DIAGNOSTIC NUCLEAR MEDICINE

Recirculation Subtraction for Analysis of Left-to-Right Cardiac Shunts: Concise Communication

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The object of this study is to improve the techniques for describing the lung dilution curve for shunt quantification by separating the effects of systemic recirculation on the curve from those of direct shunt return.

The time of the systemic recirculation peak was estimated by determination of transit times from the right and left ventricles and lung. A gamma variate fit based on the distribution of points at that segment was applied to the recirculation curve and subtracted from the original lung dilution curve. Similar gamma variate fitting was performed for both primary and shunt curves. Rather than fitting the gamma variate of the shunt curve by the leading edge only, a larger portion could now be used since the trailing edge of the curve is clearer following recirculation subtraction. The algorithm is completely automatic, requiring no operator intervention or selection of curve-fitting regions. The correlation coefficient for comparison of the dilution-curve analysis with oximetry determinations was 0.92 in a series of 29 patients.

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The analysis of time-activity curves from indicator dilution has been used for cardiac shunts for over 20 yr (*1–5*). Most of the techniques now being used involve recording the dilution curve from the lung field following a compact bolus injection, then measuring the departure of the recorded curve from an expected exponential clearance (*6*) or gamma variate fit (*7*) that would indicate normal blood flow through the lung. When a left-to-right cardiac shunt occurs, the trailing edge of the primary dilution curve is distorted, with the relative area of the distortion dependent upon the magnitude of the shunt.

Although distortion may readily be observed in large shunts, in many cases it may be obscured by activity returning by systemic recirculation. The object of this study is to improve the quantification of the shunt curve by separating the effects of recirculation from those of direct shunt return.

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MATERIALS AND METHODS

From a group of 51 patients referred to the section of pediatric cardiology for shunt evaluation, 29 were selected for comparison of results obtained by the oximetry technique with those of various curve-analysis algorithms applied to radionuclide techniques. The remaining 22 patients were primarily normal and did not undergo cardiac catheterization and oximetry for shunt evaluation. Hydrogen electrode measurements were not available at this time. The patients' ages ranged from 3 to 54 yr. For adults a dose of 20 mCi of technetium-99m-labeled human serum albumin was injected as a bolus into an antecubital vein and flushed manually into the circulation with 20 ml normal saline in 3 sec (*8*). For patients under 16 yr of age, the doses were reduced to 200 μCi/kg.

For precordial recording of the radionuclide passage,

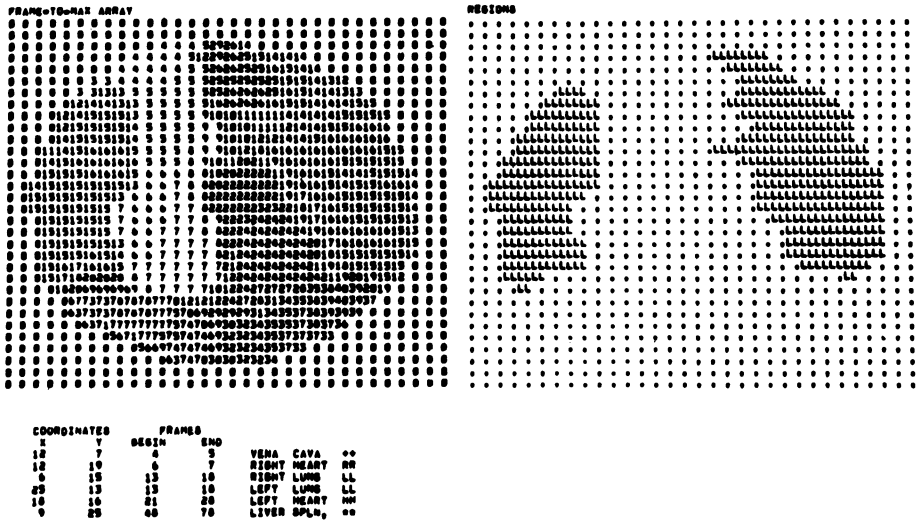

FIG. 1. Parametric scan of thorax, showing lung fields identified by pixels displaying number of frame in which maximum count was recorded. The lung regions (13–18) should reach a maximum at the times following the right-heart regions (6–7) and before the left-heart regions (21–28).

the subjects were viewed with a portable scintillation camera with a medium-sensitivity, low-energy collimator (*9*). The camera head was positioned anteriorly over the patient's body and orthogonal to both the longitudinal and horizontal axes. The camera output was recorded on magnetic tape in 32 × 32-byte matrix mode, recorded every 0.05 sec for analysis on an off-line computer. Later analysis has been based on list-mode acquisition and framing at intervals of 0.15–0.5 sec. These rates are adjusted automatically, dependent upon the time of passage from the right to the left ventricle (*10*).

