Removal of Bolus Fragmentation Artifacts from Pulmonary Curves as Applied to QP:QS Shunt Determination

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A computer method has been developed to correct errors from fragmented boluses in pulmonary time-activity curves. Improved QP:QS quantitation for cardiovascular shunt determination has been achieved in the 15 cases tested. The technique uses a series of subtractions of time-displaced minified curves from both bolus and pulmonary time-activity curves. The result is an improved bolus and lung curve that correlates very highly with QP:QS as determined by x-ray angiocardiography.

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The detection and quantitation of cardiovascular shunts by radionuclide angiography are well established (*1–7*). The accuracy of the QP:QS ratio determined from the pulmonary time-activity curve is notably affected by the contour of the injected bolus (*8*). Deconvolution analysis (*9*) of the pulmonary curve to improve shunt quantitation will correct for some imperfect injections (*8,10*), and pulmonary curves from prolonged boluses are successfully corrected by this means (*10*). Theoretically, mathematical deconvolution by means of Fourier transforms should correct a pulmonary curve for any imperfect bolus. In practice, however, present deconvolution analysis is not consistently successful in correcting pulmonary activity curves obtained from fragmented boluses (*8,10*). The calculated shunt ratio is underestimated and, in some cases, may actually be worse after correction by deconvolution analysis (*10*). A technique using multiple subtraction of minified curves is presented as an adjunct to deconvolution analysis to correct pulmonary curves resulting from fragmented boluses.

METHOD

Measurement of left-to-right shunts by means of radionuclide angiocardiography is an easily performed, minimally invasive technique (*11*). The patient and the intravenous infusion site are prepared as described by Berger et al (*11*). An online computer collects digital data with half-second intervals for 60 sec during the anterior flow study. Bolus and lung time-activity curves are generated from the stored data. When the bolus is sharp and without fragmentation, we proceed to measure the size of L-R shunts. The gamma-function technique of Maltz and Treves (*8*) is used on the pulmonary transit curve to obtain the QP:QS ratio. If the bolus is prolonged (>2.5 sec at half-maximum), deconvolution analysis, using fast Fourier transforms (*9,12,13*) is performed before quantitation, with successful results. When the bolus is asymmetric or fragmented, the technique of multiple curve subtraction is used before quantitation.

A bolus time-activity curve (Fig. 1B) is produced from a region of interest (ROI) at the superior vena cava (Fig. 1A). Arterial and pulmonary circulations should be excluded from this ROI so that fragmentation artifacts are not produced in the bolus curve. The pulmonary time-activity curve (Fig. 1D) is produced from a region of interest over the lungs (Fig. 1C). A second bolus curve can be generated by computer as a minified image of our original bolus curve, carrying the same number of points but displaced in time by T sec and reduced in amplitude (Fig. 2A). Theoretically this second bolus produces, at the lung ROI, an observed pulmonary parenchymal curve (Fig. 2D) that is a minified image of the pulmonary curve, displaced by time T and with similar but reduced amplitude. Both minified image curves are created by the computer from the original bolus and lung data. The time displacement T and the amplitude reduction are chosen by the user in such a way that the maximum spike of the minified bolus curve (Fig. 2A) will be located directly under the fragmentation portion of the original bolus curve (Fig. 2B). Similarly the new minified pulmonary curve will also underlie the original pulmonary curve at identical time displacement and amplitude reduction (Fig. 2E). Subtraction of the minified bolus curve from the original parent curve removes a portion of the fragmentation and results in an improved bolus. It can be shown that the pulmonary curve produced by this improved resultant bolus is simply the subtraction of the minified pulmonary curve from the original parent pulmonary curve. The

