chapter 12

Counting Systems

Radiation counting systems are used for a variety of purposes in nuclear medicine. *In vitro* (from Latin, meaning "in glass") *counting systems* are employed to measure radioactivity in tissue, blood, and urine samples; for radioimmunoassay and competitive protein binding assay of drugs, hormones, and other biologically active compounds; and for radionuclide identification, quality control, and radioactivity assays in radiopharmacy and radiochemistry. In vitro counting systems range from relatively simple, manually operated, single-sample, single-detector instruments to automated systems capable of processing hundreds of samples in a batch with computer processing of the resulting data.

In vivo (from Latin, meaning "in the living subject") *counting systems* are employed for measuring radioactivity in human subjects or experimentally in animals. Different in vivo systems are designed for measuring localized concentrations in single organs (e.g., thyroid, kidney) and for measurements of whole-body content of radioactivity.

Most nuclear medicine counting systems consist of the following basic components: a detector and high voltage supply, preamplifier, amplifier, one or more single-channel analyzers (SCAs) or a multichannel analyzer (MCA) ("data analysis"), and a digital or analog scaler-timer, rate meter, or other data readout device. The majority of systems employ a computer or microprocessor for data analysis and readout.

At present, the most efficient and economical detector for counting γ-ray emissions* is a sodium iodide [NaI(Tl)] scintillation detector. The characteristics of various NaI(Tl) counting systems are discussed in Sections A and B in this chapter. Scintillation counters for β particles and low-energy x rays or γ rays are presented in Section C later in this chapter. Counting systems based on gas detectors and semiconductor detectors are discussed in Sections D and E, respectively. Section F deals with counting systems for in vivo applications, including thyroid uptake, sentinel node detection, and intraoperative probes.

*In this chapter the term *γ-ray emission* also includes other forms of ionizing electromagnetic radiation (e.g., x rays, bremsstrahlung, and annihilation radiation).

A. NaI(Tl) WELL COUNTER

1. Detector Characteristics

The detector for a NaI(Tl) well counter is a single crystal of NaI(Tl) with a hole in one end of the crystal for the insertion of the sample (Fig. 12-1A). Dimensions of some commonly used well detectors are given in Table 12-1. The 4.5-cm diameter × 5-cm long crystal with 1.6-cm diameter × 3.8-cm deep well, the *standard well-counter* detector, is the most frequently used in nuclear medicine. It is designed for counting of samples in standard-size test tubes. Very large well-counter detectors, up to 13-cm diameter × 25-cm length, have been employed for counting very small quantities of high-energy γ-ray emitters (e.g., ^{40}K and ^{137}Cs). Most well-counter systems employ 5 cm or greater thickness of lead around the detector to reduce background counting levels. A typical manually loaded well-counter system is shown in Figure 12-1B.

Light transfer between the NaI(Tl) crystal and the photomultiplier (PM) tube is less than optimal with well-type detectors because of reflection and scattering of light by the well surface inside the detector crystal. Energy resolution is therefore poorer [10% to 15% full width at half maximum (FWHM) for ^{137}Cs] than obtained with optimized NaI(Tl) detector designs (approximately 6% FWHM) (see Chapter 10, Section B.7).

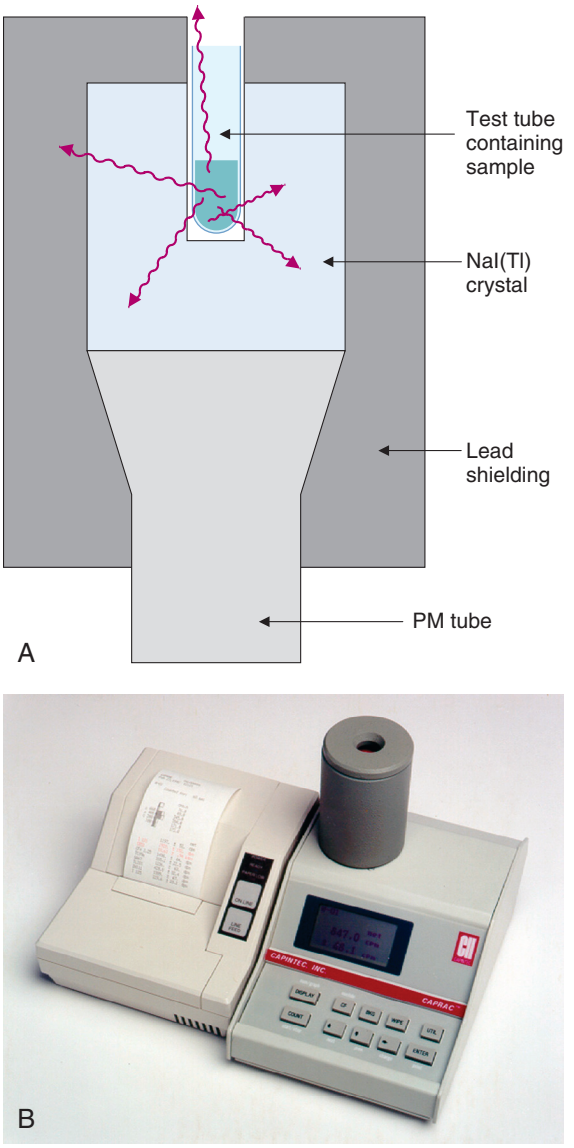


FIGURE 12-1 *A,* Cross-sectional view of a well-counter detector containing a radioactive sample. *B,* Photograph of a manually loaded well counter with a digital readout and printer output. (*Courtesy Capintec, Inc., Ramsey, NJ.*)

2. Detection Efficiency

The detection efficiency D (see Chapter 11, Section A) of the NaI(Tl) well counter for most γ-ray emitters is quite high, primarily because of their near 100% geometric efficiency g. The combination of high detection efficiency and low background counting levels makes the well counter highly suitable for counting samples containing very small quantities (Bq–kBq) of γ-ray-emitting activity. The geometric efficiency for small (≲1-mL) samples in the standard well counter is approximately 93% (see Fig. 11-3).

TABLE 12-1
DIMENSIONS OF TYPICAL NaI(Tl) WELL-COUNTER DETECTORS

Crystal Dimensions (cm)		Well Dimensions (cm)	
Diameter	Length	Diameter	Depth
4.5*	5.0*	1.6*	3.8*
5.0	5.0	1.6	3.8
7.6	7.6	1.7	5.2
10.0	10.0	3.8	7.0
12.7	12.7	3.8	7.0

*"Standard" well-counter detector.

The intrinsic efficiency ε (Equation 11-8) of well-counter detectors depends on the γ-ray energy and on the thickness of NaI(Tl) surrounding the sample; however, the calculation of intrinsic efficiency is complicated because different thicknesses of detector are traversed by γ rays at different angles around the source. Calculated intrinsic efficiencies (i.e., all pulses counted) versus γ-ray energy for 1-mL sample volumes and for different NaI(Tl) well-counter detectors are shown in Figure 12-2. Intrinsic efficiency is close to 100% for 1.3- to 4.5-cm wall thickness and $E_\gamma \lesssim 150$ keV, but at 500 keV the intrinsic efficiencies range from 39% to 82%.

Intrinsic efficiency can be used to calculate the counting rate per kBq for a radionuclide if all pulses from the detector are counted; however, if only photopeak events are recorded, then the *photofraction* f_p also must be considered (see Chapter 11, Section A.4). The photofraction decreases with increasing γ-ray energy and increases with increasing well-detector size (Fig. 12-3). At 100 keV, $f_p \approx 100\%$ for all detector sizes. At 500 keV, f_p ranges from 48% to 83% from the smallest to the largest common detector sizes (Table 12-1).

The *intrinsic photopeak efficiency* ε_p is the product of the intrinsic efficiency and photofraction

$$\varepsilon_p = \varepsilon \times f_p \qquad (12\text{-}1)$$

This may be used to estimate photopeak counting rates. Figure 12-4 shows ε_p versus γ-ray energy.

Table 12-2 lists some detection efficiencies, expressed as counts per minute (cpm) per becquerel, for full-spectrum counting of different

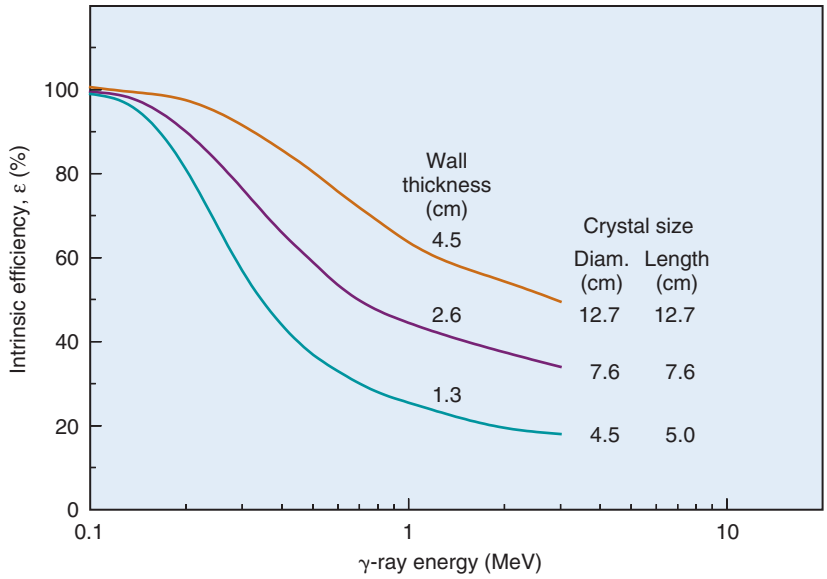


FIGURE 12-2 Intrinsic efficiency (γ-ray absorption efficiency, Equation 11-9) vs. γ-ray energy for different NaI(Tl) well-counter detectors.

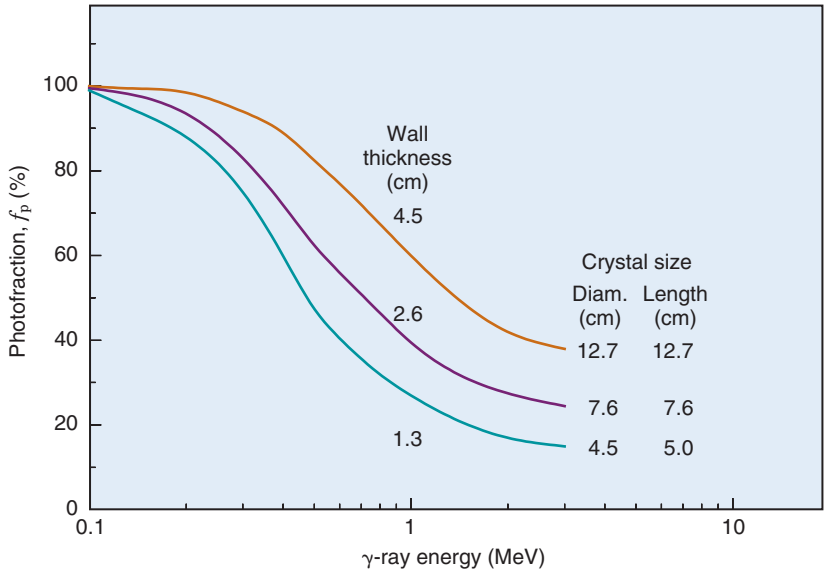


FIGURE 12-3 Photofraction versus γ-ray energy for different NaI(Tl) well-counter detectors.

radionuclides in the standard well counter. These values apply to 1-mL samples in standard test tubes.

