NSEC *Nuclear Science and Engineering Corporation*

REPORT

I-129

SURVEY OF IODINE-129 CONCENTRATIONS IN THYROID TISSUES

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I. INTRODUCTION

In accordance with the plan of work described in NSEC proposal 51-31-2004E, studies are under way of the iodine-129 concentrations in human and other mammalian thyroid tissues. Emphasis to date has been on (a) assembling a suite of thyroid specimens from a variety of sources, collected at times varying from 1930 to the present; (b) development of I-129 analytical techniques to their ultimate sensitivity; and (c) analysis of a number of thyroid specimens of recent collection, in which I-129 concentrations were expected (and found) to be sufficiently high that ultimate sensitivity was not required in their determination. The limited supply of samples of less recent vintage, expected to contain less I-129, has been reserved pending complete determination of the optimum conditions (of neutron flux, sample size, etc.) for ultimate sensitivity measurements.

Success in applying the activation-analysis technique to natural iodine specimens has paralleled expectations (1) at thermal neutron flux values of the order of 10^{13}. Absolute sensitivities, in terms of I-129/I-127 ratios, may be limited by either fast neutron-induced reactions or third-order thermal neutron capture in I-127.

Background levels in the measurement of I-130 have been reduced by a factor of at least 10^{2} as compared with those reported by the Argonne group (2) by use of a β-γ coincidence counting arrangement. This improvement in sensitivity has made it possible to obtain finite values for I-129 in analyses of individual adult human thyroid glands of recent collection date. Evaluation of the extent to which this may be the case with the glands of older collection date, or to which sensitivity limitations may be overcome by pooling of specimens, awaits results of the studies of the nuclear parameters of I-129/I-127 mixtures at higher neutron-flux values.

Progress in the various concurrent phases of the program is discussed in this report, and recommendations for future work are presented.

II. COLLECTION PROGRAM

Attempts have been made to obtain an array of human and animal thyroid specimens spanning the time period from the onset of the nuclear age to the present, in order that analyses will both reveal the pre-nuclear I-129 levels and yield some data on the rate at which this fission product is accumulating in the biosphere.

A. Human Specimens Collected 1962-63

Routine collections of surgical and post-mortem human thyroid specimens have been carried out for the past six months at five Pittsburgh hospitals and, with the cooperation of Dr. Merril Eisenbud, at the NYU-Bellevue Medical Center. These collections have yielded several hundred glands from pre-natal to geriatric, which are available for statistical studies of the current biospheric addition rates and/or of age variations in the thyroid I-129/I-127 ratio.

The collection of Dr. Henry N. Wellman of the Division of Radiological Health, U. S. Public Health Service, Cincinnati, has also been placed at our disposal. These specimens come from a widespread collection network, and have already been measured for I-131 shortly after collection.

B. Older Human Specimens

Preserved human thyroid single lobes, about seventy in number, have been obtained from a collection of Dr. Shields Warren of the New England Deaconess Hospital. These specimens were collected during the period 1945-50. Additional sources of specimens collected during 1945 or earlier are being sought.

C. Other Mammalian Specimens

Additional analytical samples of mammalian thyroid tissue covering a collection period extending from 1930 to 1962 have been assembled. These are listed below, with their sources and dates of collection:

1. Sheep thyroid glands, whole, frozen
   Source: Pittsburgh slaughterhouse
   Date: 1962
   Quantity: Approximately 50

2. Hog thyroid, desiccated
   Sources: Various pharmaceutical and meat packing companies
   Dates: 1957-1962
   Quantity: Several pounds

3. Thyroid nucleoprotein tablets (probably hog thyroid)
   Source: Schieffelin and Co.
   Dates: 1930-1956
   Quantity: 1500 (iodine content 0.002 to 0.01 mg. each)

4. Thyroid tablets, 1/4 grain USP (hog)
   Source: Wilson Laboratories, Chicago
   Date: Pre-1945
   Quantity: 4000 tablets

III. EXPERIMENTAL PROCEDURE

Although I-129 is a radioactive nuclide, its extremely long half-life (1.6×10^7 years) results in a specific radioactivity of only 0.16 μc/mg. Furthermore, the low energy of its radiations (150-Kev β and 38-Kev γ) also make detection by ordinary counting techniques very insensitive. A reasonably large cross section (~27 barns) for thermal neutron capture, leading to the formation of the activation product, 12.6-hr I-130, makes the detection of I-129 by neutron-activation analysis highly practical (1).

