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IN-VIVO COUNTING METHODS IN MEDICAL RESEARCH

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ABSTRACT

This article describes, briefly and simply, the methods by which in vivo measurements are made and data are recorded by use of such devices as scintillation counters, G-M counters, and pulse-height analyzers.

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Purpose of In-Vivo Counting

The purpose of in-vivo radioactive tracer counting is to determine the amount of a radioactive isotope at a given location and time in an animal or human subject. Sometimes the absolute amount of isotope present must be determined, but often only the relative amount as a function of time is of interest, since the rate of appearance or disappearance and the time of peak uptake are the important quantities. The relative amount of uptake is measured by directing a suitably collimated counter at all or a portion of the organ being considered and recording the counting rate as a function of time. It is important to keep the geometry constant and to correct the results for scattered and direct radiation from adjacent tissues that may be included in the acceptance angle of the counter.

In case the absolute uptake in a given organ is to be determined, such as a measurement of I^{131} uptake in the thyroid, it is important that all the organ be included within the acceptance angle of the counter. The depth below the surface at which the organ lies should also be known so that corrections can be made for the scattering by surrounding tissue and the absorption by overlying tissue. This is considered in more detail later.

In-Vivo Counting Methods

The radiations emitted by the isotope and the thickness of tissue they must penetrate to reach the counter determine the counting method used.

If beta particles are the only radiations emitted by the isotope, only exposed tissue such as the skin and cornea of the eye, or tissues exposed by surgery, can be counted, since the range of beta particles in soft tissue is only a few millimeters. Beta particles are usually detected with a thin-window Geiger-Müller counter or a scintillation counter with a thin organic scintillator crystal and a thin window. A collimator may be used to define the acceptance angle of the counter.

If the isotope emits gamma rays, deep-seated tissues can be counted, since gamma rays of moderate energy penetrate several inches of tissue without much loss. Scintillation counters are usually preferred over G-M counters as detectors for gamma rays.

If the isotope being used emits positrons, gamma-ray counting is still possible since each positron, after traveling a few millimeters in tissue, decays into two gamma rays of 0.51 Mev energy. The two gamma rays are emitted at the same instant and travel in opposite directions, permitting a highly directional coincidence counting system to be used.[2]

Comparison of Counting Methods for Gamma Rays

The principal methods used to detect gamma rays are the Geiger-Müller counter, the scintillation counter, and the scintillation counter with pulse-height analyzer. Much higher counting efficiencies are obtainable from scintillation counters, as well as a higher efficiency-to-background ratio. Another advantage results when a pulse-height analyzer is used with a scintillation counter. The pulse-height analyzer window is adjusted so that only the photoelectric peak in the curve of counting rate versus pulse height is counted.[6] The heights of the pulses resulting from the photoelectric absorption of the original gamma ray have a distribution about a peak value, whereas gamma rays that have undergone Compton scattering or pair production before entering the detector give smaller pulses. The background is reduced from perhaps 100 to only a few counts per minute, while the counting efficiency is reduced by a factor of only three or four. The formula

$$I = I_0 e^{-\mu x}$$

can now be used to calculate the number of gamma rays lost because of scattering and absorption in the overlying tissue. The quantity I in the formula is the intensity of gamma rays at the surface of an absorbing tissue, I_0 is the intensity at the same point without absorber, μ is the attenuation coefficient of the tissue, and x is the thickness of tissue between the source and the surface.[3] If the source is small enough to be considered a point source, I_0 may be calculated from the formula

$$I_0 = \frac{N}{4\pi r^2},$$

where N is the number of gamma rays emitted per unit time and r is the distance from the source to the counter.

The amount of scattered radiation is frequently large and, if a pulse-height analyzer is not used, it is counted with greater efficiency than the unscattered radiation, since scintillation counters have a peak of counting efficiency in the low-energy region. When pulse-height selection is not used, the net counting efficiency may be determined by counting a phantom which duplicates the subject in dimensions, scattering properties, and location of the radioactive source. If the placement of the counter relative to the phantom is identical with the placement relative to the subject, the absolute amount of isotope in the subject can then be calculated.

The counting technique using scintillation counters and pulse-height analyzers can be combined with multiple detectors to measure two isotopes simultaneously. A further refinement is illustrated in Fig. 1, where a single detector is used to measure two or more isotopes simultaneously.[8] Here the output from a scintillation detector is amplified and fed to two or more differential discriminators followed by scalers or counting rate meters and recorders. The acceptance angle of the counter, the attenuation by overlying tissue, and the efficiency of counting may not be the same for each isotope. Furthermore, the channel adjusted to the low-energy isotope will, in general, also count the high-energy isotope, although at reduced efficiency.