3. Sample Volume Effects

The fraction of γ rays escaping through the hole at the end of the well depends on the position of the source in the well. The fraction is only about 7% near the bottom of the well but increases to 50% near the top and is even larger for sources outside the well. Thus the geometric efficiency of a well counter depends on sample positioning. If a small volume of radioactive solution of *constant activity* in a test tube is diluted progressively by adding water to it, the counting rate recorded from the sample in a standard well detector progressively decreases, even though total activity in the sample remains constant (Fig. 12-5). In essence, the geometric efficiency for the sample decreases as portions of the activity are displaced to the top of the well.

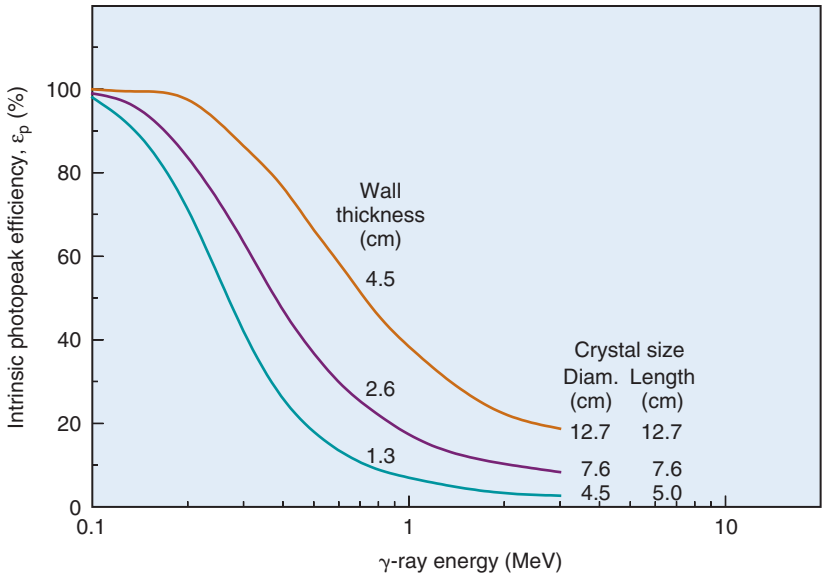


FIGURE 12-4 Intrinsic photopeak efficiency vs. γ-ray energy for different NaI(Tl) well-counter detectors.

TABLE 12-2
COUNTING EFFICIENCY FOR 1-mL SAMPLES IN A STANDARD SODIUM IODIDE WELL COUNTER (ASSUMING ALL PULSES COUNTED)

Radionuclide	γ-ray Energies (MeV) (% per Disintegration)	Counting Efficiency per Disintegration (%)	Counts per Minute per Becquerel
^{51}Cr	0.320 (8%)	4.3	2.6
^{60}Co	1.17 (100%) 1.33 (100%)	43	25.8
^{198}Au	0.411 (96.1%), 0.68 (1.1%), 1.09 (0.26%)	43.5	26.1
^{199}Au	0.051 (0.3%), 0.158 (41%), 0.209 (9%)	46	27.6
^{131}I	0.08 (2%), 0.28 (5%), 0.36 (80%), 0.64 (9%), 0.72 (3%)	48.3	28.9
^{59}Fe	0.19 (2.8%), 1.10(57%), 1.29 (43%)	27.3	16.4
^{203}Hg	0.073 (17%), 0.279 (83%)	67	40.3
^{42}K	1.53 (18%)	4.0	2.4
^{22}Na	0.511 (180%), 1.28 (100%)	81	48.6
^{24}Na	1.37 (100%), 2.75 (100%)	38	22.8

Adapted from Hine GJ: γ-ray sample counting. In Hine GJ (ed): *Instrumentation in Nuclear Medicine.* New York, 1967, Academic Press, p 282.

If the volume of a sample is increased by adding radioactive solution at a *constant* concentration, the counting rate first increases linearly with sample volume (or activity) but the proportionality is lost as the volume approaches and then exceeds the top of the well. Eventually there is little change with increasing sample volume, although the total activity is increasing (see Fig. 12-5). For example, an increase of sample volume in a standard test tube from 7 to 8 mL, a 14% increase in volume, increases the counting rate by only about 1%.

Thus sample volume has significant effects on counting rate with well counters. Sample volumes should be the same when comparing two samples. One technique that is used when adequate sample volumes are available is to fill the test tubes to capacity because with full test tubes, small differences in total volume have only minor effects on counting rate (curve B in Fig. 12-5); however, this requires

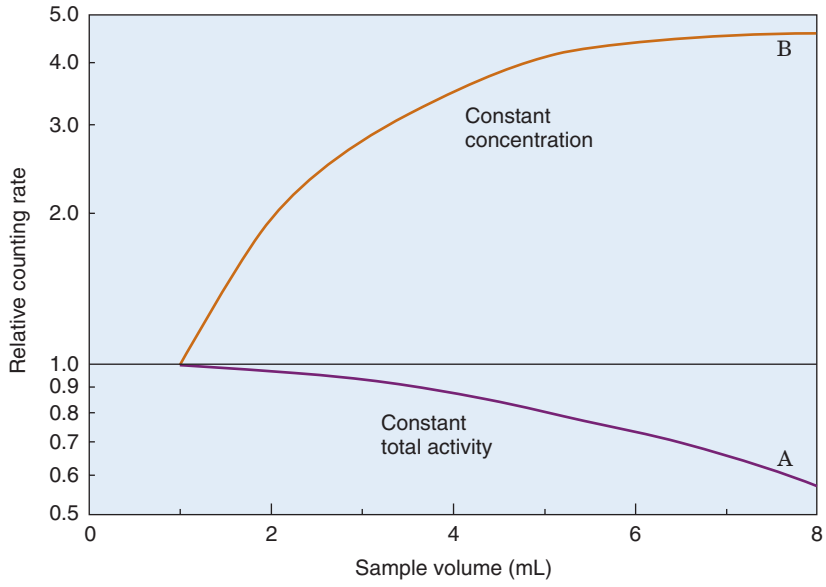


FIGURE 12-5 *A,* Change in counting rate in a standard NaI(Tl) well counter for a sample of constant *activity* but diluted to increasing sample volume in a test tube. *B,* Change in counting rate with volume for constant *concentration*.

that identical test tubes be used for all samples, so that the volume of activity inside the well itself does not differ between samples.

Absorption of γ rays within the sample volume or by the walls of the test tube is not a major factor except when low-energy sources, such as ^{125}I (27-35 keV) are counted. Identical test tubes and carefully prepared samples of equal volume should be used when comparing samples of these radionuclides.

4. Assay of Absolute Activity

A standard NaI(Tl) well counter can be used for assay of absolute activity (Bq or Bq/mL) in samples of unknown activity using the calibration data given in Table 12-2. Alternatively, one can compare the counting rate of the unknown sample to that of a calibration source (see Chapter 11, Section A.6). "Mock" sources containing long-lived radionuclides are used to simulate short-lived radionuclides, for example, a mixture of ^{133}Ba (356- and 384-keV γ rays) and ^{137}Cs (662-keV γ rays) for "mock ^{131}I." Frequently, such standards are calibrated in terms of "equivalent activity" of the radionuclide they are meant to simulate. Thus if the activity of a mock ^{131}I standard is given as "A(Bq) of ^{131}I," then the activity of a sample of ^{131}I of unknown activity X would be obtained from

$$X(\text{Bq}) = A(\text{Bq}) \times [R(^{131}\text{I})/R(\text{mock } ^{131}\text{I})] \quad (12\text{-}2)$$

where $R(^{131}\text{I})$ and R(mock ^{131}I) are the counting rates recorded in the well counter for the sample and the calibration standard, respectively.

Another commonly used mock standard is ^{57}Co (129 and 137 keV) for ^{99m}Tc (140 keV). If the ^{57}Co is calibrated in "equivalent Bq of ^{99m}Tc," then Equation 12-2 can be used for ^{99m}Tc calibrations also. If it is calibrated in becquerels of ^{57}Co, however, one must correct for the differing emission frequencies between ^{57}Co and ^{99m}Tc (0.962 γ rays/disintegration vs. 0.889 γ rays/disintegration, respectively). The activity X of a sample of ^{99m}Tc of unknown activity would then be given by

$$X(\text{Bq}) = A(\text{Bq}) \times [R(^{99\text{m}}\text{Tc})/R(^{57}\text{Co})] \times (0.962/0.889) \quad (12\text{-}3)$$

where A is the calibrated activity of the ^{57}Co standard and $R(^{99m}\text{Tc})$ and $R(^{57}\text{Co})$ are the counting rates recorded from the ^{99m}Tc sample and the ^{57}Co standard, respectively.

5. Shielding and Background

It is desirable to keep counting rates from background radiation as low as possible with the well counter to minimize statistical uncertainties in counting measurements (see Chapter 9, Section D.4). Sources of background include cosmic rays, natural radioactivity in the detector (e.g., ^{40}K) and surrounding

shielding materials (e.g., radionuclides of Rn, Th, and U in lead), and other radiation sources in the room. Additional sources of background in a hospital environment include patients who have been injected with radionuclides for nuclear medicine studies or for therapeutic purposes. These sources of radiation, although usually located some distance from the counter, can produce significant and variable sources of background. External sources of background radiation are minimized by surrounding the detector with lead. The thickness of the lead shielding is typically 2.5-7.5 cm; however, even with lead shielding it is still advisable to keep the counting area as free as possible of unnecessary radioactive samples.

In well counters with automated multiple-sample changers (Section A.9), it also is important to determine if high-activity samples are producing significant backgrounds levels in comparison with activity samples in the same counting rack. In many nuclear medicine procedures, background counting rates are measured between samples, but if the background counting rate becomes large (e.g., from a radioactive spill or contamination of the detector), it can produce significant statistical errors even when properly subtracted from the sample counting rate (see Chapter 9, Section D.4).

