed line is the line of identity and the solid line the linear regression line through all the points. The individual regression lines are: end diastole, y=0·71x+55 (r=0·85), end systole, y=0·71x+22 (r=0·88).*

ferent from the line of identity.

Discussion

INVASIVE TECHNIQUES

The importance and difficulty of determining left ventricular volume can be judged by the length of its history, which goes back at least 70 years.[4] Methods based on *x* ray contrast ventriculography have been extensively studied and rely on measurements made from either a biplane or a single plane ventriculogram and assume that the left ventricle is the shape of an ellipsoid or of a prolate spheroid respectively. The method first proposed by Chapman *et al*[5] is very similar to that used in this study in that the areas of sections through the left ventricle are summed. This method, however, was too tedious for routine use and was eclipsed by the methods of Arvidsson[6] and Dodge *et al*[7] in which the minor axes of the ellipsoid are either measured directly or calculated from the projected area of the left ventricle. Adaptation of the technique for single plane ventriculograms[8,9] and for oblique biplane ventriculograms[10] has been successful, and the subject has been well reviewed.[11,12]

The major problem of all these methods, however, is that it is necessary to assume a shape for the left ventricle, and this assumption is always incorrect to a greater or lesser extent. Volumes calculated by these methods must therefore be suspect, especially for ventricles of irregular shape. In addition, the effect of rapid injection of contrast medium into the left ventricle is unknown, and there is dispute whether it affects volume[12] or not.[13] Reason predicts that there will be a change in volume over the few contractions after injection, which will depend on the volume and rate of injection and maybe on the timing of injection with respect to the cardiac cycle.

RADIONUCLIDE TECHNIQUES

The above techniques can be applied to a radionuclide

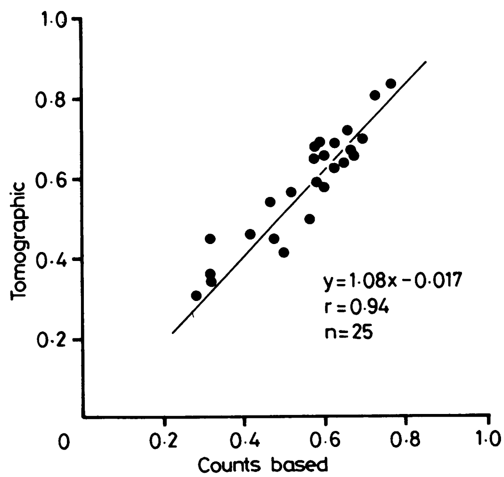

Fig. 7 *Tomographic left ventricular ejection fraction correlated with the counts based ejection fraction from a planar radionuclide ventriculogram. The linear regression line is shown.*

ventriculogram,[14 15] but the relatively poor spatial resolution dictates that non-geometric methods will be better for planar radionuclide studies.[16] Left ventricular volume can be calculated non-geometrically either from a first pass radionuclide ventriculogram,[17-19] or from an equilibrium radionuclide ventriculogram.[20 21] The equilibrium techniques equate counts within the left ventricular image to volume and so make no assumption about shape, but they do suffer from the problem of attenuation of counts by surrounding structures.[22 23] This problem can be overcome in different ways,[2 24 25] and we use a modification of the technique of Links *et al*,[2] in which attenuation is estimated in each patient by measuring the depth of the left ventricle and an attenuation coefficient is assumed. This method has been shown to correlate closely with volumes determined by single plane *x* ray contrast ventriculography. In contrast to Links *et al*, however, we used an attenuation coefficient of 0·10 cm^{-1}, which is closer to reality than the theoretical value for water of 0·15 cm^{-1},[3] which pertains to attenuation of a narrow beam of photons by an infinitely thin section of water. Unfortunately, attenuation varies between individuals, and this is the most important source of error in this technique.

ECHOCARDIOGRAPHIC TECHNIQUES

Planar radionuclide methods for the determination of left ventricular volume overcome the geometric problems of contrast ventriculography by equating counts to volume, but it is also possible to overcome them by making multiple measurements in three dimensions. The tomographic method used in this paper is such a method, and its advantage is that it makes no assumptions about the shape of the left ventricle, except that it can be represented by the sum of a series of tomographic sections. Cross sectional echocardiography can also image multiple sections through the heart and has been used to measure left ventricular volume.[26 27] Unfortunately, this is of limited applicability at present for several reasons. Firstly, a complex mechanical arm is required for the ultrasound transducer in order to record the position of each section as it is imaged. Secondly, the short axis sections generated are not parallel but pivot around the transducer head, and, thirdly, it is not always possible to image the whole endocardial surface, especially at the apex. Simpler echocardiographic methods are available,[28] but they all make some assumption about ventricular geometry.

GATED BLOOD POOL EMISSION TOMOGRAPHY

Single photon emission computed tomography is not a new technique,[29] and it has been used before to determine organ volume.[30] It is only recently, however, that commercially available computers have been able to handle electrocardiogram gated emission tomography, and so allow tomographic imaging of the intracardiac blood pools,[31-33] and application of the technique to the determination of left ventricular volume has been limited.[33 34] There are of course problems to be overcome, but the three dimensional representation of the left ventricle obtained suggests that it should become the most direct and accurate method for measuring left ventricular volume.

We have used the horizontal long axis sections to determine volume since in these sections the left ventricular contours are easiest to define. The basal short axis sections can be difficult because of the proximity of the left atrium and aorta, and the septal vertical long axis sections can be difficult because of the proximity of the right ventricle. Even in the horizontal long axis sections it can sometimes be difficult to define the base of the left ventricle, although the position of the mitral and aortic valves can be decided by reviewing all the available sections. It was possible in all our patients to calculate left ventricular volume, whereas Nixon *et al* found only nine of 16 subjects suitable for echocardiographic volume measurements.[27]

A second problem is the choice of contour to use for definition of the endocardium. The phantom experiments show that for the system of acquisition and processing used here 43% of maximum counts within the phantom gives best results. This value will, however, change for different processing methods, and in particular we have shown how back projection, using a filter that produces heavier smoothing, leads to apparently greater volumes. Tauxe *et al* found a 45% contour to give the best results for volumes less than 1 litre,[30] but it is not surprising that the best contour will vary with the processing system used. It will also vary with volume, and below approximately 100 ml a higher percentage contour may be needed since the relatively poor spatial resolution of emission tomography "smears out" the images and in particular makes small objects appear larger.[35] This most likely explains why the tomographic volumes at end systole are slightly larger than the counts based volumes, whereas there is much better agreement at end diastole.

It has also been assumed that the best contour to use is independent of scattering, and, although Tauxe *et al* found different scattering media around a phantom to make little difference to calculated volume,[30] our experience is different. Our phantom was surrounded by water which will have different scattering properties from the soft tissue, lung, and bone surrounding the left ventricle, and this may have some effect. In addition, the best contour to use may vary with the shape of the object studied.[30]

Finally, it is relevant to consider whether 100 ms frames are sufficiently short to determine the volume of a moving object accurately. Hamilton *et al* have shown that in planar radionuclide ventriculography, at 100 ms per frame, end diastolic volume is underestimated and end systolic volume is overestimated by approximately 6%.[36] This, however, is for a counts based method, and for a geometric tomographic method the errors will not be so great, particularly at end diastole. This problem could be overcome by reducing frame duration, but this would mean longer acquisition times for an equivalent number of counts.

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