A. Counting Procedures and Instrumentation

The activation of material containing I-129 for subsequent measurement of the I-130 produced leads to several interferences which cannot be circumvented except through the proper choice of the measurement method. For example, the normal presence of I-127 in the matrix leads to the formation of 25-minute I-128 by the (n, γ) reaction and to the formation of 13-day I-126 by the (n, 2n) reaction. The interference of the 25-minute I-128 may be reduced or eliminated through radioactive decay prior to measurement of the I-130. However, the 13.2-day I-126 which may be present must be discriminated against instrumentally. An examination of the decay schemes of I-126, I-128, and I-130 reveals that the maximum total energy of the gamma cascades in the decay of the respective nuclides is 1.41 Mev, 0.99 Mev, and 2.34 Mev. Therefore, it was anticipated that the use of a large diameter, well-type NaI gamma-scintillation detector, with a proper choice of gamma-energy discrimination, would permit the measurement of I-130 without serious interference from the other two iodine isotopes. The use of this type of detector reduces the Compton continuum and enhances the higher energy portion of a gamma spectrum like that of I-130; i.e., the larger the crystal, the greater the probability of total absorption of the energy of gamma cascades. The use of a 5-in diameter by 5-in long well-crystal yields ~40 percent detection efficiency for the radiations from the I-130 when the lower discrimination level is set at 1.6 Mev (a choice which excludes all but a very small amount of the radiation from the I-126). An

upper level of discrimination (2.5 Mev) is also useful in reducing to a minimum the counting rate due to cosmic radiation, which is rather high in a crystal of this size. However, without prohibitively excessive shielding, high background count rates (hundreds per minute) are still encountered.

To reduce the background to a truly low value and thus increase the sensitivity of the measurement technique, a β-γ coincidence counting system has been applied. This system (Figure 1) utilizes the NaI crystal described above, which has a 1-in diameter well, 3-in deep. A thin β-sensitive plastic phosphor, with a configuration such that a sample is nearly completely surrounded by a 1/16-in thick layer of the phosphor, is positioned within the well. A lucite light pipe and a small photomultiplier tube complete the detector assembly. Coincidence conditions are imposed on the output of the β-phosphor and the discriminated output of the large gamma scintillator by a coincidence circuit with a resolving time of approximately 0.08 microseconds, and the coincidence count rate is measured. The overall detection efficiency for I-130 counted in this system varies from 10 percent to 40 percent, depending on the sample thickness and the choice of the lower gamma-energy discrimination level. Typical samples usually exhibit efficiencies in the lower portion of this range. The background counting rate for the system is of the order of only 0.06 - 0.07 counts per minute. Thus, a relatively small sacrifice in efficiency, from 40 percent to $\sim$15 percent, results in an extremely valuable reduction in background counting rate of 3 orders of magnitude, and the sensitivity of the measurement is enhanced by a factor of 100 or more.

B. Chemical Procedures

1. Pre-irradiation Chemistry

a. Extraction of Iodine from Thyroid Glands and Thyroid Powder. The procedure used for extraction of iodine in an inorganic form from the organic material of a whole thyroid gland or from desiccated thyroid powder involves the digestion of the organic material with sodium hydroxide. Typically, the procedure used is as follows.

A whole human thyroid gland (or approximately 10-20 grams of dry thyroid powder) is placed in a 5-in porcelain evaporating dish, approximately 2-3 grams of sodium bisulfite and 30 ml of 6 N NaOH solution are added, and the mixture is slowly (~2 hours) evaporated to dryness. The material is transferred to a 100-ml nickel crucible which is then heated gently with a Meker burner until combustion of the organic material is complete. The crucible is then placed in a muffle furnace at ~1000° C for 2-3 minutes. Upon removal from the furnace, the crucible is allowed to cool until no red glow is visible and is then quenched in sufficient deionized water to cover it. The solidified melt is then loosened from the crucible, and the latter is removed from the solution and rinsed into it. The dissolution of the melt is completed by heating the solution on a hot plate. The solution is carefully acidified with nitric acid, and 20-30 ml of 10 percent sulfurous acid is added. Any undissolved solids remaining are removed by filtering the solution through a millipore filter.