6. Energy Calibration

Energy selection in a well counter usually is accomplished by an SCA (Chapter 8, Section C.2). Commercial well-counter systems have push-button or computer selection of the appropriate SCA window settings for different radionuclides. In these systems compensation has been made by the manufacturer for the nonlinear energy response of the NaI(Tl) detector. However, because of the possibility of drifts in the electronics and the PM tube gain with time, the response of the well counter should be checked regularly with a long-lived standard source, such as ^{137}Cs, as a quality assurance measure. Some modern well counters incorporate MCAs, allowing the entire spectrum to be measured and analyzed.

7. Multiple Radionuclide Source Counting

When multiple radionuclides are counted simultaneously (e.g., from tracer studies with double labels), there is "crosstalk" interference because of overlap of the γ-ray spectra of the two sources, as shown in Figure 12-6 for ^{99m}Tc and ^{51}Cr. If SCA windows are positioned on the ^{99m}Tc (window 1) and ^{51}Cr (window 2)

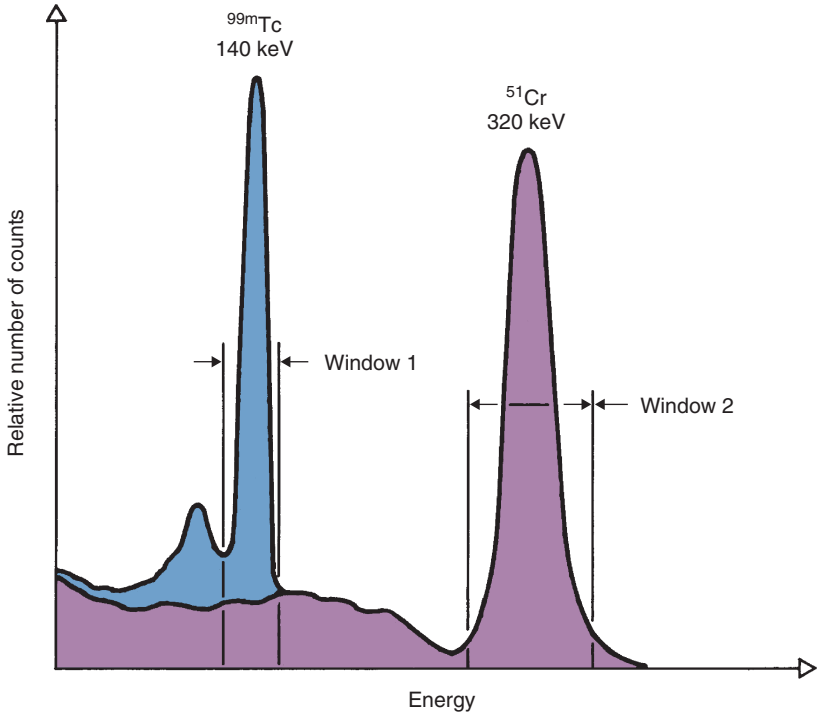


FIGURE 12-6 Window settings used for simultaneous measurement of ^{99m}Tc and ^{51}Cr in a mixed sample. Crosstalk from ^{51}Cr into the ^{99m}Tc window must be corrected for, using methods described in the text.

photopeaks, a correction for the interference can be applied as follows: A sample containing only ^{51}Cr is counted and the ratio R_{12} of counts in window 1 to counts in window 2 is determined. Similarly, a sample containing only ^{99m}Tc is counted and the ratio R_{21} of counts in window 2 to counts in window 1 is determined. Suppose then that a mixed sample containing unknown proportions of ^{99m}Tc and ^{51}Cr is counted and that N_1 counts are recorded in the ^{99m}Tc window (window 1) and that N_2 counts are recorded in the ^{51}Cr window (window 2). Suppose further that room and instrument background counts are negligible or have been subtracted from N_1 and N_2. Then the number of counts from ^{99m}Tc in window 1 [$N_1(^{99m}Tc)$] can be calculated from

$$N_1(^{99m}Tc) = (N_1 - R_{12}N_2)/(1 - R_{12}R_{21}) \quad (12\text{-}4)$$

and the number of counts from ^{51}Cr in window 2 [$N_2(^{51}Cr)$] from

$$N_2(^{51}Cr) = (N_2 - R_{21}N_1)/(1 - R_{12}R_{21}) \quad (12\text{-}5)$$

Equations 12-4 and 12-5 permit calculation of the number of counts that would be recorded in the photopeak window for each radionuclide in the absence of crosstalk interference from the other radionuclide. These equations can be used for other combinations of radionuclides and window settings with appropriate changes in symbols. For greatest precision, the ratios R_{12} and R_{21} should be determined to a high degree of statistical precision (e.g., ±1%) so that they do not add significantly to the uncertainties in the calculated results. The technique is most accurate when crosstalk is small, that is, R_{12} and/or $R_{21} \ll 1$. Generally, the technique is *not* reliable for the in vivo measurements described in Section F, because of varying amounts of crosstalk caused by Compton scattering within body tissue.

EXAMPLE 12-1

A mixed sample containing ^{99m}Tc and ^{51}Cr provides 18,000 counts in the ^{99m}Tc window and 8000 counts in the ^{51}Cr window. A sample containing ^{51}Cr alone gives 25,000 counts in the ^{51}Cr window and 15,000 crosstalk counts in the ^{99m}Tc window, whereas a sample containing ^{99m}Tc alone gives 20,000 counts in the ^{99m}Tc window and 1000 crosstalk counts in the ^{51}Cr window. What are the counts due to each radionuclide in their respective photopeak windows? Assume that background counts are negligible.

Answer

The crosstalk interference factors are, for ^{51}Cr crosstalk in the ^{99m}Tc window

$$R_{12} = 15{,}000/25{,}000 = 0.6$$

and for ^{99m}Tc crosstalk in the ^{51}C window

$$R_{21} = 1000/20{,}000 = 0.05$$

Therefore the counts in the ^{99m}Tc window from ^{99m}Tc in the mixed sample are (Equation 12-4)

$$\begin{aligned} N_1(^{99m}Tc) &= (18{,}000 - 0.6 \times 8000)/(1 - 0.6 \times 0.05) \\ &= 13{,}200/0.97 \\ &\approx 13{,}608 \text{ counts} \end{aligned}$$

and the counts in the ^{51}Cr window from ^{51}Cr are (Equation 12-5)

$$\begin{aligned} N_2(^{51}Cr) &= (8000 - 0.05 \times 18{,}000)/(1 - 0.6 \times 0.05) \\ &= 7100/0.97 \\ &\approx 7320 \text{ counts} \end{aligned}$$

8. Dead Time

Because NaI(Tl) well counters have such high detection efficiency, only small amounts of activity can be counted (typically 10^2 to 10^4 Bq). If higher levels of activity are employed, serious dead time problems can be encountered (see Chapter 11, Section C). For example, if the dead time for the system (paralyzable) is 4 μsec, and 50 kBq of activity emitting one γ ray per disintegration is counted with 100% detection efficiency, then the true counting rate is 50,000 cps; however, the recorded counting rate would be approximately 41,000 cps because of 18% dead time losses (see Equation 11-18).

9. Automated Multiple-Sample Systems

Samples with high counting rates require short counting times and provide good statistical precision with little interference from normal background radiation. If only a few samples must be counted, they can be counted quickly and conveniently using manual techniques; however, with long counting times or large numbers of samples, the counting procedures become time consuming and cumbersome. Systems with automated sample changers have been developed to alleviate this problem (Fig. 12-7). Typically, these systems can accommodate 100 or more

FIGURE 12-7 A NaI(Tl) well counter with automated sample-changing capabilities. Hundreds of samples can be loaded and measured in a single run. This system also incorporates a multichannel analyzer for spectral analysis. (*Courtesy PerkinElmer, Inc. Waltham, MA.*)

samples, and each sample is loaded automatically into the counter in a sequential manner.

Most multiple sample systems use a variation of the well-counter detector known as the *"through-hole" detector*. As shown in Figure 12-8, the sample hole passes through the entire length of the NaI(Tl) crystal, and the PM tube is connected to the side of the scintillator. A key advantage of the through-hole detector is that samples can be automatically positioned at the center of the NaI(Tl) crystal, irrespective of sample volume. This results in the highest detection efficiency and minimizes efficiency changes with volume. Figure 12-9 shows the smaller changes in efficiency with volume for a through-hole versus a well-type counter for ^{59}Fe.

Systems with automated sample changers not only save time but also allow samples to be counted repeatedly to detect variations caused by malfunction of the detector or electronic equipment or changes in background counting rates. Background counting rates can be recorded automatically by alternating sample and blank counting vials. In these

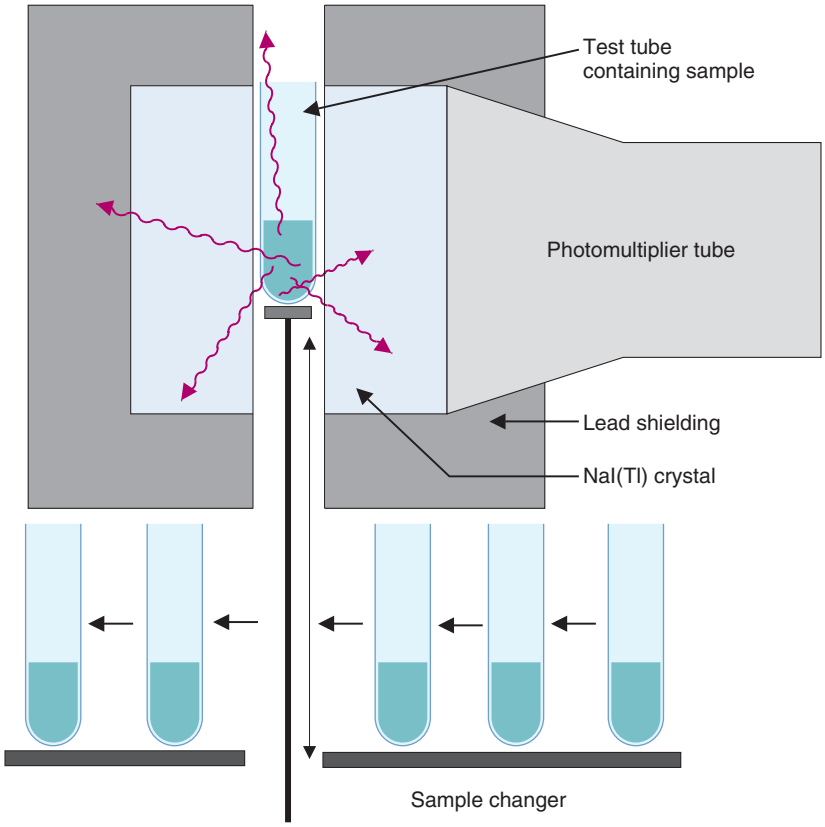


FIGURE 12-8 Schematic cross-sectional drawing of through-hole detector and sample-changing system. Placement of the sample can be automatically adjusted to center the sample volume in the detector.

