Instrumentation for I^{131} Use in Medical Studies[*]

By Benedict Cassen,[†] Lawrence Curtis,[†] Clifton Reed[‡] and Raymond Libby[§]

Scintillation counters have proved useful for the detection of gamma radiation from tissue. Several types of such counters have been designed at this laboratory to detect the gammas from I^{131}. The success of one of these for delineation of thyroid glands has led to the construction of a device for automatic scanning of the gland area and recording of the result

1. *Localizing Counter*

A scintillation counter specially designed in this laboratory for the localization of radioiodine in biological systems has been reported.[¶] Further tests have shown that the intrinsic sesitivity of this counter is, in practice, greater than that reported.

Several improvements have been made, notable among them being the use of a better cement (Hyrax) for making optical contact between the calcium tungstate and the phototube envelope. With this counter it is easy to detect, with ¼-in. resolution, the boundary of a region containing only 0.2 μc of radioiodine per cm^2.

It has been shown possible[‖] to delineate with fair accuracy the thyroid glands of patients given a dose of about 150 μc of radioiodine. (With this type of counter it is also possible to localize, readily and exactly, metastasized thyroid tissue in lymph nodes.) The procedure described here for delineating the thyroid glands is tedious but has been greatly improved by mounting the tube on a rack so that it can be moved in either of two directions at right angles to each other. This is done with lead screws turned by small hand cranks.

The outlines thus obtained were compared with the shape of the gland after removal by operation, or on autopsy, and were surprisingly accurate. The results indicated the desirability of an automatic scanning and recording device. Such a device has been built and is described in the last part of this paper.

2. *Hand-Held Localizing Counter*

A hand-held localizing counter that can be used for rapid determination of the boundaries of a thyroid gland, or other active tissue, by marking the outline on the patient's neck with a skin pencil, has been developed. This method is not as accurate as the point by point or scanning procedure, but is much less tedious and makes possible very rapid clinical location and classification of abnormalities and metastases.

---

[*] The information presented is based on work performed under Contract AT-04-1-GEN-12 between the Atomic Energy Commission and the University of California at Los Angeles. Section 5 of this paper has been reviewed in the Veterans Administration and published with approval of the Chief Medical Director. The statements and conclusions of the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Mr. Reed is co-author for Sections 1–4: Dr. Libby is co-author for Section 5.

[†] School of Medicine, University of California at Los Angeles.

[‡] Formerly at the School of Medicine, University of California at Los Angeles. Now at the R. C. Scientific Instrument Co., Playa del Rey, California.

[§] Radioisotope Laboratory, Wadsworth General Hospital, Veterans Administration Center, Los Angeles.

[¶] B. Cassen, L. Curtis, C. Reed, Nucleonics **6**, No. 2, 78 (1950); UCLA-49 (1949).

[‖] H. Allen, Jr., R. Libby, B. Cassen, *J. Clin. Endocrinol.* **11**, 492 (1950).

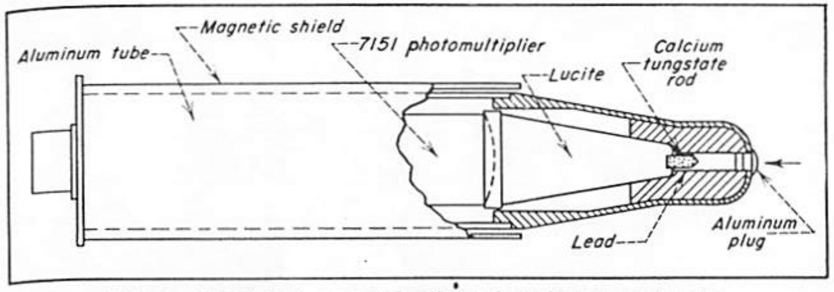

FIG. 1. Hand-held counter for tissue-boundary determination

Figure 1 shows this counter. An RCA 7151 photomultiplier tube is used. The scintillator is a single rod of clear calcium tungstate. The light produced is guided to the photosensitive surface by a conical Lucite light pipe that is cemented to the face of the phototube with Hyrax cement. This cement is also used to hold the calcium tungstate rod in place.

To obtain a sharp localizing effect with this arrangement, it is necessary to surround the calcium tungstate rod with a lead annulus of sufficient thickness and depth to shield most of the crystal from radiation coming in from outside a small angle. It is also necessary to surround the phototube with a mu-metal shield so the counting rate is not affected by the earth's or stray magnetic fields.

