Physics in Nuclear Medicine

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Nuclear Counting Statistics

All nuclear medicine procedures are based on radiation counting measurements. Like any other measurements of physical quantities, they are subject to measurement errors. This chapter discusses the types of errors that occur, how they are analyzed, and how, in some cases, they can be minimized.

A. TYPES OF MEASUREMENT ERROR

Measurement errors are of three general types:

Blunders are errors that are adequately described by their name. Usually they produce grossly inaccurate results and their occurrence is easily detected. Examples in radiation measurements include the use of incorrect instrument settings, incorrect labeling of sample containers, injecting the wrong radiopharmaceutical into the patient, etc. There is no way to "analyze" errors of this type, only to avoid them by careful work.

Systematic errors produce results that differ consistently from the correct result by some fixed amount. The same result may be obtained in repeated measurements, but it is the wrong result. For example, length measurements with a "warped" ruler, or radiation counting measurements with a "sticky" timer or other persistent instrument malfunction, could contain systematic errors. Observer "bias" in the subjective interpretation of data (e.g., scan reading) is another example of systematic error. Measurement results having systematic errors are said to be *inaccurate*.

It is not always easy to detect the presence of systematic error. Measurement results affected by systematic error may be very repeatable and not too different from the expected results, which may lead to a mistaken sense of confidence. One way to detect systematic error is by the use of measurement *standards,* which are known from previous measurements with a properly operating system to give a certain measurement result. For example, radionuclide standards, containing a known quantity of radioactivity, are used in various "quality assurance" procedures to test for systematic error in radiation counting systems. Some of these procedures are described in Chapter 12, Section D.

Random errors are variations in results from one measurement to the next, arising from physical limitations of the measurement system or from actual random variations of the measured quantity itself. For example, length measurements with an ordinary ruler are subject to random error because of inexact repositioning of the ruler and limitations of the human eye. Random error is *always* present in radiation counting measurements because the quantity that is being measured—namely, the rate of emission from the radiation source—is itself a randomly varying quantity.

Random error affects measurement *reproducibility*. Measurements that are very reproducible—in that nearly the same result is obtained in repeated measurements—are said to be *precise*. It is possible to minimize random error by using careful measurement technique, refined instrumentation, etc; however, it is impossible to eliminate it completely. There is always *some* limit to the precision of a measurement system. The amount of random error present is sometimes called the *uncertainty* in the measurement.

It is also possible for a measurement to be precise (small random error) but inaccurate (large systematic error), or vice versa. For example, length measurements with a warped ruler may be very reproducible (precise); nevertheless, they are still inaccurate. On the other hand, radiation counting measurements may be imprecise (because of inevitable variations in radiation emission rates) but still they can be accurate, at least in an average sense.

Because random errors are always present in radiation measurements, it is necessary to be able to analyze them and to obtain estimates of their magnitude. This is done using methods of statistical analysis. (For this reason, they are also sometimes called *statistical errors*.) The remainder of this chapter describes these methods of analysis.

B. RANDOM ERRORS IN RADIATION COUNTING MEASUREMENTS

1. The Poisson Distribution

Suppose that a long-lived radioactive sample is counted repeatedly under supposedly identical conditions with a properly operating counting system. Because the disintegration rate of the radioactive sample undergoes random variations from one moment to the next, the numbers of counts recorded in successive measurements (N_1, N_2, N_3, etc.) are not the same. Given that different results are obtained from one measurement to the next, one might question if a "true value" for the measurement actually exists. One possible solution is to make a large number of measurements and use the average $\overline{N}$ as an estimate for the "true value":

$$\text{True Value} \approx \overline{N} \tag{6-1}$$

$$\overline{N} = (N_1 + N_2 + \cdots + N_n)/n \tag{6-2}$$

$$= \sum_{i=1}^{n} \frac{N_i}{n} \tag{6-3}$$

where n is the number of measurements taken. The notation Σ_i indicates that a sum is taken over values of the parameter with the subscript i.

