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LETTER TO THE EDITOR

A Least Squares Test of General Use in the Radioisotope Laboratory[2,3]

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Interpretation of many tests performed routinely in nuclear medicine involves fitting a number of observed data points by a single exponential function in order to determine the Y intercept of the extrapolated curve or its half-time of disappearance. This is usually done by plotting the observed points on semi-logarithmic paper and fitting the data with a straight line. We have found this to be a subjective and often misleading method. As an alternative, regression analysis, the application of least squares testing, provides a direct and completely objective method of determining the Y intercept and the half-time of disappearance of the single exponential curve which best fits such a set of data. An analysis of this type can be performed by a radioisotope technologist using a calculator and a table of logarithms in two or three minutes, roughly the same time required to plot the data on graph paper.

The equations needed for such an analysis are presented below. They are based on the principal of minimizing the sum of the squares of differences between the logarithms of the data points and the logarithm of the predicted function.

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[3]This Letter is essentially a reprint of the letter published in the April, 1966 issue of the Journal of Nuclear Medicine (pp. 314-317). Minor modifications have been made in the formulae at the suggestion of Dr. Donald W. Brown.

Equation I

$$\lambda = \frac{2.30\left[\sum_{i=1}^{n} t_i \cdot \sum_{i=1}^{n} \log_{10} D_i - n\sum_{i=1}^{n} (t_i \cdot \log_{10} D_i)\right]}{n\sum_{i=1}^{n} t_i^2 - \left(\sum_{i=1}^{n} t_i\right)^2}$$

Equation II

$$T_{\frac{1}{2}} = \frac{0.301\left[n\sum_{i=1}^{n} t_i^2 - \left(\sum_{i=1}^{n} t_i\right)^2\right]}{\sum_{i=1}^{n} t_i \cdot \sum_{i=1}^{n} \log_{10} D_i - n\sum_{i=1}^{n} (t_i \cdot \log_{10} D_i)}$$

Equation III

$$\log_{10}(Y_0) = \frac{1}{n}\left(\sum_{i=1}^{n} \log_{10} D_i + 0.434\,\lambda \cdot \sum_{i=1}^{n} t_i\right)$$

Equation IV

$$\log_{10}(Y_0) = \frac{\sum_{i=1}^{n} \log_{10} D_i \cdot \sum_{i=1}^{n} t_i^2 - \sum_{i=1}^{n} t_i \cdot \sum_{i=1}^{n} (t_i \cdot \log_{10} D_i)}{n\sum_{i=1}^{n} t_i^2 - \left(\sum_{i=1}^{n} t_i\right)^2}$$

Equation V

$$\text{Standard log error} = \sqrt{\frac{\sum_{i=1}^{n} \left(\log_{10} D_i - \log_{10}\left[Y_0 e^{-\lambda t_i}\right]\right)^2}{(n-2)}}$$

λ is the exponential decay constant (e.g. $Y_t = Y_0 e^{-\lambda t}$),

$T_{\frac{1}{2}}$ = half-time = $(\ln 2)/\lambda$, n = number of data points.

D_i and t_i are the individual data points and their respective times.

For greater accuracy, the 2.30 in Equation I is the natural logarithm of ten, the 0.301 in Equation II is the natural logarithm of two divided by the natural logarithm of ten, and the 0.434 in Equation III is the reciprocal of the natural logarithm of ten.

RESULTS

To illustrate the importance of the application of these methods in the clinical radioisotope laboratory, we have analyzed ten consecutive plasma iron clearance tests and 24 consecutive ^{51}Cr-labelled red-blood-cell survival tests. These tests were performed on a routine clinical basis and the results expressed as half-times were determined by the plotting method and reported in the patient's clinical records. The half-times were redetermined using regression analysis and digital computation. Surprising discrepancies between the results obtained by the two methods were noted (Fig. 1).

When the computed half-time is assumed to be correct and the manually determined half-time incorrect, the percent error is determined as the difference between the two results multiplied by 100 and divided by the computed half-time. When this was done, the mean error in the plasma iron clearance determinations is found to be 10.1 percent with a standard deviation of 8.4 and a range of 1.2 to 21.8 percent. In the chromium red-blood-cell survival tests, the mean error was 11.6 percent with a standard deviation of 9.5 and 0.1 to 30.8 as the range.

It was noted that the error increased as the half-time decreased. One plasma iron clearance was found to be normal, 132 minutes, as opposed to the abnormal time, 160 miuutes, reported in the patient's clinical record. One red cell survival test was found to be 29.6 instead of 23.5 days and another was 24.0 instead of 31.4 days. These results show clearly that the application of regression analysis can make a significant difference in the values reported in these widely used clinical tests.

