PRECISE GEOMETRY-INDEPENDENT RADIOASSAY OF LARGE BIOLOGICAL SAMPLES

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Precise, quantitative radioassay of large intact biological samples with various sizes and shapes has always presented many technical problems. Self-absorption of gamma rays, nonhomogeneous distribution of the radioisotope and variations in sample size and shape are common variables that reduce the accuracy of radioassaying intact, large-volume biological samples. Consequently, these measurements are only approximate estimates rather than precise values as usually assumed. The instrument and counting method described here let one radioassay samples of various shapes, sizes (up to at least 500 ml) and nonhomogeneous radioisotope distribution. The results approximate expected statistical counting error. Common types of samples that can be assayed intact with no sample preparation are small live laboratory animals and individual stool or urine samples. The sample size can vary from that of a point source to at least 500 ml without requiring correction for size or shape, providing the greatest sample dimension is less than 15 cm.

DESCRIPTION OF INSTRUMENT

The instrument, an opposed-head counter, consists of two matched 2 × 1-in. NaI(Tl) crystal detectors and photomultipliers that are connected in parallel to a pulse-height spectrometer, as shown in the block diagram (Fig. 1). The detectors are opposed, one above the other, and the crystal faces are separated by 63 cm. This distance minimizes inverse-square effects while retaining an acceptable sensitivity. The detectors are enclosed in a 4-in.-thick shield built with lead bricks. The samples to be assayed are held on a shelf made of ⅛-in. Lucite 30 cm above the face of the lower crystal; another sheet of ⅛-in. Lucite separates the sample chamber and the upper detector to equalize scattering into both detectors. Cubical samples as large as 15 cm on a side can be contained within the sample chamber. The output of each detector assembly can be disconnected, and separate gain adjustors are provided so that individual energy calibration can be made. A photograph of the instrument is shown in Fig. 2.

EXPERIMENTAL BASIS FOR COUNTING METHOD

Spectra of a point source of ^{131}I in air and the same amount of ^{131}I uniformly distributed in 500 ml of water are shown in Fig. 3. Inspection suggests that the total area under the spectrum for the 500-ml source is greater than that for the point source. The area under the primary peak (310–410 kev) is greater for the point source, but the area under the scatter portion of the spectra (50–310 kev) is greater for the 500-ml source. Therefore these spectra suggest that there should be some threshold above which the areas under the curves (and thus the counting rates) are equal. Experiment showed that this is so: with these two extremes of sample volume and with ^{131}I as the source, the threshold lies at 200 kev. Further experiments showed that this counting condition is also geometry-independent for samples of

TABLE 1. GEOMETRY-INDEPENDENT COUNTING PARAMETERS

Isotope	Threshold (kev)	Window (kev)
^{203}Hg	180	200
^{51}Cr	190	200
^{131}I	200	200
^{198}Au	220	300
^{137}Cs	280	∞
^{58}Co	330	∞
^{86}Rb	380	∞
^{59}Fe	440	∞

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* Commercially available quart cardboard ice-cream containers, 13 cm in diameter and 9 cm tall.

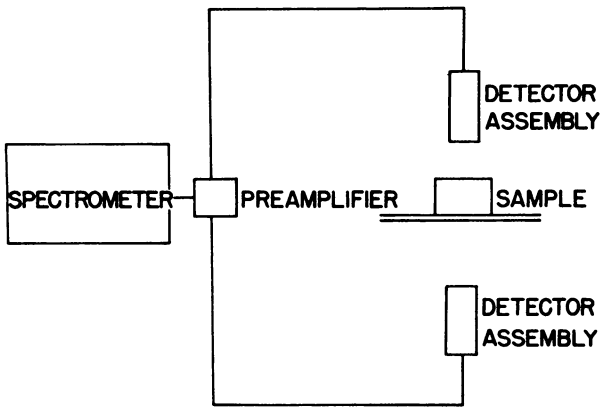

FIG. 1. Block diagram shows opposed-head instrument for geometry-independent gamma radioassay of large biologic specimens with various volumes and shapes.

intermediate volumes. The experimental procedure used to prove this independence was to place a small volume (less than 0.1 ml) of ^{131}I in a convenient sample container* and count it with the spectrometer threshold set at 200 kev. The volume of the sample was then changed successively by adding 10-ml aliquots of water to the container until the 500-ml limit was reached. Counts were made after each increment in sample volume. Between 0.1 and 500-ml sample volumes, the observed counting rates after each addition of water varied only slightly more than would be expected from statistical theory.

