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Effects of Noise on the Determination of Ejection Fraction from Left Ventricular Time–Activity Curves

D. B. Twieg, E. M. Stokely, R. W. Parkey, J. T. Willerson, and L. R. Nardizzi

Southern Methodist University, and Southwestern Medical School, University of Texas Health Science Center at Dallas, Dallas, Texas

The effects of Poisson noise on three estimates of ejection fraction made from left-ventricular time–activity curves have been investigated. All three methods are based on a sinusoidal model of left-ventricular volume changes. The first, developed by Schelbert et al., overestimates the ejection fraction for low-activity levels and low ejection fractions. The second estimate, which is merely a first-order correction for the contribution of Poisson noise to the first estimate, appears to be more accurate when both estimators are applied to simulated time–activity curves, and the resulting ejection fractions are compared. A third, "maximum likelihood" estimator, when applied to the same data, is apparently more accurate than the first two.

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Methods have been developed for determination of ejection fraction (EF) by analysis of left-ventricular time–activity curves following vascular injection of a radionuclide tracer (*1–4*). A particularly convenient technique, originated by Schelbert et al. (*1*), is available as part of a standard commercial software package.*

The background-subtracted left-ventricular time–activity curve is composed of a high-frequency cyclic curve representing cardiac contraction, superimposed upon a low-frequency curve representing the profile of tracer concentration as the bolus passes through the left ventricle. Over any given cardiac cycle, the ratio of the amplitude of variation (end-diastolic minus end-systolic) to the peak activity value (end-diastolic) gives the ejection fraction. Thus, the problem of ejection fraction estimation reduces to one of determining the relative amplitudes of cyclic variations in the noisy data.

It can be shown Poisson noise introduces a positive error in the amplitude and ejection fraction as estimated by this technique for any finite count rate. In the case of large tracer doses or with large ejection fractions, the error is small but still is often significant. We have observed this effect in the analysis of simulated noisy data curves with known EF and have devised a correction that removes most of the bias by taking the noise into account.

Analysis. The sinusoidal volume model assumes that ventricular volume varies in an approximately sinusoidal manner and that a sinusoid fitted to the high-frequency curve has an amplitude proportional to the amplitude of ventricular volume changes. In the technique of Schelbert et al., the sinusoidal fit is made by determining the root mean square deviation of the data points about the low-frequency curve.

The mean square deviation (MSD) of a sinusoid from its mean, taken over an integral number of cycles, is related to the amplitude A of the sinusoid (*1*) by

$$\mathrm{MSD} = \tfrac{1}{2}\mathrm{A}^2. \qquad (1)$$

Thus, a deterministic estimate A_0 of the amplitude is given by

$$\mathrm{A}_0 = \sqrt{2\mathrm{MSD}}. \qquad (2)$$

Equation 1, however, holds true only if the data are not noisy. It can be shown Poisson noise con-

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For reprints contact: D. B. Twieg, Dept. of Radiology, University of Texas Health Science Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75235.

tributes to the mean square deviation of data gathered as random counts. If σ_n^2 is the average variance of the Poisson noise over the data interval being used, the expected mean square deviation for noisy data (5) is

$$MSD = \frac{1}{2}A^2 + \sigma_n^2. \quad (3)$$

Thus, a more accurate estimate of A is

$$A^* = \sqrt{2MSD - 2\sigma_n^2}. \quad (4)$$

Note that since σ_n^2 is positive, the deterministic estimate A_0 is always larger than the estimate A^* that takes noise into account.

If all data points are normalized such that the low-frequency level B is constant, then EF is related to amplitude A by

$$EF = \frac{2A}{A + B}. \quad (5)$$

Thus, if A_0 is an overestimate of A, then the deterministic estimate EF_0 computed by substituting A_0 into Eq. 5 can be expected to exceed the actual value.