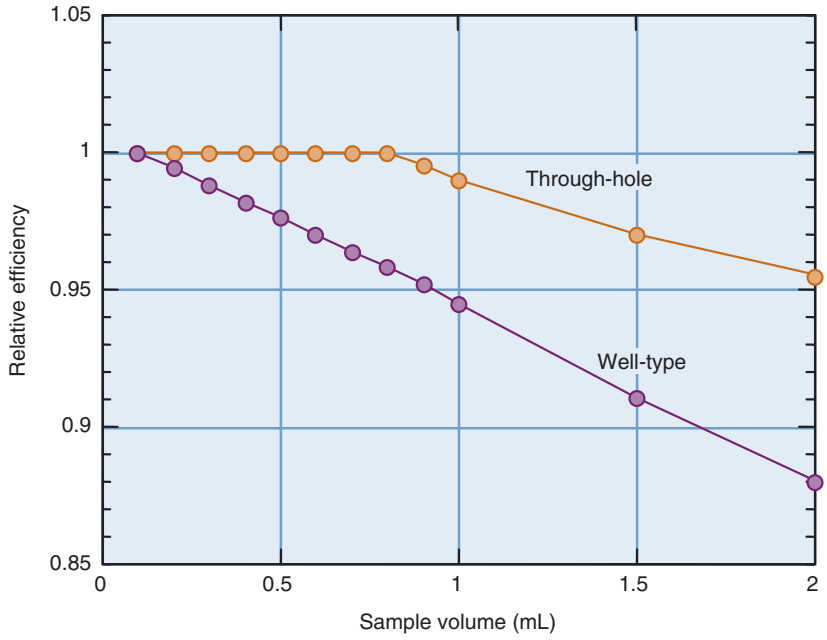


FIGURE 12-9 Efficiency of a well counter versus a through-hole counter for a constant total activity of ^{59}Fe. The efficiency of the through-hole detector shows less variation with sample volume because the sample can be centered in the detector. (*Adapted from Guide to Modern Gamma Counting. Packard Instrument Company, Meriden, CT, 1993.*)

systems, counting vials loaded into a tray or carriage are selected automatically and placed sequentially in the NaI(Tl) well counter. Measurements are taken for a preset time or a preset number of counts selected by the user. The well counter usually is shielded with 5 to 7.5 cm of lead, with a small hole in the lead shielding above and beneath the detector for insertion of the sample. One disadvantage of automated systems is that there is no lead shielding directly above or below the sample being counted. Therefore the system is not as well shielded as a manual well counter, which can cause an increase in background counting rates, particularly from other samples in the carriage. This can be a problem when low-activity samples are counted with high-activity samples in the carriage.

Commercial systems usually have MCAs or multiple SCAs to allow the selection of many different counting windows. The MCA also can be used to display the entire spectrum recorded by the NaI(Tl) detector on a computer. The displayed spectrum allows the user to inspect visually and select the positions of the single-channel windows for counting and to examine crosstalk interference when multiple radionuclides are counted simultaneously. It is also very useful for quickly and reliably checking to see if there are any significant photopeaks in the spectrum from background sources, which could indicate a radioactive spill or contamination, or for checking the general condition of the NaI(Tl) detector.

Modern well-counter systems are interfaced to computers or have dedicated circuits that control sample changing, placement and counting time, and perform corrections for radionuclide decay and background. Programs for spectral analysis and correction of multiple isotope samples are also generally available. All interactions with the well-counter system generally are through the keyboard, where the user selects from a range of predefined protocols and provides information regarding the radionuclide, desired counting time, and sample volume.

For very high throughput, there are even multidetector systems that may contain as many as 10 NaI(Tl) scintillation detectors. This permits 10 samples to be counted simultaneously and many hundreds or even thousands of samples to be counted per hour. The individual detectors are carefully separated and shielded from each other by lead to prevent crosstalk; however, when counting high-energy γ rays ($\gtrsim$300 keV) some crosstalk may occur. This is in addition to the source of crosstalk described in Section A.7, which occurs from the samples waiting to be counted in the sample changer system. Background

measurements in one detector while counting a sample in an adjacent detector can be used to estimate the magnitude of this crosstalk.

10. Applications

NaI(Tl) well counters are used almost exclusively to count x-ray or γ-ray-emitting radionuclides. Radionuclides with β emissions can be counted by detecting bremsstrahlung radiation, but the counting rate per becquerel is small because efficiency of bremsstrahlung production is very low (see Example 6-1). Well counters are used primarily for radioimmunoassays (e.g., measurement of thyroid hormones triiodothyronine and thyroxine), assay of radioactivity in blood and urine samples, radiochemical assays, and radiopharmaceutical quality control. They also are used for wipe tests (see Chapter 23, Section E.3) in radiation safety monitoring. Systems with multiple SCAs or MCAs allow multiple radionuclide sources to be counted simultaneously. These capabilities, combined with automated sample changing and automatic data processing, make the NaI(Tl) well counter an important tool for nuclear medicine in vitro assays.

B. COUNTING WITH CONVENTIONAL NaI(Tl) DETECTORS

1. Large Sample Volumes

The principal restriction on the use of most NaI(Tl) well counters is that they are useful only for small sample volumes (a few milliliters, typically) and small amounts of activity (≲100 kBq). For activities greater than approximately 100 kBq of most radionuclides, the counting rate becomes so high that dead time losses may become excessive. Large sample volumes and larger amounts of activity can be counted using a conventional NaI(Tl) detector with the sample at some distance from the detector. Placing the sample at a distance from the detector decreases the geometric efficiency (see Example 11-1) and allows higher levels of activity to be counted than with the well detector. The sample-to-detector distance can be adjusted to accommodate the level of activity to be measured. Typically, shielding from background sources with these arrangements is not as good as with the well counter because the front of the detector is exposed; however, owing to the high counting-rate applications of these systems, background counting rates usually are not significant unless there are other high-activity samples in the immediate vicinity.

The detection efficiency of a conventional detector depends on a number of factors, such as detector-to-sample distance, detector diameter, and sample size (see Chapter 11, Section A). If the sample-to-detector distance is large compared with the sample diameter, then usually the counting efficiency is relatively constant as the sample size is increased; however, this cannot always be assumed to be true, and sample size effects should be evaluated experimentally for specific counting conditions to be employed.

2. Liquid and Gas Flow Counting

NaI(Tl) detectors are used frequently as γ-ray monitors in conjunction with gas or liquid chromatographs. Chromatographs are used to separate and identify different chemical compounds by passing a gas or solution through columns containing beads that can selectively retain or control the rate of movement of different chemical species based on molecular size (gel filtration chromatography), net electric charge (ion exchange chromatography), or binding characteristics (affinity chromatography). By comparing the flow of radioactivity with the flow of chemical species, one can determine the radiochemical identity of different radioactive species (Fig. 12-10). The SCA typically is used to count only the photopeak to reduce background caused by scattered radiation from activity in the flow line outside the detector and in the chromatograph. MCAs or multiple SCAs also can be employed to detect multiple radionuclides simultaneously.

With simple systems the data output from the SCA is recorded with a ratemeter (digital or analog) and sent to some form of data recorder. With more sophisticated systems the data are collected with computers that have extended capability for data analysis.

C. LIQUID SCINTILLATION COUNTERS

1. General Characteristics

For *liquid scintillation* (LS) counting, the radioactive sample is dissolved in a scintillator solution contained in a counting vial and placed in a *liquid scintillation counter* (LSC) that consists of two PM tubes in a darkened counting chamber (Fig. 12-11). LSCs are used for counting β emitters, such as ^{3}H and ^{14}C, which would be strongly absorbed in the glass

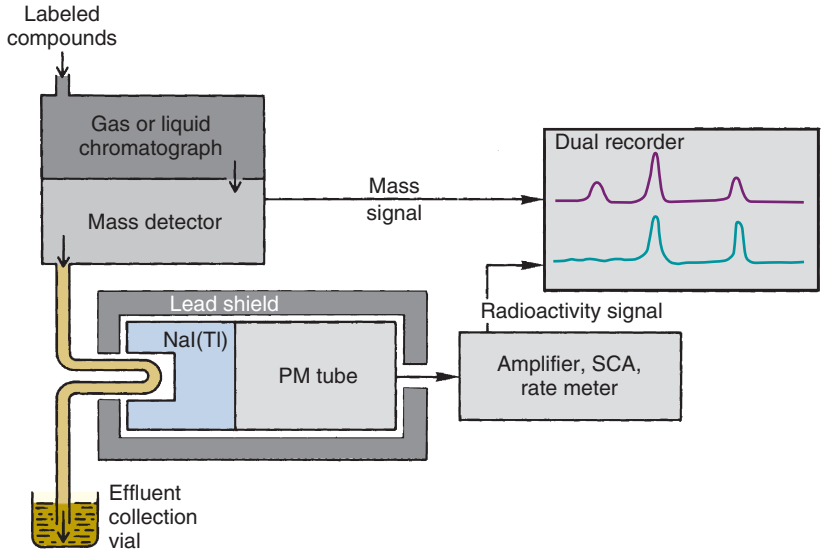


FIGURE 12-10 NaI(Tl) detector system used in conjunction with a gas or liquid chromatograph. The "mass detector" is used to detect chemical species, and the radiation detector is used to detect the radioactivity associated with these species for radiochemical identification.

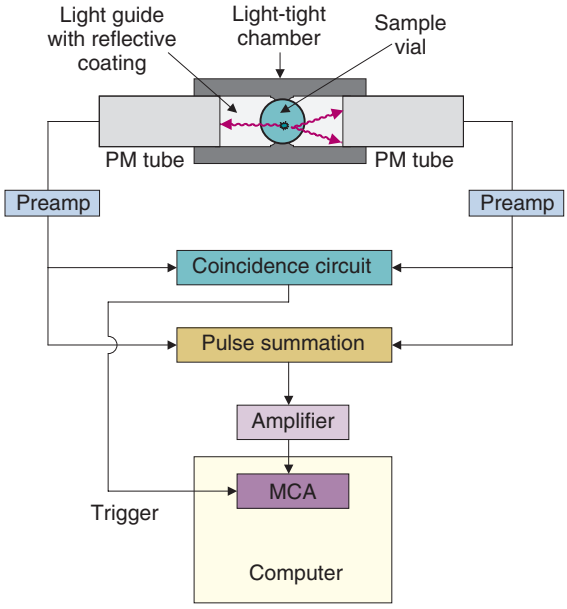


FIGURE 12-11 Basic components of a liquid scintillation counter.

or plastic of the test tube used to contain the sample in a standard well counter. They are also used for counting emitters of low-energy x rays and γ rays, which cannot be detected efficiently with NaI(Tl) detectors because of the thickness of canning material required around the detector.