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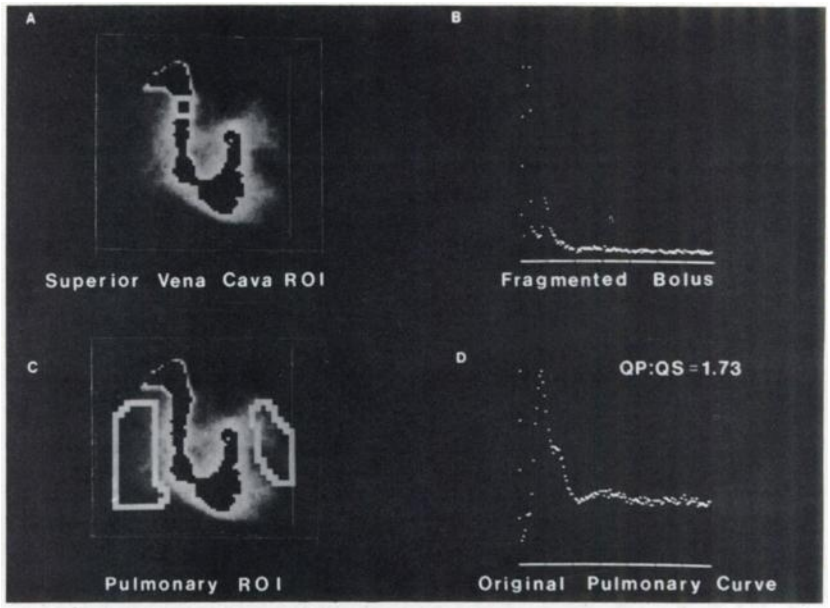

FIG. 1. Regions of interest over superior vena cava (A) and lungs (C) generate corresponding time-activity curves (B and D). ROIs in both lung fields (C) must be far from central circulation.

degree of pulmonary-curve improvement is measured by the degree of fragmentation removal seen in the bolus curve.

The minified bolus curve does not have the same shape as the fragmentation it underlies. Therefore, when this curve is subtracted from the original bolus, the fragmentation will be lessened, but not totally removed. The technique is now repeated using the resultant bolus and lung curves, minified. New time displacements and amplitude reductions are chosen in such a way that each minified curve always underlies the unwanted fragments left in the previous resultant bolus curve. Subtracting minified resultant curves is just as valid as subtracting minified original curves. Since the resultant curves have diminished fragmentation, they provide more controlled minified curve subtraction. For reasons covered in the discussion section, the fragmentation farthest left should be reduced first. The continuing process of subtracting minified resultant bolus curves from previously generated curves results in a bolus of negligible fragmentation. Likewise, the pulmonary curve, generated simultaneously, evolves from the minified curve subtractions (Fig. 2F) and provides improved QP:QS quantitation. This final pulmonary curve can be shown to be a convolution of the true lung curve and the final resultant bolus curve.

Specifically, we pick a point P (Fig. 3) on the fragmented portion of the bolus curve (f = amplitude at point P). A minified bolus curve is positioned under point P in such a way that the main spike of the minified bolus directly underlies P and has an amplitude equal to 0.3f. The value of 0.3 produces curves that will not produce negative points in the resultant curves, while keeping the subtractions required for fragmentation removal to a tolerable number of 4–12. The ratio R of the amplitude b (minified bolus spike) to amplitude B (the original bolus spike), as well as the time displacement T, are also computed (Fig. 3B). The computer then creates a minified lung curve using the same ratio and time displacement.

Activity artifacts that precede the original lung curve (such as

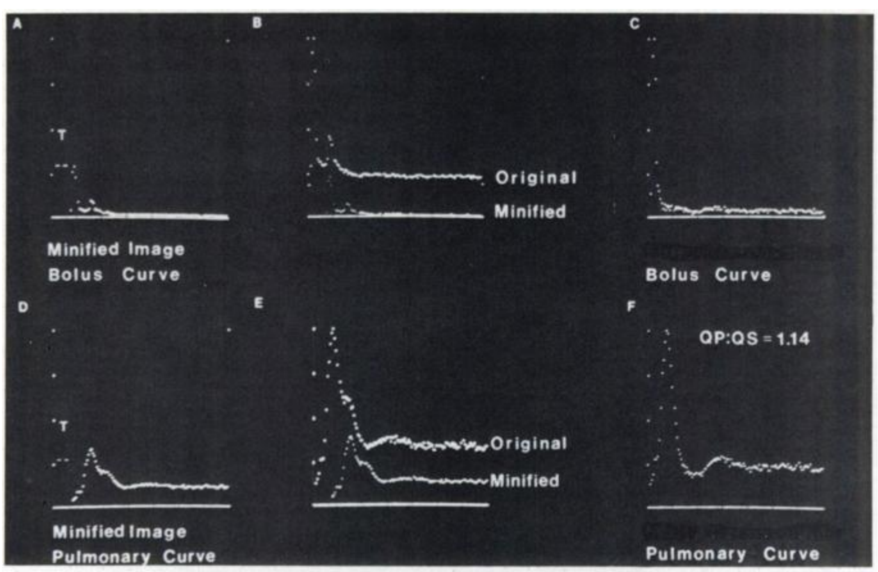

FIG. 2. Minified time-activity curves of bolus and pulmonary curves created, with time displacement T (A and D). B shows minified bolus curve under original, and E shows minified pulmonary curve under its original curve. Multiple subtractions of minified curves chosen by the user will yield a suitable bolus (C) and improved pulmonary curve (F).