Pulmonary dilution curves were recorded from the right and left lung regions selected automatically by a technique previously described (*10,11*). In the location of regions, the cardiac chambers and lung areas are delineated by a functional image that plots the frame number in which the maximum count of each pixel is recorded (Fig. 1, left). By following the time course of the passage of the radioactive material through the various chambers, the right heart and lung regions may be identified as shown in Fig. 1, right.

The dilution curves from these regions were analyzed by the technique described by Maltz and Treves (*12*). A gamma variate function is fitted to the primary dilution curve A as shown in Fig. 2. This function is subtracted from the original data, and a second gamma variate function is fitted to the initial segment of the curve of the difference, as described by area B. The difference curve is related to the reappearance of radioactivity in the lung field which, if it occurs in the early phase, would indicate a left-to-right shunt. The ratio of area B to area A is the shunt ratio, and thus the relationship of the pulmonary flow $\dot{Q}p$ to the systemic flow $\dot{Q}s$ may be expressed by the ratio of the area of the primary curve A to the difference in area between curve A and derived curve B (*12*).

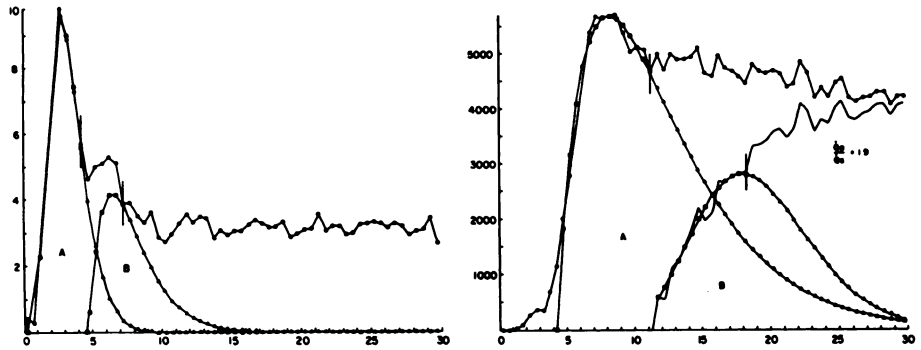

FIG. 2. (Left) dilution (time-activity) curve recorded from lung of subject with shunt, showing rapid clearance and obvious shunt contribution. Analysis was successful without recirculation subtraction. (Right) dilution curve recorded from lung of subject with large shunt, showing extremely slow clearance because of continual reinfusion. Arbitrary selection of inflection point.

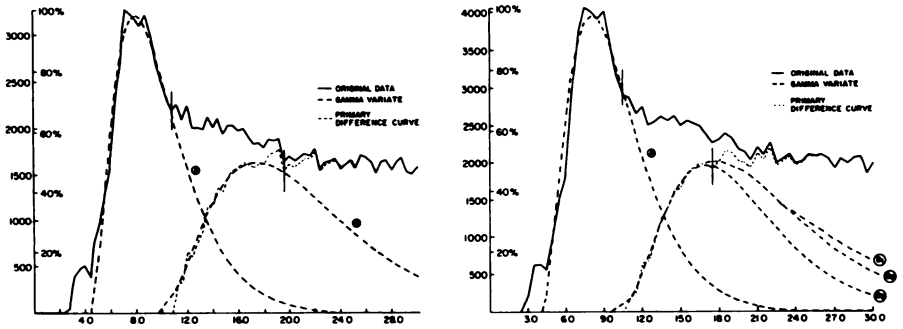

FIG. 3. (Left) typical difference curve derived from gamma variate fit of pulmonary curve and original data. (Right) various gamma variate fittings of above curve based on arbitrary criteria. Variations in $\dot{Q}p/\dot{Q}s$ values with different criteria as shown exceed 80%.

EFFECT OF RECIRCULATION

The conventional analysis, as illustrated in Fig. 2, can be performed quite easily when the shunt region is well delineated. However, this analysis ignores the effects of systemic recirculation which, if bronchial collateral circulation is present, can occur very rapidly. Such recirculation would be added to area B and, thus, give a falsely high $\dot{Q}p/\dot{Q}s$ ratio.