This technique has been used[4] in measurements with Na^{24} and I^{131}.*

Recording of Counting Data

If the counting rate of a counter is constant within statistical variations, a scaler with a register and a timer suffices to give the counting rate. When the counting rate is changing rapidly, the data may be recorded by photographing a register at intervals, using a printing register, or by recording each register pulse on a strip chart moving at constant speed.

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*When this arrangement is employed for the simultaneous determination of I^{131} and Na^{24}, the counting rate for Na^{24} is reduced by a factor of 2 and that of I^{131} by 3.7 from that obtained without the differential discriminator. None of the I^{131} is detected in the Na^{24} counting channel, while 3% of the Na^{24} counting rate appears in the I^{131} channel. This measurement was made with known amounts of the isotopes in a 500 ml. flask, and a thallium-activated sodium iodide crystal 1.75 inches in diameter and 1 inch thick. The amount of discrimination can be adjusted to suit the experiment.

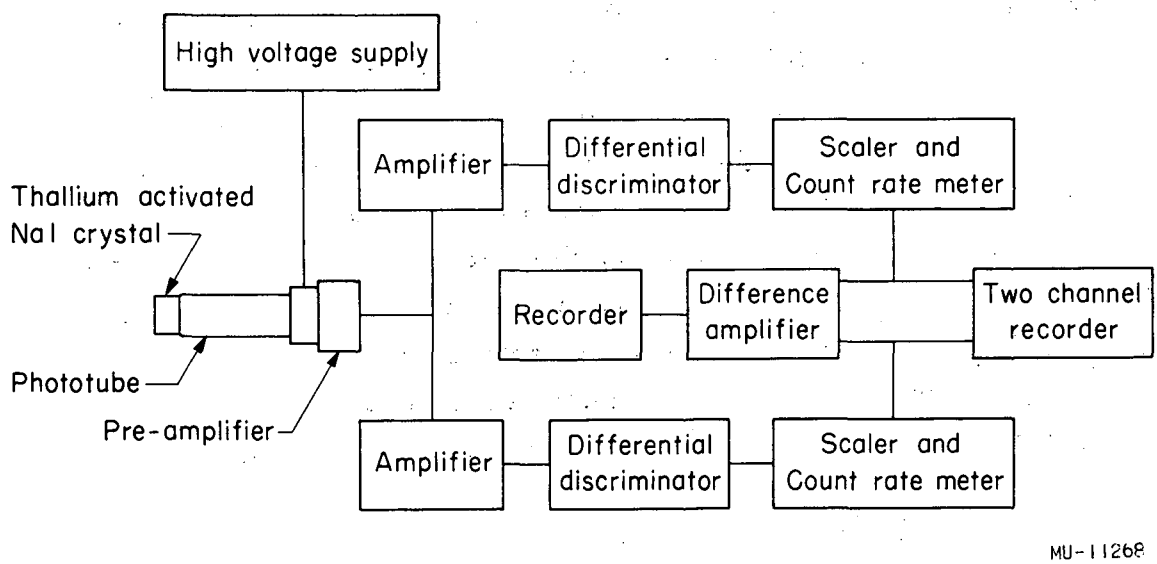

Fig. 1. A scintillation counter is shown whose output is amplified and fed to two differential discriminators. The lower and upper energy-acceptance levels of the discriminators are independently variable so that only those pulses within a given energy range are fed to the scaler and counted. The outputs from the count-rate meters are shown connected to a difference amplifier and recorder.

A recording counting-rate meter, which draws a curve of counting rate versus time, eliminates much of the labor involved in plotting such data. Most counting-rate meters integrate the counts by means of a parallel resistor-and-capacitor combination in which a charge is placed on the capacitor for each count and the charge leaks off exponentially.[5] Another type uses a capacitor with no parallel resistance; here the charge is integrated, then read, and discharged by shorting periodically.[1]

In the first instrument the probable error is

$$\% \text{ pe} = \frac{67.45}{\sqrt{2\ n\ RC}},$$

where RC is the time constant of the capacitor and resistor and n is the counting rate. The time required for the meter to reach approximate equilibrium--or actually, true equilibrium less the numerical value of the probable error--is

$$T = RC\left(\frac{1}{2}\ln 2nRC + 0.394\right),$$

at which time the error in the indicated counting rate is

$$\text{Error} = \overline{-\text{pe}} \pm \text{pe}.$$

In the second type of count-rate recorder the probable error is simply

$$\% \text{ pe} = \frac{67.45}{\sqrt{nt}},$$

where t is the sampling interval. This type of recorder follows rapid changes in counting rate with less error than the first instrument, since all the counts received in the counting period are given equal wieght.

The output from two or more counting-rate meters can be fed to a difference amplifier or computer to obtain difference curves or other information automatically (see Fig. 1). A ratio recorder can be used when the ratio between two counting rates is required, as when the abundance of one is changing with respect to the other, or when a counting rate is changing as a function of some other measurable physiological process.[7]

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