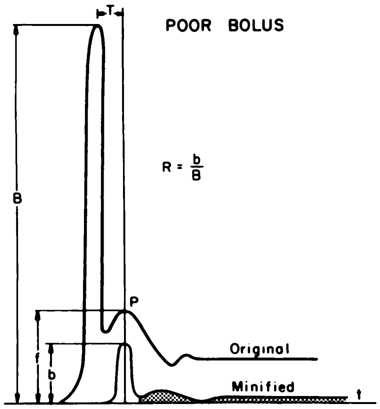

FIG. 3. Computer generates minified bolus curve (amplitude b = 0.3f) positioned under fragmentation point P before subtraction. Ratio R and time displacement T, determined from minified bolus curve, will be used to generate minified lung curve.

injection-site backscatter) should be removed before creating minified lung curves from the original. In addition, all curves must first be corrected for dead-time losses so that the original bolus curve, when taken at reduced amplitude, will generate the original pulmonary curve at reduced amplitude. Any number of minified bolus and lung curve subtractions, at any time displacement and any minification factor, are mathematically valid. For physical validity, however, the minified curve subtractions are acceptable only so long as negative points are not produced on the resultant curves, since we cannot subtract out more bolus than originally existed. Negative points will occur beyond the 60-sec interval of the resultant curve as a natural consequence of this technique, but these will not affect the integrity of the curves within that 60-sec interval.

RESULTS

Preliminary results from fifteen radionuclide angiograms with fragmented boluses were evaluated (Table 1). The first ten studies were performed on expected normal-shunt patients (reference QP/QS of 1.00). The QP/QS ratios determined from the uncorrected pulmonary curves of fragmented boluses are compared with the QP/QS ratios determined from pulmonary curves after minified curve subtractions, as well as after deconvolution analysis. Studies 11 and 12 are the result of two unsuccessful injections for shunt calculation from the same patient. Each of these two injections displayed significant fragmentation, which elevated the uncorrected QP/QS ratio. The QP/QS for this patient, as determined by x-ray angiocardiography, was 2.13:1. The thirteenth study displayed the worst fragmentation to date, as evidenced by the uncorrected QP/QS ratio of 9.87. The x-ray QP/QS for this patient was 2.7:1. The bolus of the fourteenth and fifteenth studies exhibited both fragmentation and prolongation. Deconvolution analysis of the curve-subtracted data exhibits the greatest change in these two studies. The QP/QS data determined by radionuclide angiography were calculated in each case as a "blind study;" that is, the x-ray angiocardiography was performed after the nuclear medicine QP/QS ratios were reported.

The QP/QS ratios determined from the uncorrected data (Table 1) show a linear least-squares correlation of r = 0.771, with the reference QP/QS values. Improved correlation (r = 0.988) is achieved with the technique of multiple curve subtraction. The QP/QS ratio was also determined by deconvolution analysis of the original data for the bolus and lung curves using the fast Fourier transform algorithm of Cooley and Tukey (*12,13*). Although improved correlation with deconvolution (r = 0.864), the size of the shunt was underestimated for all the fragmented boluses evaluated. Deconvolution analysis can be applied to the resultant curve-subtracted bolus and lung curves to correct for any prolongation and to produce the true lung curve. A correlation of r = 0.985 is seen when the lung curves derived by multiple curve subtraction are subjected to deconvolution analysis.

Four different investigators performed shunt quantitation using deconvolution analysis and curve subtractions on five patient studies (Table 2). Although the fragmentation following the bolus is "chipped away" in slightly different manner for each investigator through minified curve subtraction, a correlation of r = 0.914 is found, as opposed to r = 0.825 with deconvolution analysis.