As a localizing detector, this counter is much more sensitive than the previous type. The over-all optical efficiency of the instrument is greater because the light can get to the photosensitive surface without reflections at air or vacuum interfaces. Also, the calcium tungstate rod is much closer to the layer of radioactive material. But the collimation of the gamma radiation is not as good and the spatial resolution suffers somewhat. If bias and amplification are set so that the background is about 4 cps, this counter, with a ¼-in. diameter circular aperture, is 3 to 4 times as sensitive as the earlier type with the same aperture.

Earlier, a modification of this type of detector was constructed using the larger 5819 photomultiplier tube and a much longer Lucite light pipe. The possibility was suggested of making radioactive the pontamine sky blue dye that Dr. Weinberg of the Long Beach Veterans Hospital injects into the mediastinal lymph plexus when making a radical removal of a lung. Usually the dye diffuses to the lymph nodes and makes those near enough to the surface visible so they can be excised in case of suspected lung cancer. Mixing radioactive di-iodofluorescein with the blue dye was suggested since with a gamma locater it would seem possible to locate more lymph nodes for excision, even if they were somewhat below the surface. Preliminary tests on rabbits have shown that the radioactivity of the di-iodofluorescein follows along with the visible dye.

For this application, the counter was made with a long light pipe so that the crystal and aperture could be introduced into a deep operation cavity. As yet it has not been used in a human operation.

3. *Sensitive Wide-Angle Counter*

Since a relatively small volume of calcium tungstate will absorb a high percentage of the incident 0.37-Mev gammas from radioiodine, a scintillation counter can be built with an over-all sensitivity from 30 to 100 times greater than that of an ordinary G-M tube. Specially designed G-M tubes can do better than the usually available types. However, it was thought worth while to investigate scintillation counters for use in thyroid-gland uptake and biological half-life studies with radioiodine.

By removing the lead shield from the counter discussed in Section 1 of this article, it was found that the thyroid-uptake studies could be made with an administered dosage of only 1–5 μc of radioiodine. The calcium tungstate crystals which were cemented to the face of the 1P21 tube were placed close to the patient's thyroid gland and a series of cases were followed.

Somewhat later calcium tungstate crystals were cemented to the face of a 5819 tube. The arrangement is shown in Fig. 2. Tests showed that 0.002 μc of radioiodine placed 1 in. from the face of the crystal assembly could easily be detected at about twice a background of 4 cps. Thyroid uptake and biological half-life studies could easily be made with 1 μc, or less, administered dose.

It appears likely that this tube is sensitive enough to make a direct measurement of radioiodine in tissue by placing the counter over a part of the body. In such use the crystals would have to be particularly well shielded from the thyroid gland. Measurements along these lines are in progress.

4. Counter Characteristics

In Fig. 3 performance characteristics of the wide-angle counter tube discussed in Section 3 are given. The data plotted are from a 0.62-μc I^{131} source at a distance of 40.5 cm from the face of the crystals.

It was found that, over a limited range of photomultiplier plate voltage, the net counts of a sample at a fixed distance from the counter are approximately the same for the same background count. To get the same background count when the plate voltage is raised, the bias must be raised. If the plate voltage is raised too much, the sensitivity to the sample will decrease somewhat, even though the bias is adjusted to give the same background.

The three sets of points in Fig. 3 are for three different fixed bias settings, the plate voltage being varied to obtain various background levels. Background counts is chosen for the abscissa because the sample count is relatively independent of the physical factors, as long as the background is set at the same value.

The net counts increase rapidly with low background and then flatten out. The ratio of gross to background counts reaches a maximum value and then slowly decreases.

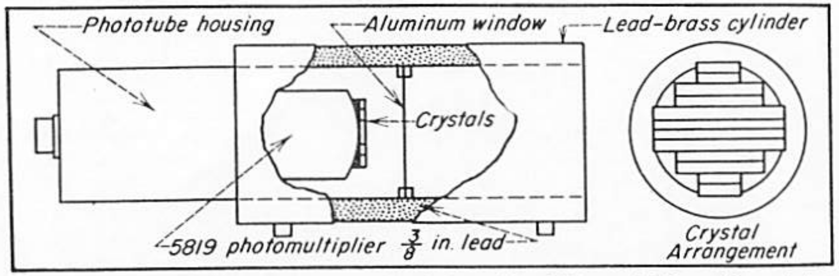

FIG. 2. Wide-angle scintillation counter designed for high sensitivity. The calcium tungstate crystals are cemented to the face of the photomultiplier

As is well known, the ratio of the standard deviation of the net counts, σ_{g-b}, to the net counts, $g - b$, is

$$\frac{\sigma_{g-b}}{g-b} = \frac{1}{\sqrt{g}} \frac{\sqrt{r^2+r}}{r-1}$$

where g = gross counts, b = background counts, and $r = g/b$.