The LS solution has a low atomic number ($Z \sim 6$ to 8) and density ($\rho \sim 1$) in comparison with other scintillators, such as NaI(Tl). However, this is sufficient for high-efficiency detection of low-energy x rays, γ rays, and β particles. Because the radioactivity is in direct contact with the scintillator, LS counting is the preferred method for the detection of low-energy β-emitting radionuclides, such as ^{3}H and ^{14}C. Numerous other β-emitting radionuclides, including some (β,γ) emitters, also are counted with a LSC (Table 12-3). Positron (β^+) emitters, however, are generally

TABLE 12-3
RADIONUCLIDES COMMONLY COUNTED WITH LIQUID SCINTILLATION DETECTORS

Radionuclide	Half-Life	Maximum β Energy (MeV)
^{3}H	12.3 yr	0.019
^{14}C	5700 yr	0.156
^{35}S	87.5 d	0.167
^{45}Ca	163 d	0.257
^{65}Zn	243 d	0.325
^{59}Fe	45 d	0.467
^{22}Na	2.6 yr	0.546
^{131}I	8.06 d	0.606
^{36}Cl	3×10^5 d	0.714
^{40}K	1.3×10^9 yr	1.300
^{24}Na	15.0 hr	1.392
^{32}P	14.3 d	1.711

counted in a standard well counter, because of the penetrating 511-keV γ rays produced from the annihilation (see Chapter 3, Section G) of positrons with electrons in the sample, or in the walls of the tube containing the sample.

Because LSC systems are used primarily to count very low-energy particles, the system must have very low electronic noise levels. For example, with ^{3}H, the energy range of the β particle is 0-18 keV. Under optimal conditions, β particles from ^{3}H decay produce only 0 to 25 photoelectrons at the PM tube photocathode, with an average of only about eight ($\bar{E}_\beta \approx 1/3E_\beta^{max}$). Background electronic noise is due mainly to spontaneous thermal emission of electrons from the photocathode of the PM tube. Background noise also is present from exposure to light of the scintillator solution during sample preparation. This exposure can produce light emission (phosphorescence), which persists for long periods (i.e., hours).

Several methods are employed in LS detectors to reduce this noise or background count rate. Thermal emission is reduced by refrigeration of the counting chamber to maintain the PM tubes at a constant low temperature (typically about −10° C). Constant PM tube temperature is important because the photocathode efficiency and electronic gain of the PM tube are temperature dependent, and variations in temperature produce variation in the amplitude of the output signal.

Pulse-height analysis also may be used to discriminate against noise because true radiation events usually produce larger signals than thermal emission noise; however, thermal emission noise still is superimposed on the radiation signals, which can cause deterioration of the energy resolution and linearity of the system.

The most effective reduction of noise is achieved by *coincidence detection* techniques (see Fig. 12-11). When a scintillation event occurs in the scintillator, light is emitted in all directions. Optical reflectors placed around the counting vial reflect the light into two opposing PM tubes to maximize light collection efficiency. Pulses from each of the PM tubes are routed to separate preamplifiers and a *coincidence circuit* (see Chapter 8, Section F). The coincidence circuit rejects any pulse that does not arrive simultaneously with a pulse from the other PM tube (i.e., within approximately 0.03 μsec). Noise pulses are distributed randomly in time; therefore the probability of two noise pulses occurring simultaneously in the two PM tubes is very small. Random coincidence rates R_r (cps) can be determined from

$$R_r = (2\tau)R_n^2 \qquad (12\text{-}6)$$

where 2τ is the resolving time of the coincidence circuit and R_n is the noise pulse rate for each PM tube (assumed to be equal) caused by PM tube noise and phosphorescence in the sample. For $2\tau = 0.03$ μsec and $R_n = 1000$ cps, one obtains $R_r = 3 \times 10^{-8} \times (10^3)^2 = 0.03$ cps. Thus most of the noise pulses are rejected by the coincidence circuit.

The output signals from the two PM tubes and preamplifiers are fed into the coincidence circuit as described earlier and also into a summation circuit, which adds the two signals together to produce an output signal proportional to the total energy of the detected event (see Fig. 12-11). The output signals from the summing circuit are sent to an amplifier to boost the signal, which is then digitized in an MCA. The output from the coincidence circuit is fed to the MCA to enable data collection only when both PM tubes have registered a pulse, thus rejecting noise. The MCA provides a spectrum of the energies of the detected events, which can be further processed by a computer, including routines for separating the counts from two radionuclides that are being counted simultaneously and for performing quench corrections as discussed in Section C.5.

2. Pulse-Height Spectrometry

Pulse-height analysis is used with LS counting to further reduce the background counting rate by selecting only the energy region corresponding to the radiation of interest or to select different energy regions when simultaneous sources are being counted. An example of *two-energy window analysis* for a source containing ^{3}H and ^{14}C is shown in Figure 12-12. Because of the continuous energy distribution in β decay, pulse-height analysis cannot separate completely the two spectra, and there is crosstalk interference. Methods to correct for this situation are discussed in Section C.4.

3. Counting Vials

Counting vials containing the radioactivity and the liquid scintillator solution usually are made of polyethylene or low-potassium-content glass. The low-potassium-content glass is used to avoid the natural background of ^{40}K. When standard laboratory glass vials (lime

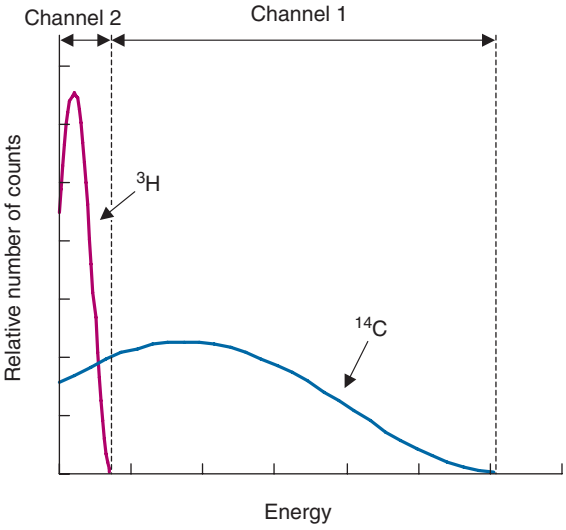


FIGURE 12-12 Example of pulse-height spectra obtained from ^{3}H and ^{14}C by liquid scintillation counting.

glass) are used, the background for ^{3}H and ^{14}C is increased by 30-40 cpm because of ^{40}K in the glass. Polyethylene vials frequently are used to avoid this problem and also to increase light transmission from the liquid scintillator to the PM tubes. Polyethylene vials are excellent for dioxane solvents but should not be used with toluene as the scintillator solvent because toluene will cause the vials to distort and swell, which may jam the sample changer. Materials such as quartz, Vicor, and others also are used for counting vials.

Exposure of the vial and liquid scintillator solution to strong sunlight produces a background of phosphorescence that may take hours to decay; therefore samples frequently are stored temporarily in a darkened container before counting. This is referred to as *dark adaptation* of samples.

4. Energy and Efficiency Calibration

Beta emission results in a continuous spectrum of β-particle energies from zero to a maximum β-particle energy E_β^{max} that is characteristic of the nuclide, with a mean value at approximately $\bar{E}_\beta \approx 1/3 E_\beta^{max}$. Usually, most of the β-particle spectrum lies above the electronic noise, allowing almost the entire spectrum to be used and resulting in detection efficiencies of 80% or higher. An exception is ^{3}H. The low-energy β emission of ^{3}H (E_β^{max} = 18 keV) reduces the counting efficiency to approximately 40% to 60% because some of the events produce pulses below typical noise pulse amplitudes that are rejected by pulse-height analysis (see Section C.1).

Modern LS counters have prestored calibrations that enable them to convert the detected cpm into disintegrations per minute for a wide range of radionuclides. These calibrations, however, depend on the material composition and thickness of the sample vial and on the effects of quenching, which are discussed in Section C.5).

Frequently, samples containing a mixture of two radionuclides (e.g., ^{3}H and ^{14}C) are counted. By selecting separate energy windows on each of the β spectra (see Fig. 12-12), the activities of each of the radionuclides can be determined. The optimal window for each radionuclide is determined individually by using separate ^{3}H and ^{14}C sources. If possible, the energy windows should be adjusted so that counts from the lower-energy emitter are not included in the window used for the higher-energy emitter. The method and equations used to correct for crosstalk interference—described in Section A.7 for well-counter applications—can be also used on the LS counter. There are also a number of increasingly sophisticated methods for dealing with samples containing radionuclides with very similar spectra. These methods are described in detail in reference 1.

5. Quench Corrections

Quenching refers to any process that reduces the amount of scintillation light produced by the sample or detected by the PM tubes. The causes of quenching in LS counting were described in Chapter 7, Section C.6. The principal effect of quenching is to cause an apparent shift of the energy spectrum to lower energies (Fig. 12-13). This results in a

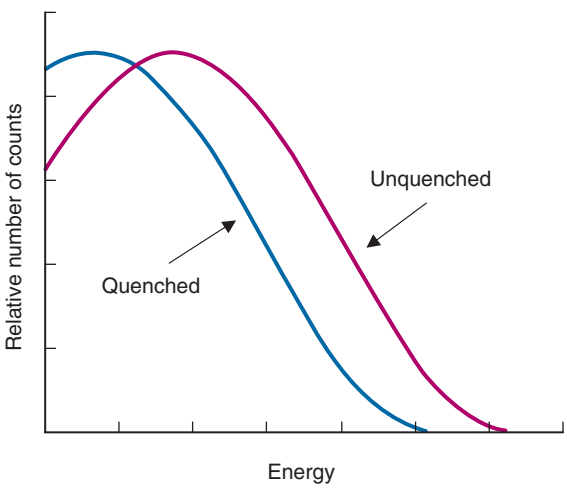


FIGURE 12-13 Effect of quenching on a liquid scintillation counter pulse-height spectrum.

loss of counts because events can either be shifted below the noise levels of the LS counter, or if pulse-height analysis is used, they may be shifted out of the energy window. Thus inaccurate counting rates are recorded. The error depends on the amount of quenching, which may vary from one sample to the next.

To obtain accurate results, it is necessary to correct the observed counting rate for quench-caused spectral shifts. Several methods have been developed.

With the *internal standardization method,* the sample-counting rate is determined; then a known quantity of the radionuclide of interest (from a calibrated standard solution) is added to the sample and it is recounted. The counting efficiency, ε_c, is calculated by

$$\varepsilon_c = \frac{\text{cps(standard + sample)} - \text{cps(sample)}}{\text{standard(Bq)}} \qquad (12\text{-}7)$$

From the efficiency, the activity of the sample is obtained from

$$\text{sample(Bq)} = \frac{\text{cps(sample)}}{\varepsilon_c} \qquad (12\text{-}8)$$

With internal standardization, the sample must be counted twice and the added activity of the standard must be distributed in the scintillator solution in the same manner as the sample. The method is not accurate if the sample and standard are not dissolved in the same way in the scintillator. Also, self-absorption of the emitted β particle by the labeled molecule might not be accounted for unless the standard is also in the form of the labeled molecule.