A check on a typical yield of the above procedure was provided in the following way. A weighed sample of thyroid powder was digested in the manner described above and the iodine precipitated as silver iodide. The silver iodide after careful washing and drying, was weighed, and the percent of iodine in the original sample was calculated. This result, 0.30 percent, agreed very well with that obtained on a duplicate sample by a recognized microanalytical laboratory using standard techniques for organic iodine analysis. The independent result, 0.31 percent, indicates that the iodine extraction method used here is very nearly quantitative.

The total iodine extracted from whole human thyroid glands has been, on the average, approximately that expected for normal glands.

b. Purification of Iodine and Preparation for Irradiation. Extremely careful purification of the iodine with respect to two contaminants, cesium and uranium, is necessary prior to irradiation. The presence of either of these can lead to the formation of I-130 in a neutron flux. An (n, α) reaction

on cesium or the fission of uranium can produce I-130 in sufficient quantities to vitiate the results of the activation, particularly when there is only a very small quantity of I-129 present.

The solution obtained in section (a) above is purified by two cycles of extraction as elemental iodine and back-extraction as iodide as follows.

Sodium nitrite solution is added to the solution resulting from the dissolution of the organic material until the brown color of I_2 is observed. The elemental iodine is then extracted into carbon tetrachloride. After the organic phase is washed with deionized water, the iodine is back-extracted into a dilute solution of sulfurous acid, oxidized with sodium nitrite again, and the cycle is repeated. The final aqueous solution is boiled to remove carbon tetrachloride, allowed to cool, and palladous chloride ($PdCl_2$) is added to precipitate palladium iodide. The precipitate is removed by filtering through a fritted glass funnel, and is then washed with several portions of deionized water followed by alcohol and ether. The frit and precipitate are dried by placing for 15 minutes or more in an evacuated vacuum desiccator.

The dried palladium iodide is subsequently placed in one leg of a clean quartz* U-tube which is then evacuated and sealed. The compound is decomposed by gentle heating with a torch and the iodine distills into the other leg of the tube which is cooled in ice-water. The second leg, now containing elemental iodine is then sealed off and is ready for irradiation.

In the event that a thyroid gland contains an amount of iodine which is too small for handling in the above procedure (i.e., <3 mg), the following procedure is used for the preparation of the sample for irradiation. Five milligrams of silver, as a nitrate solution, is added to the final aqueous phase and sufficient dilute HCl is added to precipitate all of the silver. The silver chloride-iodide precipitate is filtered, washed, and dried in an oven at 110° C. The dry solid is placed in one arm of a clean quartz* U-tube

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*The quartz tubes are cleaned by soaking in a solution consisting of ~20% HNO_3 and ~5% HF for 10-15 minutes and rinsing thoroughly with deionized water.

with ~50 mg of aluminum wire, and the U-tube is evacuated and sealed. The solid mixture is heated gently with a torch until a substantial amount of aluminum chloride is distilled into the second leg of the U-tube which is cooled in an ice bath. The leg containing iodine and aluminum chloride is sealed off and is ready for irradiation.

2. Post-irradiation Chemistry and Preparation for Counting. There are several interfering radioactivities which may be produced from impurities in the iodine or in the quartz irradiation capsule and which would be detected in the coincidence system described above. The most important of these impurities is 36-hour Br-82, because it is most likely to survive the pre-irradiation purification chemistry by virtue of its chemical similarity to iodine. The method described below is specifically designed to decontaminate the sample from any Br-82 which may be present, but in so doing will also remove to an even greater extent, any other impurities, such as Na-24 or K-42, which may be present.