TABLE 1. RESULTS WITH FRAGMENTED BOLUS INJECTIONS

Study No.	Reference QP/QS	Fragmented bolus, uncorrected	QP/QS by deconvolution analysis	QP/QS by multiple minified curve subtractions	Curve subtractions followed by deconvolution analysis
1	1.00	1.25	1.00	1.03	1.00
2	1.00	1.27	1.00	1.00	1.00
3	1.00	1.39	1.00	1.06	1.02
4	1.00	1.52	1.04	1.10	1.06
5	1.00	1.63	1.00	1.05	1.02
6	1.00	1.67	1.00	1.04	1.00
7	1.00	1.88	1.02	1.05	1.00
8	1.00	2.55	1.00	1.02	1.00
9	1.00	3.29	1.26	1.15	1.08
10	1.00	5.58	1.04	1.09	1.05
11	2.13	4.87	1.62	2.15	2.05
12	2.13	6.95	1.54	1.94	1.90
13	2.70	9.87	1.93	2.72	2.62
14	4.10	7.13	1.71	4.88	3.12
15	1.75	2.66	1.49	1.85	1.63
Correlation coefficients:		r = 0.771	r = 0.864	r = 0.988	r = 0.985

TABLE 2. RESULTS WITH FOUR INVESTIGATORS

Reference QP/QS	Fragmented bolus uncorrected	QP/QS deconvolution analysis	QP/QS by multiple minified-curve subtractions
1.0	2.55	1.00	1.02
1.0	1.95	1.00	1.06
1.0	2.87	1.01	1.10
1.0	3.13	1.00	1.09
1.0	1.88	1.02	1.05
1.0	2.35	1.04	1.08
1.0	1.62	1.00	1.06
1.0	1.35	1.00	1.04
4.1	7.13	1.71	4.88
4.1	10.80	1.99	2.20
4.1	6.21	1.85	4.32
4.1	8.86	1.61	3.97
2.7	9.87	1.93	2.72
2.7	14.55	2.01	2.91
2.7	12.33	1.80	2.50
2.7	10.41	2.12	2.58
2.13	6.95	1.62	1.94
2.13	1.3	1.54	1.73
2.13	6.08	1.73	2.02
2.13	5.58	1.43	2.27
Linear correlation	r = 0.702	0.825	0.914

DISCUSSION

The minified curve that is subtracted, like the original curve, may have numerous spikes in it, so there may be uncontrolled and inappropriate subtraction of data from regions of the original curve following the fragment of interest (spike P in Fig. 3). This problem, which may lead to the formation of negative points, is best controlled by beginning the minified curve subtractions on the bolus fragmentation farthest to the left. Bolus fragments and trailing activity to the right of the extreme left fragment (point P) act as an umbrella to cover uncontrollable irregularities to the right of the main spike in the minified bolus curve (Fig. 3, shaded). This umbrella, which prevents the formation of negative points during curve subtractions, is adequately present in all 30 fragmented bolus curves we have observed.

The multiple minified-curve-subtraction technique does not represent deconvolution and will not return a true lung curve and delta spike bolus curve. Whenever a prolonged symmetrical bolus curve is encountered, application of this technique will merely minify, not improve, the bolus and lung curves involved. However, whenever there is asymmetry in the bolus curve, the subtraction technique consistently provides superior correlation with QP:QS as determined by x-ray angiography (Tables 1 and 2). Minified-curve subtractions display gradual improvements in the bolus and the lung curves, continuing until the fragmentation is reduced to a negligible level. This visual control of the subtraction provides a reliable alternative to the choosing of a suitable filter frequency, as is demanded in deconvolution analysis. At our institution, multiple minified curve subtractions have provided a fast, accurate method for correcting lung curves from fragmented boluses.

SUMMARY

Multiple curve subtraction effectively improves pulmonary curves derived from fragmented and asymmetric boluses. Deconvolution analysis of the curve-subtracted data will return the true lung curve and will sometimes further improve the QP/QS finding. The multiple-curve-subtraction technique has provided improved QP/QS ratios for the preliminary studies where it was applied. When compared with Fourier inverse transforms, the multiple-curve-subtraction technique has been shown in this preliminary report to be a sensitive method for quantifying left-to-right shunts in radionuclide angiograms involving fragmented boluses. However, further correlation from other centers will be necessary to confirm our positive experience with the technique.

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