Unfortunately, multiple measurements are impractical in routine practice, and one must usually be satisfied with taking only one measurement. The question then is, how good is the result of a single measurement as an estimate of the "true value," i.e., what is the uncertainty in this result? The answer to this depends on the *frequency distribution* of the measurement results. Figure 6-1 shows a typical frequency distribution curve for a series of radiation counting measurements. It is a graph showing the different possible results, (i.e., number of counts recorded) versus the probability of getting each result. The curve is peaked at a mean value m, which is the "true value" for the measurement. Thus if a large number of measurements were made and their results averaged, one would obtain

$$\overline{N} \approx m \tag{6-4}$$

The curve in Figure 6-1 is described mathematically by the *Poisson distribution*. The probability of getting a certain result N when the true value is m is

$$P(N;m) = e^{-m} m^N/N! \tag{6-5}$$

where e (= 2.718 . . .) is the base of natural logarithms and $N!$ (*N factorial*) is the product of all integers up to N (i.e., $1 \times 2 \times 3 \times \cdots \times N$). From Figure 6-1 it is apparent that the probability of getting the exact result $N = m$ is rather small; however, one could hope that the result would at least be "close to" m.

The probability that a measurement result will be "close to" m depends on the relative width, or dispersion, of the frequency distribution curve. This is related to a parameter called the *variance*, σ^2, of the distribution. The variance is a *number* such that 68.3 percent (~⅔) of the measurement results fall within

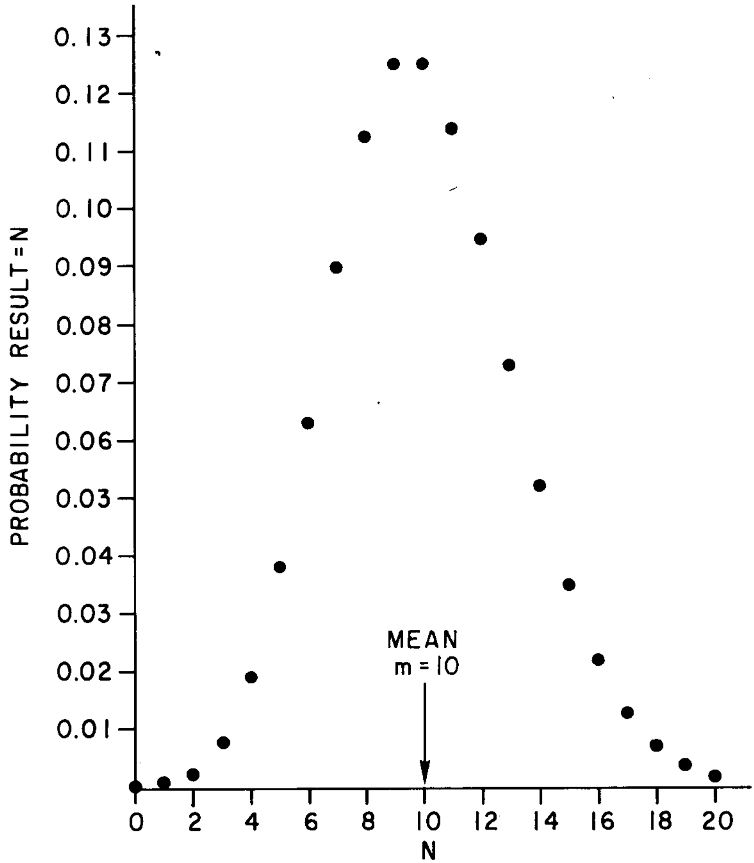

Fig. 6-1. Poisson distribution for $m = 10$.

$\pm\sigma$ (i.e. square root of the variance) of the true value m. For the Poisson distribution, the variance is given by

$$\sigma^2 = m \tag{6-6}$$

Thus one expects to find approximately ⅔ of the counting measurement results within the range $\pm\sqrt{m}$ of the true value m.

Given only the result of a single measurement, N, one does not know the exact value of m or of σ; however, one can reasonably assume that $N \approx m$, and thus that $\sigma \approx \sqrt{N}$. One can therefore say that if the result of the measurement is N, there is a 68.3 percent chance that the true value of the measurement m is within the range $N \pm \sqrt{N}$. This is called the "68.3 percent *confidence interval*" for m; i.e., one is 68.3 percent confident that m is in the range $N \pm \sqrt{N}$.

The range $\pm\sqrt{N}$ is the uncertainty in N. The *percentage uncertainty* in N is

$$V = (\sqrt{N}/N) \times 100\% \tag{6-7}$$

$$= 100\%/\sqrt{N} \tag{6-8}$$

Example 6-1.

Compare the percentage uncertainties in the measurements $N_1 = 100$ counts and $N_2 = 10{,}000$ counts.

Answer.