Following neutron-irradiation, the quartz capsules are broken open after thorough cleaning of the outside and immediately submerged in a solution of sodium bisulfite. For samples containing only a small amount of iodine, there is a danger of loss due to volatilization. These samples are opened in the apparatus shown in Figure 2. The vertical section of the tube is first filled with sodium bisulfite. The quartz tube is scratched and placed with the scratch mark over the joint. The joint is closed and held closed with a clamp (not shown). The joint is then flexed to break the capsule and the apparatus manipulated (without opening) so that the quartz is thoroughly rinsed with the bisulfite solution.

Following dissolution of the iodine, ~5-10 mg of bromine is added as a hold-back carrier in the form of a solution of sodium bromide, the iodide is oxidized to elemental iodine with nitrite, and the I_2 is extracted into carbon tetrachloride. A cyclic procedure similar to that described for the pre-irradiation chemistry is followed, except that bromine hold-back

carrier is added to each aqueous extract (except the last) and three complete cycles are used*. Finally, the iodine is precipitated as silver iodide which is removed by filtering, washed, and dried. The silver iodide is weighed on a mylar film sample holder (Figure 1), evenly spread, and covered with another mylar film. The decay of the I-130 is followed for several days and a slight "tail" due to I-126 is usually obtained and subtracted. The area of the sample is measured and a self-absorption correction applied. The I-127 (stable) content of the sample is calculated from the weight of the silver iodide.

For samples containing an amount of iodine too small for precipitation or accurate weighing, a small amount of iodide carrier is added prior to the first extraction. The I-127 (stable) content of the sample is then obtained by comparison of its 13-day I-126 activity with other, larger, samples in the same irradiation after the I-130 has completely decayed.

Two comparators and two blank samples are run with each irradiation. The blanks are processed, after the addition of iodine carrier, in the same manner as the samples. These normally show no I-130 radioactivity.

The comparators consist of a known amount of I-129 in the form of NaI from a stock solution which has been irradiated with no prior treatment. After irradiation, a known amount of iodine carrier is added, and one purification cycle is performed to remove the Na-24 which is present. Silver iodide is precipitated and weighed, and the yield and self-absorption corrections are calculated in the usual manner.

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*The identical procedure was used on a sample which contained a deliberately added, known amount of bromine in order to examine the effectiveness of the decontamination procedure. No Br-82 was detectable in the purified sample and a decontamination factor of $2(10^5)$ was conservatively estimated as a lower limit.

IV. RESULTS

Nine individual whole human thyroid glands and four samples of desiccated hog thyroid have been successfully analyzed thus far in this program. All of the whole human thyroid samples were current, having been obtained from autopsies at three hospitals in the Pittsburgh area during late 1962. The thyroid powders were of recent (1957-1962) manufacture from hog thyroid by Parke-Davis and Company, Detroit, Michigan, by the Pharmaceutical Division of Wilson Laboratories, Chicago, Illinois, and by Canada Packers Limited of Toronto, Canada.

The results, shown in Table I, are to be regarded as tentative inasmuch as several of these were obtained during the actual refinement of the procedure for analyses at the required level of sensitivity. The isotope ratio I-129/I-127 varies from 9×10^{-11} to 4.3×10^{-9} for the human thyroid samples, while the hog thyroid tissues exhibit values in the upper part of this range. The ages of the subjects from whom the thyroid glands were taken and the dates of manufacture of the thyroid powder samples are given.

The data show clearly that current biospheric I-129 levels are higher by factors of 10^4 to 10^6 than those anticipated (1) as a result of spontaneous fission and cosmic-ray production processes. The limited range of collection dates of the human specimens analyzed to date prohibits conclusions as to the current rates of biospheric accumulation. Similarly, the small number of samples so far analyzed is not considered to be statistically adequate for conclusions regarding variation of I-129 level with age of the individual. If the wide variation in isotope ratio is borne out in the analyses of a large number of additional samples, a considerable dietary effect is certainly suggested.

Geographical variations, and perhaps a biospheric increase in the period 1957-1962, are suggested by the results on the desiccated hog thyroid samples. Since these are normally prepared from large numbers of glands collected in a short period of time at a given location, individual differences should be pretty well eliminated. Again, however, it is clear that additional analyses will be required to justify any firm conclusions.