DISCUSSION

The method of analysis presented has proved useful in several tests performed routinely in nuclear medicine. These include: 1) determination of the

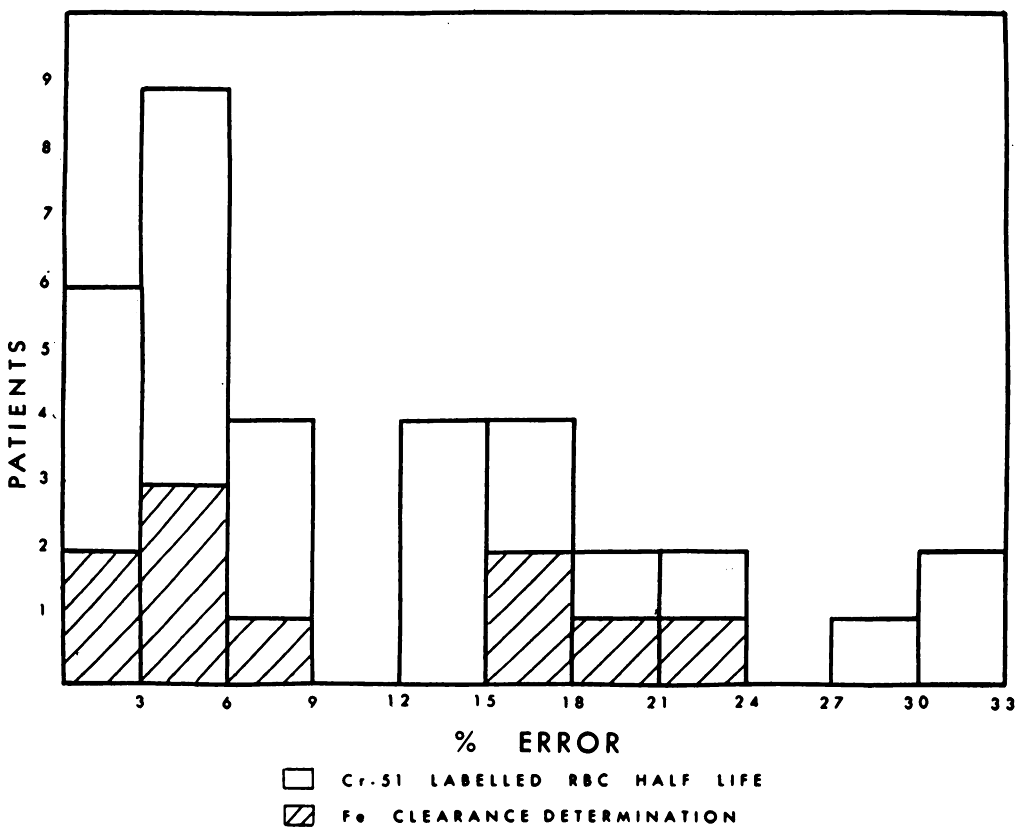

Fig. 1. The percent difference in half-times determined by regression analysis and semi-log plotting in ten plasma iron clearance and 24 ^{51}Cr-labelled red-blood-cell survival tests.

half-time of disappearance of radioactivity due to radioactive decay, 2) determination of the half-time of disappearance of radioactive iron from plasma, 3) determination of ^{51}Cr-tagged red-blood-cell survivals and 4) determination of blood volumes when multiple samples are obtained. A number of other uses can be envisioned.

In these radioisotope tests, the variance of the differences between the logarithms of the observed data points and predicted function tends to approximate a constant as opposed to the variance of the differences between the values themselves, especially when dealing with higher counting rates. Thus, it is found that the introduction of logarithms yields highly satisfactory weighting of the data for the least squares test. Without this, far too much weight would be given to the initial larger counts.

Using the above equations, it is a simple matter to program a digital computer to perform this type of analysis. In our program the computer determines the unknown values λ, $T_{\frac{1}{2}}$, and Y_0, and then tests each data point against the predicted function. If there is a probability greater than 90% that the data point represents a spurious result, that point is cast out and the unknowns are recomputed. The computer also has the option of producing an x-y plot of the resulting output[1].

SUMMARY

A set of simple and frequently useful equations for least squares analysis of a set of data points which fit a single exponential function is presented. They can be solved quickly using a calculator and table of logarithms without knowledge of advanced mathematics. We have found them useful in determining the half-time of disappearance and Y intercept which best fit the data in several tests performed routinely in nuclear medicine. Comparison reveals a surprising discrepancy between the half-times determined by this method and those obtained by semilogarithmic plotting. It is suggested that the least squares method presented is more objective and probably superior.

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[1]A copy of the Fortran 4 computer program in use at our institution will be provided upon request.

REFERENCE

1. BROWNLEE, K. A.: Statistical Theory and Methodology In Science and Engineering, John Wiley and Sons Inc., N.Y. and London, 344-345, 1960.