In the usual clinical measurement, most of the pulmonary dilution curves do not present the discrete separation shown in Fig. 2; more commonly they show a more gradual reappearance, as shown in Fig. 3, left. This curve shows not only an influence of recirculation on the descending part of the curve, but also shows that the identification of the area to be fitted by the second gamma variate may be extremely arbitrary, involving operator intervention and additional criteria (*13*). Figure 3, right shows various gamma variate fittings of the secondary curve based on arbitrary fitting criteria. With large shunt areas, resultant variations of the $\dot{Q}p/\dot{Q}s$ value of over 80% are observed.

GAMMA VARIATE FITTING OF THE RECIRCULATION CURVE

In some cases, as in Fig. 4, the recirculation curve is obvious, and in those instances a third gamma variate function representing systemic recirculation can readily be fitted to that region and the recirculation contribution subtracted from the difference curve before the secondary curve B is fitted. In each case, the point of origin of the gamma variate is taken as the first point of departure of the pulmonary fitted curve from the original data.

However, when the recirculation is not obvious (which occurs in about two-thirds of the patients), a search must be made for the time of recirculation based on measurements of the transit times between various heart chambers and the lung. An approximate recirculation time is estimated by measuring the peak-to-peak times between various chambers—namely, right heart to lung, right heart to left heart, lung to left heart—and multiplying this time by an appropriate integer. The time at maximum of each dilution curve is identified by determining the focus of a parabolic fit of the peak of the curve. In most cases, it has been found that the pulmonary transit time is equal to approximately half of the entire circulation time. Since the pulmonary transit time is approximately twice the transit time between the right heart and the lung (*14*), the time of recirculation has been derived from the measure of peak-to-peak times between these two chambers.

Once the approximate circulation time is determined, a search for a peak time is made on the pulmonary dilution curve at times between 75% and 125% of this value, in order to select the best peak area for a gamma variate fit. The transition from the primary gamma variate fit and subtraction from the original data is shown in Fig. 5A, left; selection of recirculation curve and subtraction in Fig. 5A, right; and fit of the resultant curve for shunt quantification in Fig. 5B, left.

In some cases (Fig. 6), a definite recirculation curve cannot be determined because no area of concavity can be found in the area scanned for recirculation. When this occurs, a point on the difference curve is selected at a value of half the circulation time between lung peaks, and clearance is assumed to follow the same time constant as the primary curve from that point on.

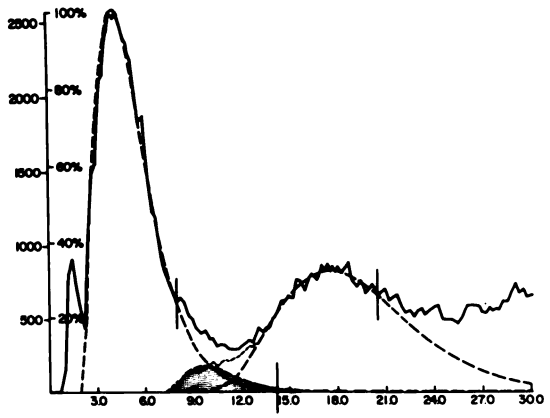

FIG. 4. Gamma variate fitting of obvious systemic recirculation component.