The final column of the table gives the total I-129 content of the human thyroid specimens, assuming a total iodine content of 15 mg. These values range from 1.3 to 64 picograms (2×10^{-4} to 10^{-2} picocuries) per adult gland, clearly demonstrating the sensitivity of the analytical method at its present level of refinement.

TABLE I

CURRENT I-129 CONTENT OF THYROID TISSUES

Sample	Date of Collection or Preparation	Age of Subject	Isotope Ratio I-129/I-127 ($\times 10^9$)	Picograms of I-129 in Thyroid Gland[a]
Individual Human Thyroid Glands				
1	9/4/62	43	2.6±0.2	39±3
2	9/20/62	44	0.6±0.1	9.0±1.5
3	9/26/62	57	0.26±0.09	3.9±1.3
4	9/26/62	74	0.09±0.06	1.3±0.9
5	10/2/62	52	2.5±0.2	37±3
6	10/18/62	42	0.2±0.1	3.0±1.5
7	11/30/62	37	1.3±0.1	20±2
8	12/19/62	38	1.6±0.1	24±2
9	12/23/62	50	4.3±0.2	64±3
Desiccated Hog Thyroid				
Parke-Davis	1957-1958	-	0.48±0.05[b]	-
Parke-Davis	1962	-	3.1±0.6[b]	-
Canada Packers Limited	1962	-	0.61±0.06[b]	-
Wilson Laboratories	1962	-	1.1±0.1[b]	-

(a) Assuming 15 mg total iodine in adult thyroid gland.
(b) Average of duplicate determinations.

V. CURRENT AND PROPOSED STUDIES

A. Additional Analyses

From the results already obtained, it is evident that much information can be developed on I-129 levels in modern thyroid materials without further refinement of the analytical technique. Sensitivity is probably adequate for individual pediatric glands of recent collection, and for commercial desiccated thyroid preparations ranging in age to a number of years. These specimens will be analyzed, as available, along with additional adult glands.

Marine levels of I-129, while doubtless not yet homogeneous, will ultimately reflect the overall biospheric levels. Efforts have been initiated, through Dr. Vaughn Bowen of the Woods Hole Oceanographic Institute, to obtain both modern and preserved whale thyroid specimens for analysis. Hopefully, samples will be obtained from both northern and southern hemispheres.

The older specimens of human and mammalian tissues, many of which are already on hand, and of milk samples of any age will almost certainly require higher analytical sensitivity than has been demonstrated, and analyses will not be undertaken in quantity until the limits of sensitivity in available reactor facilities are determined, as described below.

B. Ultimate Sensitivity of the Analysis

The ultimate limit of detection of I-129 in a given sample depends on a number of complex factors. With the experimental procedures and counting arrangement cited previously, and with neutron irradiations in a flux of $\sim 10^{13}$ neutrons/cm^2 sec, $\sim 10^{-12}$ grams of I-129 may be easily measured in a typical sample with an ultimate sensitivity approaching 10^{-13} grams. In principle, an increase in thermal neutron flux will improve the sensitivity proportionately.

1. Production of I-126. As has been already noted, the presence of a finite quantity of stable I-127 in a sample leads to the production of I-126 via the (n, 2n) reaction. This reaction occurs to an appreci-

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lower limit of the sensitivity of the method for I-129 detection and, if so, to what degree. In the event that the effect is substantial, correction factors, based on the σ_{128} measurement will be calculated and applied.

An experiment is scheduled for the very near future to determine the value for the cross section of I-128. A series of samples of iodine has been prepared by careful purification of an iodine-containing compound which is known to pre-date the atomic era. These samples will be irradiated with flux monitors for varying periods of time at a flux of $\sim 2(10^{14})$ neutron/cm^2 sec. Determinations of the I-130 produced in each of these samples will enable calculations of σ_{128} as well as estimation of the pre-atomic-era levels of I-129 in nature.

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1. R. R. Edwards: Science 137, 851 (1962).