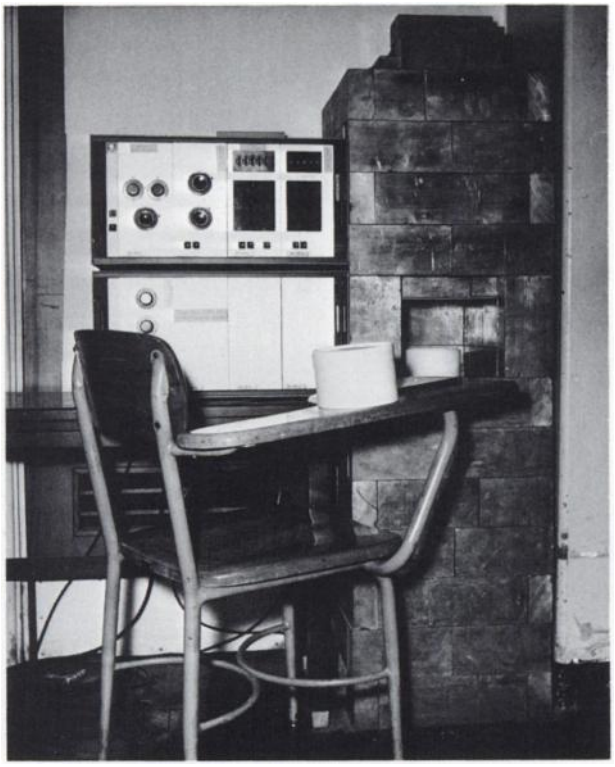

FIG. 2. Photograph shows simple construction of instrument used for gamma radioassay.

To determine whether this independence from sample volume also held true for nonuniform distributions of ^{131}I, two additional experiments were performed. A chip of balsa wood less than 0.5 ml in volume was soaked in a dilute solution of ^{131}I, coated with paraffin to seal the activity in, and stuck to the bottom of the sample container. The wood chip was covered successively with 10-ml increments of water until the 500-ml volume was reached; counts were made, as before, after each addition. The sample container was then emptied, the balsa chip was freed so that it would float and the experiment was repeated. The observed counting rates did not vary more than 1% for any position of the balsa-chip source in any sample volume in either experiment.

Similar experiments have been performed and the threshold for geometry-independent counting has been found for ^{203}Hg, ^{51}Cr, ^{198}Au, ^{68}Ga, ^{137}Cs, ^{58}Co, ^{54}Mn, ^{86}Rb and ^{59}Fe. The results are shown in Table 1.

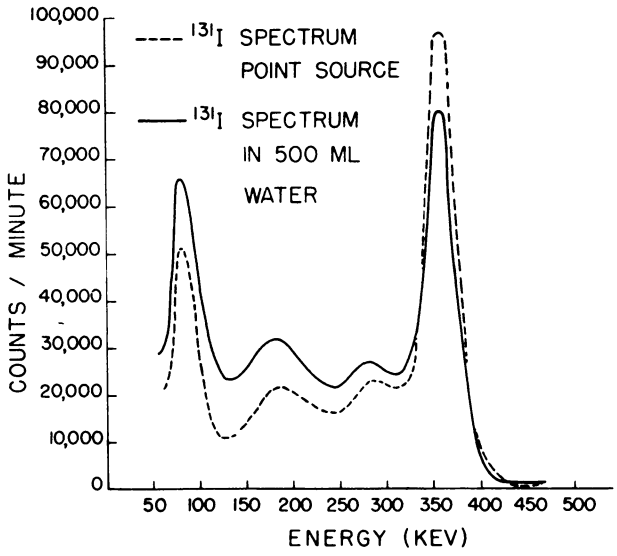

FIG. 3. Gamma-ray spectra were made with opposed-head instrument of same amount of ^{131}I in point source in air and evenly dispersed in 500 ml of water, about 9 cm deep.