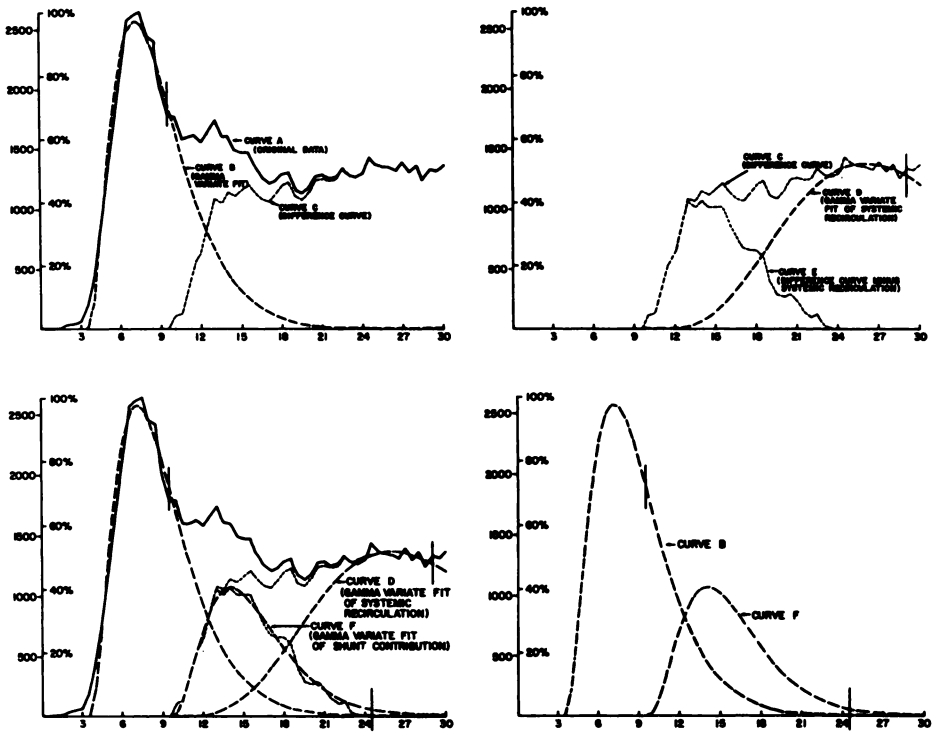

FIG. 5 (A). (Left) curve A represents original recorded dilution curve used for pulmonary gamma variate fit (Area A). Curve B shows gamma variate fit of Curve A, and Curve C shows difference between original curve and gamma variate fit. (Right) curve D shows gamma variate function fitted to region of recirculation. Curve E illustrates curve derived from subtraction of recirculation fit (Curve D) from original difference curve (Curve C). **(B)** (Left) all six curves shown simultaneously. Curve F represents gamma variate function fitted to Curve E. (Right) final areas used to determine shunt ratio (B/A) and $\dot{Q}p/\dot{Q}s$ value, using relationship $\dot{Q}p/\dot{Q}s = A/(A - B)$.

RESULTS

In the 29 patients for whom comparisons were available, correlations between the ratios for pulmonary flow to systemic flow, as calculated from catheterization and oximetry on the one hand, and from the radionuclide approach on the other, generated an r value of 0.92, as shown in Fig. 7. There were no false negatives when comparing radionuclide shunt calculations with oximetry. As expected, the $\dot{Q}p/\dot{Q}s$ was found insensitive to right-to-left and bidirectional shunting, since the inclusion of three patients with bidirectional shunting decreased the r value to 0.73, the oximetry $\dot{Q}p/\dot{Q}s$ values being low.

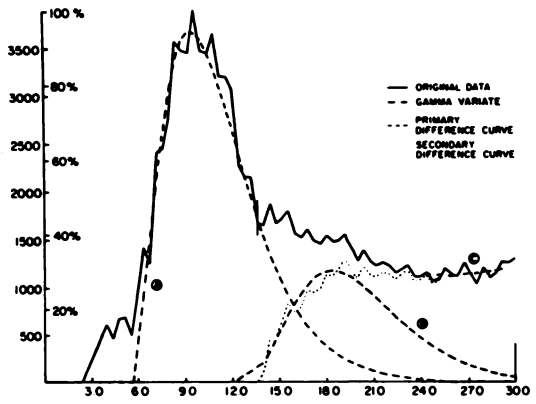

FIG. 6. Example where no time of recirculation can be found because no segment of examined area shows a concavity to be identified as time of systemic recirculation. In this case, clearance is assumed by program to follow same decay constant as in primary curve.

DISCUSSION

In the radionuclide studies without recirculation subtraction, the usual criterion for normal subjects (those without shunts) has been a $\dot{Q}p/\dot{Q}s$ ratio of 1.2 or less. Thus, up to 16% of the reappearance area is accepted

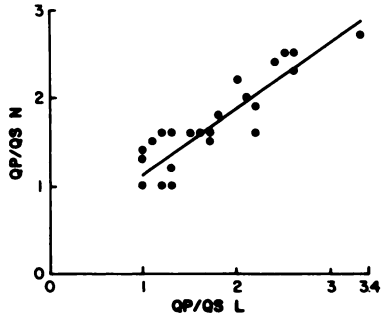

FIG. 7. Correlation of $\dot{Q}p/\dot{Q}s$ values obtained by oximetry, shown by abscissa values "L," and by calculation using subtraction of systemic recirculation component, shown by ordinate values "N." All radionuclide calculations performed automatically with no operator intervention. Coefficient of correlation is 0.92.