For $N_1 = 100$ counts, $V_1 = 100\%/\sqrt{100} = 10\%$ (Equation 6-8). For $N_2 = 10{,}000$ counts, $V_2 = 100\%/\sqrt{10{,}000} = 1\%$. Thus the percentage uncertainty in 10,000 counts is only $\frac{1}{10}$ the percentage uncertainty in 100 counts.

Equation 6-8 and Example 6-1 indicate that *large numbers of counts have smaller percentage uncertainties and are statistically more reliable than small numbers of counts.*

Other confidence intervals can be defined in terms of σ or $\sqrt{N}$. They are summarized in Table 6-1. The 50 percent confidence interval ($0.675\sqrt{N}$) is sometimes called the *probable error* (PE) in N.

2. The Standard Deviation

The variance σ^2 is related to a statistical index called the *standard deviation* (SD). The standard deviation is a number that is calculated for a series of measurements. If n counting measurements are made, with results $N_1, N_2, N_3, \ldots, N_n$, and a mean value $\overline{N}$ for those results is found, the standard deviation is

$$\text{SD} = \left(\sum_{i=1}^{n} \frac{(N_i - \overline{N})^2}{n-1} \right)^{1/2} \tag{6-9}$$

(recall that raising a quantity to the ½ power is the same as taking its square root). The standard deviation is a measure of the dispersion of measurement results about the mean and is in fact an estimate of σ, the square root of the variance. For radiation counting measurements one should therefore obtain

$$\text{SD} \approx \sqrt{N} \tag{6-10}$$

This can be used as a test to determine if the random error observed in a series of counting measurements is consistent with that predicted from random variations in source decay rate, or if there are additional random errors present, e.g., from faulty instrument performance. This is discussed further in Section E.

Table 6-1
Confidence Limits in Radiation Counting Measurements

Range	Confidence Limit for m (True Value) (%)
$N \pm 0.675\sigma$	50
$N \pm \sigma$	68.3
$N \pm 1.64\sigma$	90
$N \pm 2\sigma$	95
$N \pm 3\sigma$	99.7

3. The Gaussian Distribution

When the mean value m is "large" ($m \gtrsim 20$) the Poisson distribution can be approximated by the *Gaussian distribution* (also called the *normal distribution*). The equation describing the Gaussian distribution is

$$P(x;m;\sigma) = (1/\sqrt{2\pi\sigma^2})\, e^{-(x-m)^2/2\sigma^2} \tag{6-11}$$

where m and σ^2 are again the mean and variance. Equation 6-11 describes a symmetric "bell-shaped" curve, similar to the one shown in Figure 6-1.

The Guassian distribution with $\sigma^2 = m$ describes the results of radiation counting measurements when the only random error present is that due to random variations in source decay rate. When additional sources of random error are present—e.g., a random error or uncertainty of ΔN counts due to variations in sample preparation technique, counting system variations, etc.—the results are described by the Gaussian distribution with variance given by

$$\sigma^2 = m + (\Delta N)^2 \tag{6-12}$$

The confidence intervals given in Table 6-1 may be used for the Gaussian distribution with this modified value for the variance. For example, the 68.3 percent confidence interval for a measurement result N would be $\pm\ (N + (\Delta N)^2)^{1/2}$ (assuming $N \approx m$).

Example 6-2.

A 1 ml radioactive sample is pipetted into a test tube for counting. The precision of the pipette is specified as "± 2 percent," and 5000 counts are recorded from the sample. What is the uncertainty in sample counts per ml?

Answer.

The uncertainty in counts arising from pipetting precision is 2% $\times$ 5000 counts $=$ 100 counts. Therefore $\sigma^2 = 5000 + (100)^2 \approx 15{,}000$, and the uncertainty is $\sqrt{15{,}000} \approx 122$ counts. Compare this to the uncertainty of $\sqrt{5000} \approx 71$ counts that would be obtained without the pipetting uncertainty.

C. PROPAGATION OF ERRORS

The preceding section described methods for estimating the random error or uncertainty in a single counting measurement; however, most nuclear medicine procedures involve multiple counting measurements, from which ratios, differences, and so on are computed to determine a final result. This section describes methods for estimating uncertainties in mathematical combinations of multiple counting measurements.