DISCUSSION

When the geometry-independent thresholds listed in Table 1 are plotted against primary gamma energy of the respective radioisotope, a straight line is obtained. This linear relationship (Fig. 4) predicts that if the gamma energy to be measured is less than 150 kev, this counting method cannot be used. It lets one predict the geometry-independent counting threshold for any monoenergetic gamma-ray emitter. For polyenergetic emitters (e.g. ^{58}Co, ^{59}Fe, etc.) the energy of the most common gamma ray should be used to obtain a first estimate of the geometry-independent counting threshold. The actual threshold

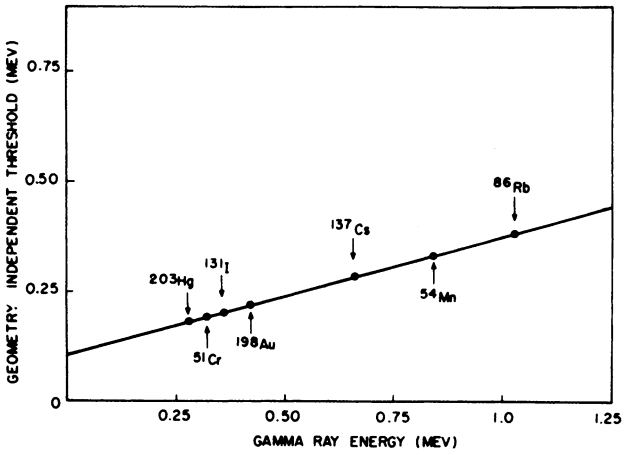

FIG. 4. Graph shows linear relation between primary gamma-ray energy of seven radioisotopes and geometry-independent counting threshold in opposed-head instrument used for radioassay.

can then be determined precisely by repeating the experiments we describe with the thresholds in a narrow range above and below this estimate.

In Table 1, the geometry-independent counting conditions for some radioisotopes permit differential counting using an upper discriminator, but those for more energetic radioisotopes require integral counting. These limitations are imposed on the counting method because the spectrometer window in our instrument has a maximum width of 300 kev unless gain changes and recalibrations are made that increase the likelihood of technician error. For every radioisotope for which the total photopeak can be included within a window defined by the geometry-independent threshold plus 300 kev or less, differential counting is used. Use of the upper discriminator improves counting statistics by reducing the background count; it is used whenever possible. With other radioisotopes integral counting is done. The minimum amount of ^{131}I that can be assayed in this instrument with a statistical error of $\pm 5\%$ and a counting time of 10 min is 0.05 μc. The maximum amount is 250 μc. The sensitivity range can be changed to suit requirements by using detectors with a different size than the 2 $\times$ 2-in. crystals we found optimum for our clinical radioassays.

Such a substitution is very likely to change the spectra, and redetermination of the geometry-independent threshold will therefore be required. However, a new linear relationship like that in Fig. 4 can be established using only three monoenergetic nuclides (say ^{203}Hg, ^{137}Cs and ^{86}Rb); then the proper thresholds for other nuclides can be read easily from the line.

This instrument and the "peak-plus-scatter" counting method have been used in our laboratory now for more than 2 years. Urine and stool samples are routinely assayed with it. Radioassay of total organs such as human thyroid, spleen and kidney has been done successfully. The instrument and method have been particularly useful in whole-body retention studies of radioisotopes in small animals such as rodents, reptiles and amphibia when radioisotope localization within the animal is changing with time.

SUMMARY

An instrument and a counting method for accurate radioassay of large, intact, biological samples are described. Within wide geometric limits the instrument and counting method requires neither a standard sample shape, standard volume nor uniformity of radioisotope distribution within the sample. Accuracy of the radioassays is limited primarily by counting statistics even when samples as large as 500 gm with a dimension of 15 cm or less are used.

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