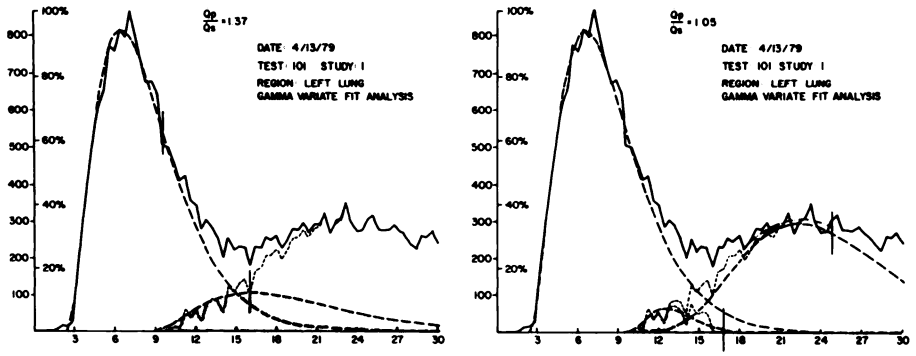

FIG. 8. Normal lung dilution curve (no shunt) showing large area B (stippled) estimated without recirculation subtraction (left) and small area B estimated with recirculation subtraction (right).

without identifying this area as due to a shunt. This reappearance is due to recirculation, and demonstrates the problem of separating the shunt-reappearance activity from systemic recirculation. With the subtraction of the systemic recirculation component, the normal values of $\dot{Q}p/\dot{Q}s$ do not necessarily become zero, but they do become smaller and are usually in the 1.05–1.10 range. This has allowed a more accurate definition of the smaller shunts that previously could not be identified. This reduction is illustrated in Fig. 8, in which dilution curves of a patient with no shunt are shown with and without the subtraction of systemic recirculation.

Although the mathematical model of the lung dilution curve recorded from a left-to-right cardiac shunt is quite straightforward, there has been considerable difficulty in analyzing the curve. In many cases, an inflection point on the reappearance curve cannot be identified readily, and an arbitrary decision must be made to delineate the region for which the gamma variate is to be fitted.

Several techniques have been proposed to aid in this analysis. One method involves the deconvolution (*15*) of the input bolus so as to produce a dilution curve from the lung such as would be recorded from an ideal bolus. This process reduces the time span of the lung dilution curve so that, in many cases, the region of the shunt distortion can be better delineated.

One of the most useful features of the recirculation subtraction method is the construction of a complete curve for fitting a gamma variate function to the reappearance curve (*16*). Without this subtraction, the leading edge is usually the only region that is unequivocal, with the peak dependent upon an arbitrary selection of inflection point (Fig. 9, left).

With the recirculation subtraction shown in Fig. 9, right, a fit can be made of the difference curve with the same criterion applied to all studies without operator intervention. This factor, along with the automatic selection of the lung area, has made the entire radionuclide $\dot{Q}p/\dot{Q}s$ determination an off-line computer measurement, independent of operator interaction.

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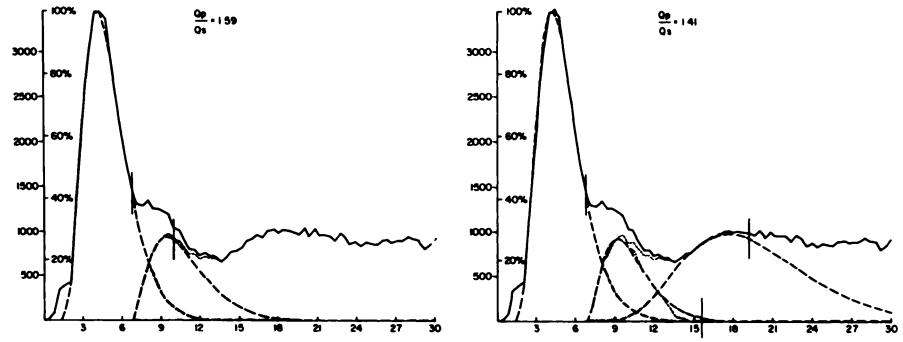

FIG. 9. Abnormal dilution curve with moderate shunt, showing large area B estimated without recirculation subtraction (left) and smaller area B estimated with recirculation subtraction (right).

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