1. Sums and Differences

If two quantities A and B are subject to random errors σ_A and σ_B, then the uncertainty in either their sum or difference is given by

$$\sigma(A \pm B) = \sqrt{\sigma_A^2 + \sigma_B^2} \tag{6-13}$$

Applying this to radiation counting measurements one obtains

$$\sigma(N_1 \pm N_2) = \sqrt{N_1 + N_2} \tag{6-14}$$

The rule is readily extended to longer sequences

$$\sigma(N_1 \pm N_2 \pm N_3 \pm \cdots) = \sqrt{N_1 + N_2 + N_3 + \cdots} \tag{6-15}$$

2. Constant Multipliers

If a quantity A having random error σ_A is multiplied by a constant k (i.e., a number having no random error), the uncertainty in the result, kA is

$$\sigma(kA) = k\sigma_A \tag{6-16}$$

Thus for a radiation counting measurement N multiplied by a constant k,

$$\sigma(kN) = k\sqrt{N} \tag{6-17}$$

The percentage uncertainty in the product kN is

$$V(kN) = [\sigma(kN)/kN] \times 100\% \tag{6-18}$$

$$= 100\%/\sqrt{N} \tag{6-19}$$

which is the same result as Equation 6-8. Thus there is no statistical advantage to be gained in multiplying the number of counts recorded by a constant to make the number larger. The percentage uncertainty still depends on the actual number of counts recorded.

3. Products and Ratios

If two quantities A and B have percentage uncertainties V_A and V_B, then the percentage uncertainty in their product or ratio is

$$V(A \overset{\times}{\div} B) = \sqrt{V_A^2 + V_B^2} \tag{6-20}$$

For radiation counting measurement N_1 and N_2, this implies

$$V(N_1 \overset{\times}{\div} N_2) = \sqrt{V_{N_1}^2 + V_{N_2}^2} \tag{6-21}$$

$$= \sqrt{1/N_1 + 1/N_2} \times 100\% \tag{6-22}$$

The rule can be extended to longer sequences:

$$V\,(N_1 \overset{\times}{\div} N_2 \overset{\times}{\div} N_3 \overset{\times}{\div} \ldots) = \sqrt{1/N_1 + 1/N_2 + 1/N_3 + \cdots} \times 100\% \tag{6-23}$$

4. More Complicated Combinations

Many nuclear medicine procedures involve both differences and ratios of counting measurements (e.g., thyroid uptakes, blood volume determinations, etc.). A general form of these calculations is

$$Y = k(N_1 - N_2)/(N_3 - N_4) \tag{6-24}$$

where N_1, N_2, N_3, and N_4 are measured counts, k is a constant, and Y is the calculated quantity (thyroid uptake, blood volume, etc.). The percentage uncertainty in Y is obtained by first applying the rule for ratios and products (Equation 6-20),

$$V_Y = \sqrt{V_{N_1-N_2}^2 + V_{N_3-N_4}^2} \tag{6-25}$$

and then the rule for sums and differences (Equation 6-14),

$$V_{N_1-N_2}^2 = [(N_1+N_2)/(N_1-N_2)^2] \times 100\% \tag{6-26}$$

$$V_{N_3-N_4}^2 = [(N_3+N_4)/(N_3-N_4)^2] \times 100\% \tag{6-27}$$

The final result is

$$V_Y = \sqrt{(N_1+N_2)/(N_1-N_2)^2 + (N_3+N_4)/(N_3-N_4)^2} \times 100\% \tag{6-28}$$

The uncertainty σ_Y can then be obtained from

$$\sigma_Y = V_Y \times Y/100\% \tag{6-29}$$

Example 6-3.

A patient is injected with a radionuclide. At some later time a blood sample is withdrawn for counting in a well counter and $N_p = 1200$ counts are recorded. A blood sample withdrawn prior to injection gives a blood background of $N_{pb} = 400$ counts. A standard prepared from the injection preparation records $N_s = 2000$ counts, and a "blank" sample records an instrument background of $N_b = 200$ counts. Calculate the ratio of net patient sample counts to net standard counts, and the uncertainty in this ratio.

Answer.

The ratio is

$$\begin{aligned} Y &= (N_p - N_{pb})/(N_s - N_b) \\ &= (1200 - 400)/(2000 - 200) \\ &= 800/1800 = 0.44 \end{aligned}$$

The percentage uncertainty in the ratio is (Equation 6–28)

$$\begin{aligned} V_Y &= \sqrt{(1200 + 400)/(800)^2 + (2000 + 200)/(1800)^2} \times 100\% \\ &= 5.6\% \end{aligned}$$

The uncertainty is $5.6\% \times 0.44 \approx 0.02$; thus the ratio and its uncertainty are $Y = 0.44 \pm 0.02$.