A second approach is called the *channel ratio method.* One channel is set to count an unquenched sample as efficiently as possible (i.e., channel 1 in Fig. 12-14), and a second channel is set to accumulate counts in the lower-energy region of the spectrum (channel 2 in Fig. 12-14). When the spectrum shifts to the left because of quenching, the lower channel gains counts, and the ratio of counts in the two channels changes. A series of standards of known activity are counted, each quenched deliberately a little more than the preceding one by adding a quenching agent, to obtain a quench curve relating counting efficiency (cps per becquerel) to the channel ratio. Then for subsequently measured samples, the channel ratio is used to determine the quench-corrected counting efficiency.

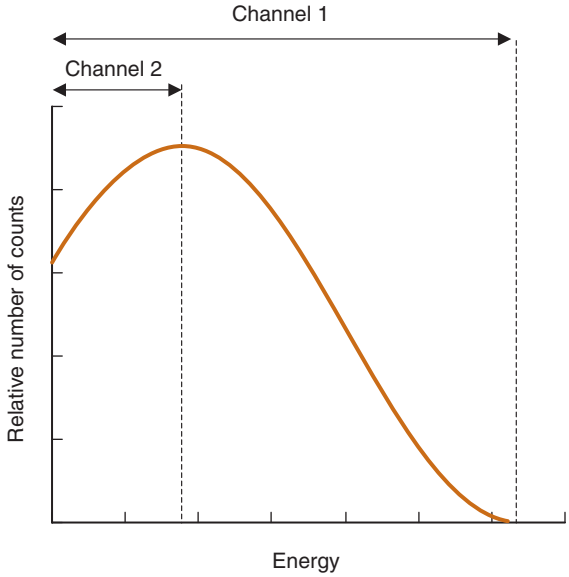


FIGURE 12-14 Setting of energy windows for quench corrections using the channel ratio method.

Once the correction curve has been obtained, only one (dual-channel) counting measurement per sample is required to determine counting efficiency. All causes of quenching are corrected by the channel ratio method. A disadvantage of the method is that at very low counting rates statistical errors in the value determined for the channel ratio can be large, which may result in significant errors in the estimated quench correction factor. Longer counting times may be employed to minimize this source of error.

A third approach is called the *automatic external standardization* (*AES*) *method*. This method incorporates features of both internal standardization and channel ratio. The sample is first counted and then recounted (usually for 1 min or less) with an external standard γ-ray source (usually ^{137}Cs) placed close to the sample (some counters count the sample plus standard first). Positioning of the standard is automatic. Compton recoil electrons produced by interactions of the γ rays with the scintillator solution are counted in two channels and a channel ratio determined, or

$$\text{AES (ratio)} = \frac{\text{cpm (sample + STD)} - \text{cpm sample channel 2}}{\text{cpm (sample + STD)} - \text{cpm sample channel 1}} \qquad (12\text{-}9)$$

where STD refers to the standard γ-ray source and channels 1 and 2 are as indicated in Figure 12-14.

A series of quenched standards containing known amounts of the radionuclide of interest is prepared, and counting efficiency is related to the AES ratio. The AES ratio is then used to correct for quenching on subsequently measured samples.

The external standard method generally provides a high counting rate and thus small statistical errors in the determination of the quench correction factor while maintaining the sensitivity of the channel ratio method for detecting quenching effects. The disadvantage of the AES method is that only chemical and color quenching are corrected; β-particle self-absorption effects or losses caused by sample distribution effects are not. For example, the AES method might not be accurate with multiphase solutions in which the sample is not soluble in the counting solution.

Representative AES quench curves and crosstalk correction factors are shown in Figure 12-15 for ^{14}C and ^{3}H for double-label studies, that is, both radionuclides counted simultaneously. It is apparent from Figure 12-15 that as quenching increases (AES ratio decreases), the efficiency for counting both ^{14}C and ^{3}H decreases. Thus even though the true efficiency may be determined accurately from the quench correction curve, counting efficiency deteriorates with increased quenching, resulting in increased statistical errors.

6. Sample Preparation Techniques

Samples can be combined with scintillator solution in several different ways, depending on the composition, state (liquid or solid) and polarity of the sample compound or material. The medium into which the sample is placed is known as the *LS cocktail,* of which there are two main groups: *Emulsifying cocktails,* also known as *aqueous cocktails,* consist of an organic aromatic solvent, an emulsifier and the scintillator. *Organic cocktails,* also known as *nonaqueous* or *lipophilic cocktails,* consist of an organic aromatic solvent and the scintillator.

Liquid scintillators were discussed in Chapter 7, Section C.6. The most popular and widely used is a combination of 2,5-diphenyloxazole (also known as PPO) and *p*-bis-(*o*-methylstyryl)benzene (abbreviated as bis-MSB). Traditional aromatic solvents include toluene and xylene, and although these are still used, they are gradually being replaced with more environmentally friendly solvents such as di-isopropylnaphthalene (DIN) and phenylxylylethane (PXE).

Most radionuclides are present in aqueous form and therefore are not readily miscible with aromatic solvents. Detergents or emulsifiers are used to form a microemulsion, in which the aqueous solution is dispersed in tiny droplets through the solvent. Commonly used

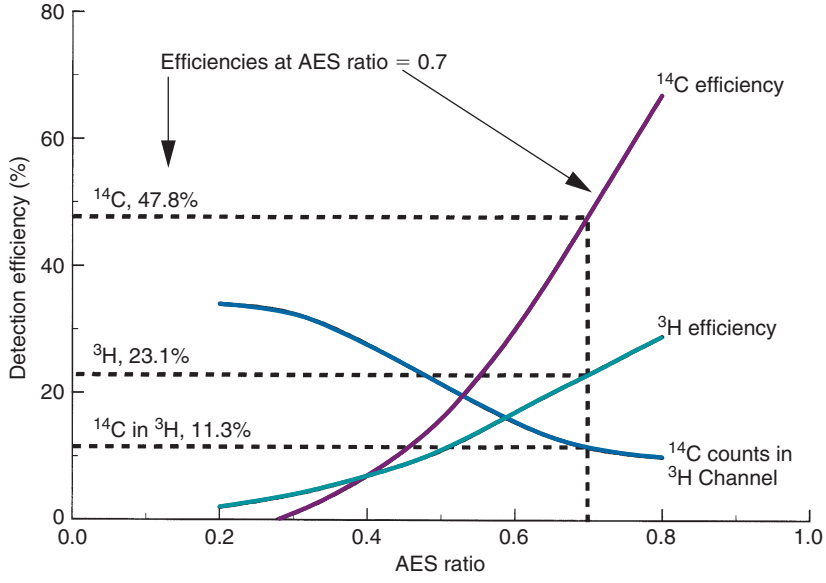


FIGURE 12-15 Representative quench correction curves based on the automatic external standardization (AES) method for counting mixed ^{14}C-^{3}H samples. For example, with an AES ratio of 0.7 (*vertical dashed line*) counts in the ^{3}H channel must first be corrected for ^{14}C crosstalk by 11.3% of the counts in the ^{14}C channel. The counting efficiency for the corrected ^{3}H counts is 23.1% and for the ^{14}C counts is 47.8% relative to an unquenched sample. Note that the AES ratio decreases with increasing quenching.

detergents include the alkyl phenol ethoxylates, alkyl and alkylaryl sulfonates, alcohol sulfates, and phosphate esters. Polar compounds also can be used by forming insoluble suspensions. For example, $^{14}CO_2$ can be precipitated as barium carbonate and then suspended in the scintillator solution with the addition of thixatropic jelling agents. Silica gels from thin-layer chromatography also can be counted in this manner. Samples deposited on filter paper such as from paper chromatography frequently are counted by placing the paper strip in the liquid scintillator. The scintillator solution also can be dissolved or suspended in the sample itself.

Another straightforward approach to counting complicated organic compounds such as proteins or sections of acrylamide gel columns with high efficiency is to combust the sample. The $^{14}CO_2$ and $^{3}H_2O$ released may be collected, dissolved in scintillator solution, and then counted.

Numerous other techniques have been developed for LS sample preparation. More discussion of these techniques is presented in reference 1. Careful sample preparation is critical for accurate application of the LS technique.

7. Cerenkov Counting

High-energy beta emitters may also be assayed in LSC systems without the use of a liquid scintillator solution by detecting optical Cerenkov radiation (see Chapter 6, Section A.5). Beta particles with an energy in excess of 263 keV will produce Cerenkov light in a water solution, which can be detected by the PM tubes in a LSC system. The calibration of the LSC system for measuring activity from the detected Cerenkov light must account for the directionality of the light cone produced and the spectral characteristics of the Cerenkov light, which is weighted toward the blue end of the visible spectrum. Because the production of Cerenkov light is a physical phenomenon, there is no chemical quenching of the signal. However, color quenching still must be accounted for. Cerenkov counting is used primarily to measure samples containing ^{32}P (E_β^{max} = 1710 keV) in which the counting efficiency can be in excess of 50%.

8. Liquid and Gas Flow Counting

In addition to counting individual samples, LSC systems also can be used for continuous monitoring of gas streams or flowing liquids. In these systems, the vial of LS solution is replaced with a cell filled with finely dispersed solid scintillator crystals through which the radioactively labeled gas or liquid is allowed to flow. The most common scintillator material for this purpose is the organic scintillator anthracene. This technique is used primarily for β-emitting radionuclides, typically ^{14}C and ^{3}H. The β particles interact with the anthracene crystals, and the resulting scintillation is detected in the same manner as from the LS vial.

These systems have been used for monitoring the effluent from amino acid analyzers, liquid chromatographs, and gas chromatographs. To monitor the effluent from gas chromatographs, the compounds usually are passed through a gas combustion furnace to convert them into $^{14}CO_2$ or $^{3}H_2O$ (vapor). Carrier gas from the gas chromatograph (e.g., He) is used to sweep the $^{14}CO_2$ or $^{3}H_2O$ through the counting cell.

Counting rates in these systems depend on the activity concentration and the flow rate. If fast flow rates and low-activity concentrations are required, the result may be data of poor statistical quality. Data from flow counting represent the time course of some process and usually are displayed as time-activity curves.