An EF estimate unbiased by noise is provided by the maximum-likelihood (ML) estimator (6). Briefly, the ML estimate of a parameter $\hat{x}$, given the set of noise-corrupted observations z'_k, is the estimate x such that the likelihood of obtaining the observation set is maximized. In the case of ejection fraction estimation, a convenient formulation involves estimating the amplitude A of volume variation from the linear observations

$$z'_k = ABh_k + B + C + n_k, \quad (6)$$

where B is the mean activity level of the ventricular curve, C is the background level, n_k is Poisson-distributed noise, and h_k is a sinusoidal curve with the same frequency as that of the heartbeat.

The ML estimate $\hat{A}$ for the K linear observations z_k (6) is given by

$$\hat{A} = \frac{\sum_{k=1}^{K} (h_k z_k / \sigma_k^2)}{\sum_{k=1}^{K} (h_k^2 / \sigma_k^2)}, \quad (7)$$

where $z_k = z'_k - B - C$, and σ_k^2 is the variance of the Poisson noise. A good estimate of σ_k^2 is obtained by smoothing the raw data z'_k.

If the value of $\hat{A}$ given by Eq. 7 is used in Eq. 5, the result is an estimate of EF unbiased by Poisson noise.

Comparison using simulated curves. In order to investigate the effect of noise on typical EF estimates, a series of 11 simulated list-mode time–activity curves with Poisson noise and with known ejection fractions was generated on a laboratory computer.† The ejection fractions simulated were 0.20, 0.40, and 0.80. The average count rates were varied from 30 to 150 counts per 40-msec data point; these levels correspond to typical peak left-ventricular activity levels in our patient studies.

The noise correction method discussed here assumes a time-invariant low-frequency curve, which is unrealistic in most patient studies. To test the effect of a nonconstant low-frequency curve, two of the simulated curves were given parabolic low-frequency components.

A group of intervals on each of the eleven 500-point test curves were analyzed by the method of Schelbert et al. using the program supplied with our computer.* A noise correction was applied to each of the resulting EF estimates, based upon the average

TABLE 1. UNCORRECTED AND NOISE-CORRECTED EJECTION FRACTION ESTIMATES FOR VARIOUS MEAN ACTIVITY LEVELS AND TRUE EJECTION FRACTIONS

Simulated data			EF estimates		
Mean activity level (B)	True EF	Number of intervals	Uncorrected	Corrected for noise	Maximum likelihood
30	0.4	3	0.575 ± 0.026 ($p < 0.01$)	0.425 ± 0.051 (—)	0.425 ± 0.035 (—)
60	0.4	3	0.507 ± 0.029 ($p < 0.01$)	0.433 ± 0.039 (—)	0.379 ± 0.031 (—)
90	0.4	4	0.486 ± 0.011 ($p < 0.005$)	0.437 ± 0.013 ($p < 0.02$)	0.417 ± 0.018 (—)
150	0.4	4	0.453 ± 0.031 ($p < 0.05$)	0.421 ± 0.015 (—)	0.392 ± 0.020 (—)
30	0.2	4	0.476 ± 0.019 ($p < 0.01$)	0.134 ± 0.105 (—)	0.206 ± 0.062 (—)
60	0.2	4	0.380 ± 0.036 ($p < 0.01$)	0.212 ± 0.077 (—)	0.200 ± 0.044 (—)
90	0.2	4	0.358 ± 0.051 ($p < 0.01$)	0.255 ± 0.086 (—)	0.196 ± 0.035 (—)
60	0.8	4	0.846 ± 0.039 ($p < 0.001$)	0.828 ± 0.043 (—)	0.803 ± 0.027 (—)
90	0.8	4	0.850 ± 0.009 ($p < 0.005$)	0.838 ± 0.009 ($p < 0.001$)	0.808 ± 0.016 (—)
60 parabolic*	0.4	4	0.502 ± 0.038 ($p < 0.02$)	0.417 ± 0.056 (—)	0.402 ± 0.041 (—)
150 parabolic*	0.4	4	0.460 ± 0.036 ($p < 0.05$)	0.426 ± 0.038 (—)	0.405 ± 0.021 (—)

* In each of the "parabolic" test curves, the low-frequency component was a parabola with B = 10 at initial and final times and peak B values of 60 and 150.

activity level of the curve in that interval. The same intervals of each data curve were then processed on another computer† using the maximum likelihood procedure, and the three sets of EF estimates were compared.