The number of counts, C_p, required for a predetermined fractional accuracy, $p = \sigma_{g-b}/(g - b)$, is

$$C_p = \frac{1}{p^2} \frac{r^2+r}{(r-1)^2}$$

The time, t_p, required for C_p counts is

$$t_p = \frac{C_p}{g} = \frac{1}{gp^2} \frac{r^2+r}{(r-1)^2}$$

The third curve in Fig. 3 is p^2t_p plotted from this equation, with values of g taken from the experimental curve.

Counting with this particular counter is most accurate, then, if the background is about 8 cps, although the accuracy does not suffer too much over quite a range of background settings. In some applications a high gross-to-background ratio would be more useful than maximum accuracy. For this counter the maximum ratio is at about 6 cps, which is practically the same setting that gives maximum accuracy. The stability of the counting rate with respect to plate voltage fluctuations is at its best at higher backgrounds, say from 10 cps up.

5. Automatic Scanner and Recorder

The scintillation counter described in Section 1 of this article has been used for *in vivo* delineation of thyroid glands. The procedure requires taking individual readings over a rectangular network of positions and then estimating the gland outline by drawing a line through positions of a given reading or range of readings. With a little practice it is possible to get extraordinarily good agreement between the outlines so obtained and the actual outline of the glands as found either post operatively or post mortemly. This procedure, however, is tedious and time consuming. An automatic scanner and recorder which would give a crude picture of the distribution of gland activity would obviously serve a very useful purpose.

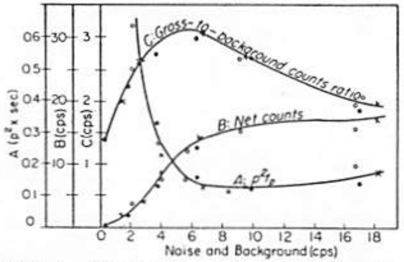

FIG. 3. Performance characteristics of a calcium tungstate scintillation counter

FIG. 4. Automatic scanner and recorder

The automatic scanner and recorder is shown in Fig. 4. The localizing scintillation counter is mounted on a carriage that is driven back and forth by a lead screw which in turn is driven by a reversing series motor operating through a reduction gear. The electrical reversing is accomplished by tripping a switch that is attached to the moving carriage, by a stationary but adjustable stop. The amplitude of back and forth motion can be adjusted by setting the positions of the stops. Each time reversal occurs the other motor is actuated for a small time interval. This interval is usually adjusted so that a scan is displaced about ⅛ in. from the previous one.

A small drawing board is rigidly mounted on the carriage that holds the counter. This drawing board is

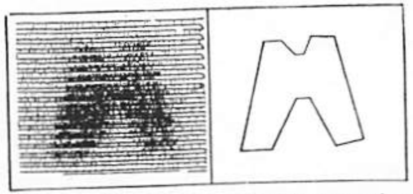

FIG. 5. Record of automatic scanning of filter paper soaked with 200 μc of I^{131} (left) and actual shape of the filter paper

scanned under an ink writing pen held rigidly on an arm attached to the main frame. The pen is attached to the arm of an electromagnet so that a short duration actuation of the magnet causes the pen to make a ⅛-in. pip in a direction at right angles to the direction of motion of the scanning table. The pen and relay assembly was adapted from one used on Esterline-Angus time-marking recorders.

The amplified pulses from the photomultiplier tube are fed into a multivibrator regularizer and scaler. The scaler can be set to feed a pulse to the pen for any power of 2 up to 256 counts. Obviously, when the ¼-in. aperture of the detector moves over an active area the pips will be closer together. The higher the signal-to-noise count ratio the higher will be the visual contrast in the scanning record. If the contrast is sufficient the effect of a picture of the gland will be obtained. However, even when the contrast is low, a sensation of a picture can often be obtained.

The first tests of the scanner were made with filter paper wetted with a solution containing radioiodine. Figure 5 shows such a record and the corresponding outline of the filter paper which had been wetted with 200 μc of I^{131}. On this record, one pip corresponds to four counts.

The next tests were made on a frozen trachea preparation with attached thyroid glands obtained from a terminal patient given 3 mc of I^{131} 14 hours before death. The gland uptake in this time was approximately 15%. A series of records were obtained from 11 to 29 days after death.

The relative success of these tests made it desirable to extend the trials to *in vivo* mapping of thyroid glands in actual patients. Tests were made and typical results are shown in Fig. 6.