9. Automated Multiple-Sample LS Counters

LSC may be used for counting large numbers of samples or for counting low-level samples for long counting times. To expedite this and to remove the tedious job of manually counting multiple samples, automated multiple-sample LSC systems have been developed. These systems have automated sample changers that frequently can handle 100 or more counting vials (Fig. 12-16). A number of

FIGURE 12-16 A liquid scintillation counter with automated sample loading can efficiently count and analyze hundreds of samples. (*Courtesy Beckman Coulter, Inc., Brea, CA.*)

different sample-changing mechanisms have been developed, but the most common ones employ either trays or an endless belt for transport of the samples. Sample vials are selected automatically and loaded into the light-tight LS counting chamber. The samples are counted sequentially in serial fashion. Empty positions in the sample changer can be bypassed, and samples below a selectable low-level counting rate may be rejected automatically to avoid long counting times on samples that contain an insignificant amount of activity when preset counts are selected.

Modern automated multiple-sample LSC systems are provided with many different ways of handling and presenting the recorded data. Computer-based systems allow automatic implementation of quench corrections, efficiency corrections, background subtraction, statistical analysis, and calculations of parameters for radioimmunoassay or other assay analysis.

10. Applications

LSC systems are used in nuclear medicine for radioimmunoassays and protein-binding assays of drugs, hormones, and other biologically active compounds. LSC systems also are commonly used in studies of metabolic or physiologic processes with ^{3}H-or ^{14}C-labeled metabolic substrates or other physiologically important molecules. They are also used for wipe tests for radiation-monitoring purposes (see Chapter 23, Section E.3).

D. GAS-FILLED DETECTORS

1. Dose Calibrators

Although they are inefficient detectors for most γ-ray energies encountered in nuclear medicine, gas-filled detectors still find some specialized applications. A dose calibrator is essentially a well-type ionization chamber that is used for assaying relatively large quantities (i.e., MBq range) of γ-ray-emitting radioactivity (Fig. 12-17). Dose calibrators are used for measuring or verifying the activity of generator eluates, patient preparations, shipments of radioactivity received from suppliers, and similar quantities of activity too large for assay with NaI(Tl) detector systems.

The detector for a dose calibrator typically is an argon-filled chamber, sealed and pressurized to avoid variations in response with ambient barometric pressure (see Chapter 7, Section A.2). Ionization chamber

FIGURE 12-17 An ionization chamber dose calibrator. Samples are inserted into the well in the sealed ionization chamber. The current is measured and displayed on a digital readout. (*Courtesy Biodex Medical Systems, Shirley, NY.*)

dose calibrators assay the total amount of activity present by measuring the total amount of ionization produced by the sample. Plug-in resistor modules, pushbuttons, or other selector mechanisms are used to adjust the electrometer readout to display the activity of the selected radionuclide directly in MBq or kBq units. Because ionization chambers have no inherent ability for energy discrimination, they cannot be used to select different γ-ray energies for measurement, as is possible with detectors having pulse-height analysis capabilities. One approach that is used to distinguish low-energy versus high-energy γ-ray emitters (e.g., ^{99m}Tc vs. ^{99}Mo) is to measure the sample with and without a few millimeters of lead shielding around the source. Effectively, only the activity of the high-energy emitter is recorded with the shielding in place, whereas the total activity of both emitters is recorded with the shielding absent. This technique can be used to detect tens of kBq quantities of ^{99}Mo in the presence of tens or even hundreds of MBq of ^{99m}Tc.

As with the NaI(Tl) well counter, dose calibrators are subject to sample volume effects (see Section A.3). These effects should be investigated experimentally when a new dose calibrator is acquired, so that correction factors can be applied in its use, if necessary. For example, a quantity of activity can be measured in a very small volume (e.g., 0.1 mL in a 1-mL syringe), and that activity can be diluted progressively to larger volumes in larger syringes and then in beakers, and so forth to determine the amount by which the

instrument reading changes with sample volume.

Another parameter worth evaluating is linearity of response versus sample activity. This may be determined conveniently by recording the reading for a ^{99m}Tc source of moderately high activity (e.g., 1 GBq, or whatever the approximate maximum amount of activity the dose calibrator will be used to assay), then recording the readings during a 24- to 48-hour period (4-8 half-lives) to determine whether they follow the expected decay curve for ^{99m}Tc. Deviations from the expected decay curve may indicate instrument electronic nonlinearities requiring adjustment or correction of readings. In applying this technique, it is necessary to correct for ^{99}Mo contamination using the shielding technique described earlier, especially after several ^{99m}Tc half-lives have elapsed.

2. Gas Flow Counters

Gas-filled detectors also are used in gas flow counters, primarily for measurement of β-emitting activity. The detector in these systems usually can be operated in either proportional counter or Geiger-Müller mode. The most frequent application for these systems in nuclear medicine is for monitoring the effluent from gas chromatographs. Gases labeled with ^{3}H or ^{14}C in helium carrier gas from the chromatograph are passed through a combustion furnace to convert them to $^{3}H_2O$ or $^{14}CO_2$, which then is allowed to flow through the counter gas volume itself with the counting gas (usually 90% He plus 10% methane). This permits a time-course analysis of the outflow from the chromatograph. These systems have good geometric and intrinsic detection efficiencies for low-energy β emitters, such as ^{3}H and ^{14}C; however, their intrinsic efficiency for γ-ray detection is only approximately 1%. Gases labeled with β emitters are therefore analyzed using NaI(Tl) detectors.

E. SEMICONDUCTOR DETECTOR SYSTEMS

1. System Components

Semiconductor detectors [germanium (Ge) and silicon (Si)] (see Chapter 7, Section B) created revolutionary advances in nuclear physics, nuclear chemistry, radiation chemistry, nondestructive materials analysis (e.g., x-ray fluorescence and neutron activation), and other fields. To date, however, they have had limited effect on nuclear medicine. Their disadvantages of small size and high cost outweigh their advantage of superior energy resolution in comparison with other detection systems [e.g., NaI(Tl)] for general-purpose applications; however, the energy resolution of semiconductor detectors allows the separation of γ rays differing in energy by only a few keV as opposed to 20-80 keV with NaI(Tl) (Fig. 12-18; see also Fig. 10-14). Therefore in applications in which energy resolution is the critical factor and the relatively small size of the semiconductor detector is not completely restrictive, Ge or Si detectors are the system of choice.

Semiconductor detectors are used extensively as charged-particle and γ-ray spectrometers in physics. Their principal application in nuclear medicine is for assessment of radionuclide purity. Si has a lower atomic number and density than Ge and therefore a lower intrinsic detection efficiency for γ rays with energies $\gtrsim$40 keV (see Chapter 11, Section A.3). Thus Si detectors are used primarily for detection of low-energy x rays and Ge, cadmium telluride (CdTe), and cadmium zinc telluride (CZT) are used for γ rays.

The basic configuration of a semiconductor system for in vitro analysis is shown in Figure 7-12. Except for a special low-noise high-voltage supply, preamplifier, and amplifier, the system components are the same as those of NaI(Tl) counting systems. Usually an MCA is employed rather than an SCA with semiconductor detectors because the detectors most commonly are used to resolve complex spectra of multiple emissions and multiple radionuclides (see Fig. 12-18).

The superior energy resolution of semiconductor detectors may result in a significant advantage in sensitivity [i.e., minimum detectable activity (MDA)] (see Chapter 9, Section D.5) in comparison with NaI(Tl) detectors for some applications. MDA depends on the ratio $S/\sqrt{B}$, in which S is the net sample counting rate and B is the background counting rate. Because the energy resolution of a semiconductor detector is 20 to 80 times better than NaI(Tl), a photopeak window 20 to 80 times narrower can be used, resulting in typically 20 to 80 times smaller background counting rate. Considering background alone, then, the MDA for a semiconductor detector could be a factor $\sqrt{20}$ to $\sqrt{80}$ smaller than a NaI(Tl) detector of comparable size. This advantage is partially offset by the larger available detector sizes with NaI(Tl) and,

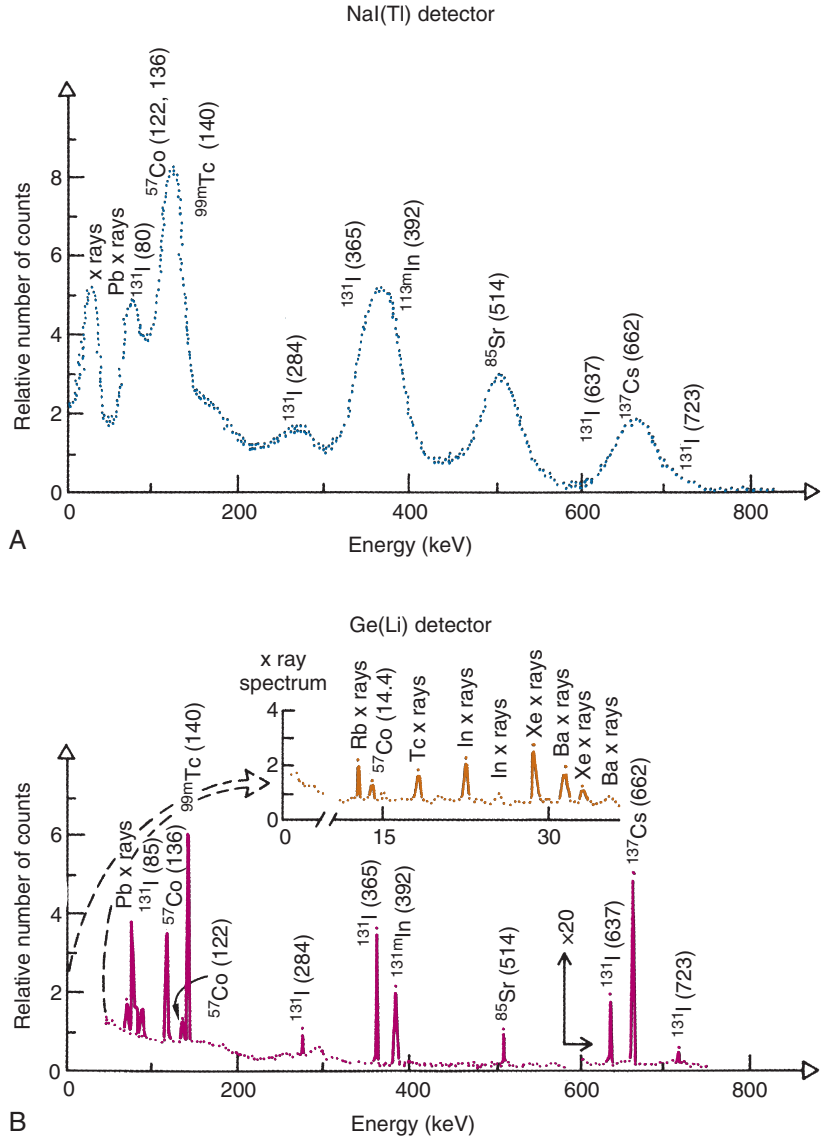


FIGURE 12-18 Comparative pulse-height spectra of a mixed radionuclide sample recorded with NaI(Tl) (*A*) and Ge(Li) (*B*) detectors. Because of its superior energy resolution, the Ge(Li) detector clearly resolves multiple γ rays and x rays of similar energies that appear as single peaks with NaI(Tl).

above approximately 200 keV, by the greater intrinsic photopeak efficiency of NaI(Tl) for comparable detector thicknesses (see Chapter 11, Section A.3); however, for lower-energy γ rays, measured in a configuration having a high geometric efficiency (e.g., sample placed directly against the detector), there is usually an advantage in MDA favoring the semiconductor detector. For higher-energy γ rays, CdTe or CZT semiconductors provide the advantage of both excellent energy resolution and good photopeak efficiency, although the cost per unit detector volume is much higher than NaI(Tl), limiting them to situations in which small detector sizes are acceptable.