The mean EF estimates for each curve are presented in Table 1, and results for the series of curves with EF = 0.40 are plotted in Fig. 1. Student's t-test was applied to determine the significance of the deviation of each averaged estimate from the actual EF value; the p values in Table 1 indicate this significance level. The confidence limits in Table 1 and Fig. 1 are the sample standard deviations.

CONCLUSIONS

The following observations can be made from the results:

1. The positive bias in the deterministic estimate was significant in all cases tested, although it decreased with increasing activity and increasing EF.
2. The corrected estimates (EF*) were always closer to the actual EF value than were the deterministic estimates (EF_0). Similarly, the ML estimates were always more accurate than the corrected estimates. Errors in the uncorrected estimates averaged 42% over all curves, the average error for corrected estimates was 10%, and for the ML estimates, 2%.
3. There was no significant decrease in the accuracy of any of the three EF estimates when a more realistic nonconstant baseline was used.

The mean activity level of the left-ventricular time–activity curve is dependent on several variables, including tracer dose, end-diastolic volume, background level, collimator and detector efficiency, and others. Because the uncorrected MSD method will significantly overestimate EF when the mean left ventricular activity level is low for any reason, users of the MSD method should be aware of whether or not their computational procedure includes a correction for Poisson noise.

The clinical usefulness of maximum-likelihood estimates in radionuclide angiographic measurement of ejection fraction and the comparison of ML estimates with other estimates of EF in patients remains an interesting subject for future investigations.

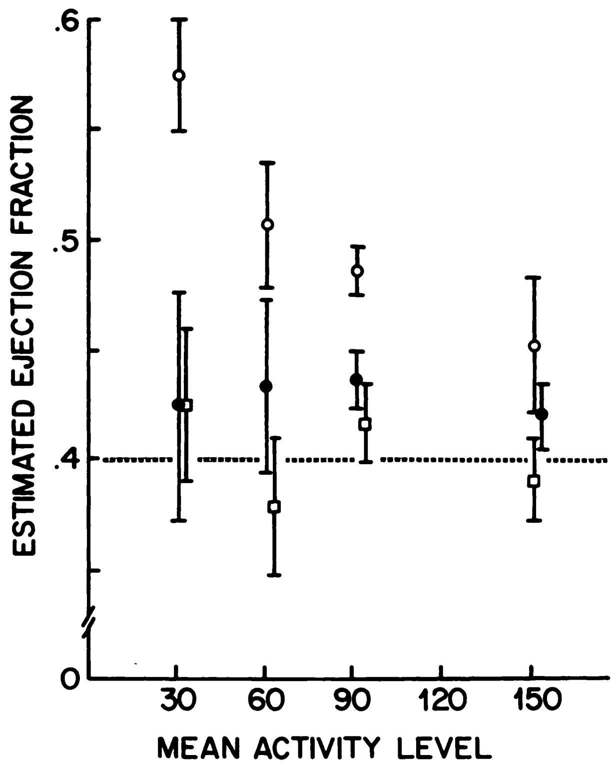

FIG. 1. Ejection fraction estimates for simulated curves with EF = 0.40. Open circles designate deterministic estimates, closed circles designate corrected estimates, and squares indicate ML estimates. Error bars represent sample standard deviations.

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FOOTNOTES

* General Electric Nuclear Data MED II computer.

† Digital Equipment Corp. PDP 8/I.

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