* * *

The parts of this program of investigation requiring testing on patients at the Radioisotope Units of the Sawtelle and Long Beach Veterans Hospitals were authorized by the Division of Medicine and Biology of the Atomic Energy Commission, and by the Veterans Administration. At the Sawtelle Hospital the clinical programs were undertaken by Dr. Herbert Allen, Jr. and Dr. Raymond Libby. At the Long Beach Hospital some other types of testing were done under the direction of Dr. M. Morton. Much of the clinical findings reflected back on improved instrumentation development, and important suggestions were made by the clinicians concerned.

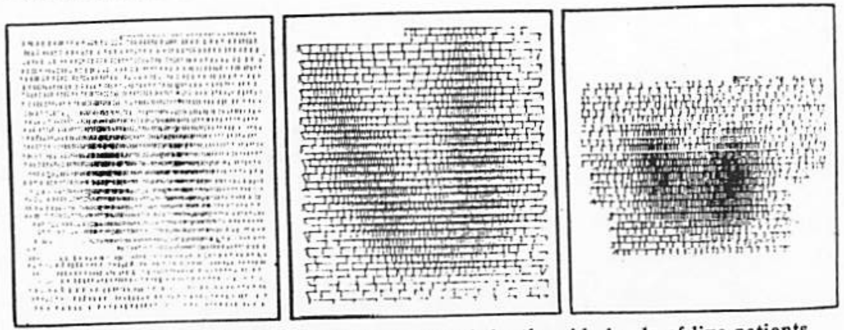

FIG. 6. Automatically recorded outlines of the thyroid glands of live patients

---

METHODS of FLUORINE and FLUORIDE ANALYSIS—III[*]

Beryllium compounds, aerosols, biologicals, glass, foods, and steel are just a few of the materials subjected to the methods of fluorine analysis noted in this series of articles for which the literature from 1816–1950 was surveyed

By F. E. McKENNA
Air Reduction Company, Research Laboratories[†]
Murray Hill, New Jersey

IN THIS LAST of three articles, the pertitanic acid and fluosilicic acid methods are discussed, the analysis of fluorocarbons, volatile fluorides, and elementary fluorine are considered, and spectrochemical methods, miscellaneous analytical methods, and the determination of fluorides in specific substances, such as foods, biologicals, and industrial materials are treated briefly.

Reactions of fluoride with peroxide-treated titanium solutions. An acidic solution of titanium after treatment with hydrogen peroxide exhibits a yellow color which has been attributed to the presence of pertitanic acid. This color is bleached by fluoride ions, but the bleaching is apparently not quantitatively proportional to the fluoride content (*300*).

The presence of alkali sulfates causes additional bleaching, while Al^{+++} and Fe^{+++} restore the color, but either a bleaching or a color restoration can occur in the presence of phosphates with a dependence on the relative concentrations of phosphate and fluoride. The optimum bleaching action due to fluoride occurs at *p*H 1.5, and there is a rapid decrease to zero effect at *p*H 2.5. The color-restoring properties of Al^{+++} and Fe^{+++} apparently indicate that the fluoride forms more stable complexes with them than with the titanium (*300–307*). The color-restoring action of aluminum is effected by the *p*H, but the restoration is not due to hydrolysis of the $Al(NO_3)_3$ solution.

At *p*H 0.9, sulfate and phosphate do not interfere (*308*). A 100-fold excess of nitrite does not effect the fluoride-titanium reaction (*205*). The color intensity of the pertitanic acid is decreased by lowering the temperature. When measured with a neutral wedge photometer (*309*), 1.00 ppm of fluoride in a 4% NaCl solution was analyzed as 1.03 ppm by its bleaching action.

Solutions of peroxidized titanium follow Beer's Law up to the solubility limits of the pertitanic acid, whether an excess of hydrogen peroxide is present or not, while Beer's Law is not obeyed in the fluoride-bleached pertitanate solutions (*310*). The bleaching action measured at 440 mμ is reproducible to 0.003% F^- and is accurate to 0.01% below 2.0% fluoride. The optical

---

[*] In Part I, published in the June NUCLEONICS (page 24) the lead chlorofluoride, calcium fluoride, aluminum, ferric, ceric, yttrium, lanthanum, and thorium fluoride methods of analysis were considered. In Part II, published in the July NUCLEONICS (page 40), discussion of the thorium fluoride method was continued, and analysis by the zirconium fluoride, zirconium lakes, and fluosilicic acid methods was considered. The isolation of fluoride as the volatile fluosilicic acid was also discussed.

[†] Certain portions of this paper were collected at the SAM Laboratories at Columbia University and at the Institute for Nuclear Studies of the University of Chicago.