2. Applications

The major in vitro applications of semiconductor detectors in nuclear medicine have been for tracer studies employing many radionuclides simultaneously and for the assay of radionuclidic purity of radiopharmaceuticals. In both of these applications the superior energy resolution of semiconductor detectors, illustrated by Figure 12-18, offers a distinct advantage. The energy resolution of the Ge

detector allows unequivocal identification of radionuclides, whereas the NaI(Tl) spectrum is ambiguous. Another application of semiconductor detectors is for analysis of samples in neutron activation analysis.

F. IN VIVO COUNTING SYSTEMS

In vivo counting systems are used to measure radioactive concentrations in patients and, occasionally, in experimental animals. Systems designed to monitor radioactivity in single organs or in localized parts of the body are called *probe systems.* For example, *single-probe* systems, employing only one detector, are used for measuring thyroidal uptake of radioactive iodine and for sentinel node detection in breast cancer. *Multiprobe* systems, although less common, have been used for renal function studies, for lung clearance studies, for obtaining washout curves from the brain, and so forth. Probe systems provide some degree of measurement localization but without the detail of imaging techniques discussed in Chapters 13-19. Because the radiation must in general pass through several centimeters of soft tissue to reach the detector, most in vivo counting systems are designed to detect γ rays.

1. NaI(Tl) Probe Systems

The simplest probe system consists of a collimated NaI(Tl) detector mounted on a stationary or mobile stand that can be oriented and positioned over an area of interest on the patient (Fig. 12-19). Such detectors are commonly used in diagnostic tests for thyroid disease. The detector is connected to the usual NaI(Tl) electronics, including an SCA for energy selection and a digital counter or computer that records the number of counts per second. A typical probe system employs a 5-cm diameter × 5-cm thick NaI(Tl) crystal, with a cylindrical or conically shaped collimator, 15-25 cm long, in front of the detector.

When calibrating a probe system for in vivo measurements, it is important to account for the effects of attenuation and scatter on the recorded counting rate (see Chapter 11, Section A.5). Usually, the depth of the source distribution within the patient is not known accurately. Because the linear attenuation coefficient for soft tissue is in the range μ_l = 0.1 to 0.2 cm^{-1} for most γ-ray energies in nuclear medicine, a 1- to 2-cm difference in source depth can result in a 10% to 40% difference in recorded counting rate. The intensity of scattered radiation is another important variable. For example, a source lying outside the direct field-of-view of the collimator can contribute to the recorded counting rate by Compton scattering in the tissues surrounding the source distribution. To minimize the contribution from scattered radiation, measurements usually are made with the SCA window set on the photopeak of the γ-ray emission to be counted. Even this is not completely effective for eliminating all the variable effects of scattered radiation on the measurement, however, especially when low-energy γ rays are counted (see Figs. 10-6 and 10-10).

FIGURE 12-19 Typical NaI(Tl) probe system for measuring thyroid uptake of radioactive iodine. (*Courtesy Capintec, Inc., Ramsey, NJ.*)

2. Miniature γ-Ray and β Probes for Surgical Use

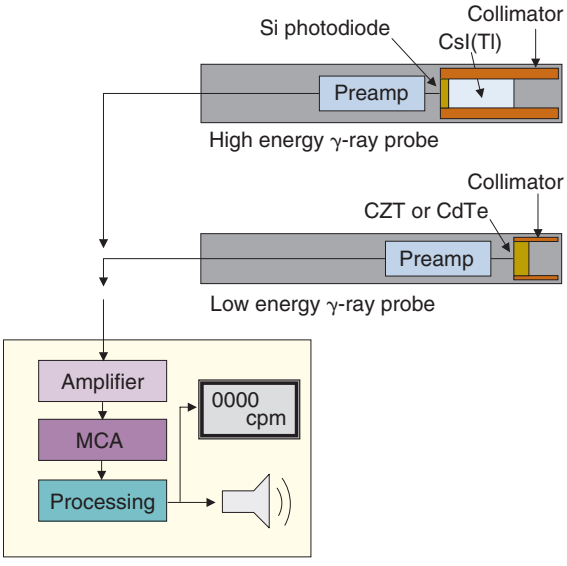
Miniature, compact γ-ray probes are designed for use in conjunction with surgical procedures, primarily in cancer applications. The most important application is the detection of the *sentinel lymph node* in patients with

breast cancer and melanoma. The sentinel node is the most likely initial site for metastatic spread of the cancer; thus biopsy of the sentinel node is important for patient management. The sentinel node is identified by direct injection of a ^{99m}Tc-labeled *colloid* (a suspension of fine particles labeled with ^{99m}Tc) into the tumor. This colloid is trapped in the first lymph node draining the tumor. During surgery, the γ-ray probe is used to identify the sentinel node, from which a biopsy sample is taken and sent to a pathology laboratory for analysis.

The second broad class of applications is in radioguided surgery. Here, tumor-seeking radiopharmaceuticals are injected into the patient. The radiopharmaceutical agent is designed to target and bind to cancer cells with high selectivity. After waiting for an appropriate length of time for selective uptake of the radiopharmaceutical agent into the tumor, the patient goes to surgery and the surgeon uses the γ-ray probe to assist in locating and removing the cancerous tissue, while sparing as much healthy tissue as possible. This procedure has been applied in parathyroid surgery and colorectal cancer, and in detecting lymph node involvement for a range of other cancers.

The requirements for γ-ray probes for intraoperative use are that they have high efficiency (so that radiolabeled tissue can be found quickly in the surgical environment), that they be lightweight and easy to use, and that they pose no hazard to the patient. The probe of choice for high-energy γ emitters, such as ^{111}In, ^{131}I, and ^{18}F, is a scintillation detector. A typical probe consists of a 5-mm diameter × 10-mm high cesium iodide [CsI(Tl)] scintillator crystal, coupled to a Si photodiode. The Si photodiode is a light-sensing semiconductor detector that replaces the PM tube found in conventional scintillation detectors and converts the scintillation light into an electrical signal (see Chapter 7, Section C.3). It is preferred in this application because of its compact size and low weight compared with a PM tube. CsI(Tl) is used in place of NaI(Tl) as the scintillator because its emission wavelengths are better matched to the spectral response of the Si photodiode. For lower-energy γ emitters, such as ^{99m}Tc, a semiconductor detector made from CZT or CdTe (see Chapter 7, Section B) that directly converts the γ rays to electric charge is typically used. This is an ideal application for these semiconductor detectors, because the required detector area is small. CZT and CdTe are better for this application than Si or Ge because they have higher stopping power for γ rays and can be operated at room temperature. A small collimator is used in front of the probe to provide directionality.

Figure 12-20 shows the components of a typical γ-ray probe system. The output signals from the probes are amplified and sent to an MCA. Discriminator levels are set automatically for each different radionuclide. The counting rate is presented on a digital display. Many systems also have an audible output proportional to the counting rate. The whole unit is battery powered and can run for many hours on a single charge, eliminating the need for power cords. Wireless probes also are



A

B

FIGURE 12-20 *A,* Schematic representation of γ-ray probes for intraoperative use. *B,* Four different wireless gamma probes shown with control unit. The geometry of the probes are tailored to suit specific clinical applications. (*Figure B courtesy IntraMedical Imaging, Los Angeles, CA.*)

available, further facilitating their use in the surgical environment. References 2 and 3 provide a detailed review of counting probe systems for intraoperative use.

Probes for β-particle detection also have been developed. These are typically used in conjunction with tumor-seeking, positron-emitting radiopharmaceuticals to aid in locating tumors during surgery or to map tumor margins during surgical resection, helping to ensure that the tumor is completely removed while sparing normal tissue. They differ from the γ-ray probes described previously in that these probes directly detect β^+ particles (positrons) rather than the 511-keV annihilation photons. Because of the short range of positrons in tissue (see Chapter 6, Section B.2), they can only detect radioactivity that is very superficial (1-2 mm) at the surgical site, but have the advantage over γ-ray probes of being very insensitive to radioactivity that may be contained in adjacent tissues and organs and that could interfere with the local measurement.

3. Whole-Body Counters

Another class of in vivo measurement systems are *whole-body counters,* which are designed to measure the total amount of radioactivity in the body, with no attempt at localization of the activity distribution. Many (but not all) of these systems employ NaI(Tl) detectors. They are used for studying retention, turnover, and clearance rates with nuclides such as ^{60}Co and ^{57}Co (labeled vitamin B_{12}), ^{24}Na, ^{42}K, ^{47}Ca, and ^{59}Fe. Most of these radionuclides emit high-energy γ rays, and several have quite long half-lives. Thus it is important that a whole-body counter have good detection efficiency, so that very small amounts of activity ($\lesssim$50 kBq) can be detected and measured accurately.

Another application for whole-body counting is the measurement of naturally occurring ^{40}K, which can be used to estimate total-body potassium content. This is another high-energy γ emitter present in very small quantities, requiring good detection efficiency for accurate measurement. Whole-body counters also are used for detecting and monitoring possible accidental ingestion of radioactive materials.

Most whole-body counters employ relatively large NaI(Tl) detectors, 15 to 30 cm in diameter × 5 to 10 cm thick, to obtain good geometric efficiency as well as good intrinsic efficiency for high-energy γ rays. Several such detectors may be employed. Also the "counting chamber" is well shielded with lead, concrete, steel, and other materials to obtain minimal background levels, thus ensuring minimum statistical error caused by background counting rates (see Chapter 9, Section D.4). Shielding materials are selected carefully for minimum contamination with background radioactivity.

REFERENCES

A detailed reference on in vitro counting systems is the following:

1. L'Annunciata MF: *Handbook of Radioactivity Analysis*, ed 2, San Diego, 2003, Academic Press.

The design and application of miniature γ probes for surgical use are reviewed in detail in the following:

2. Hoffman EJ, Tornai MP, Janacek M, et al: Intraoperative probes and imaging probes. *Eur J Nucl Med* 26:913-935, 1999.
3. Povoski SP, Neff RL, Mojzisik CM, et al: A comprehensive overview of radioguided surgery using gamma detection probe technology. *World J Surg Oncol* 7:11, 2009.