2. M. H. Studier, C. Postmus, Jr., J. Mech, R. R. Walters, and E. N. Sloth: J. Inorg. Nucl. Chem. (in press).

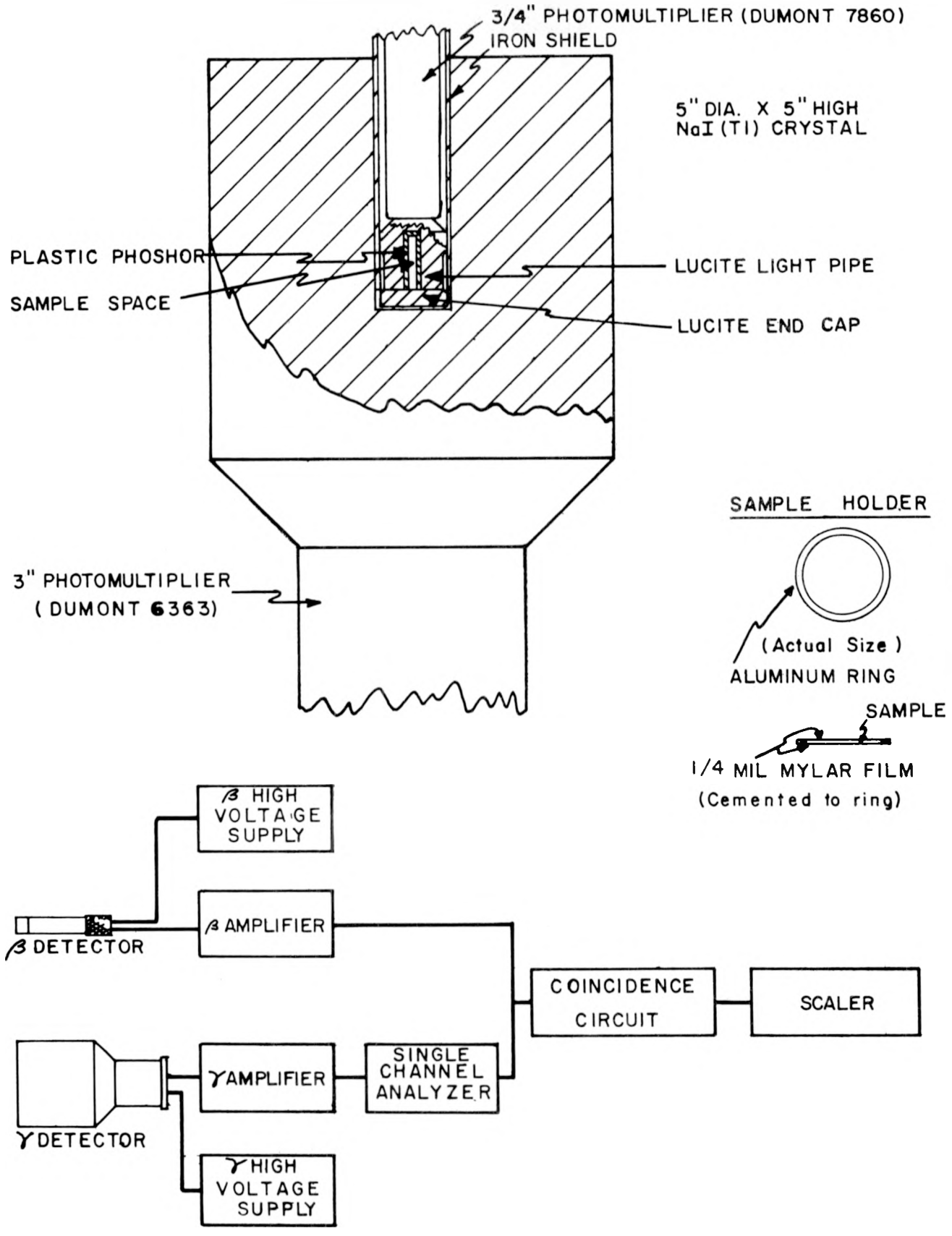

FIGURE 1 **β–TOTAL γ COINCIDENCE COUNTING ARRANGEMENT**

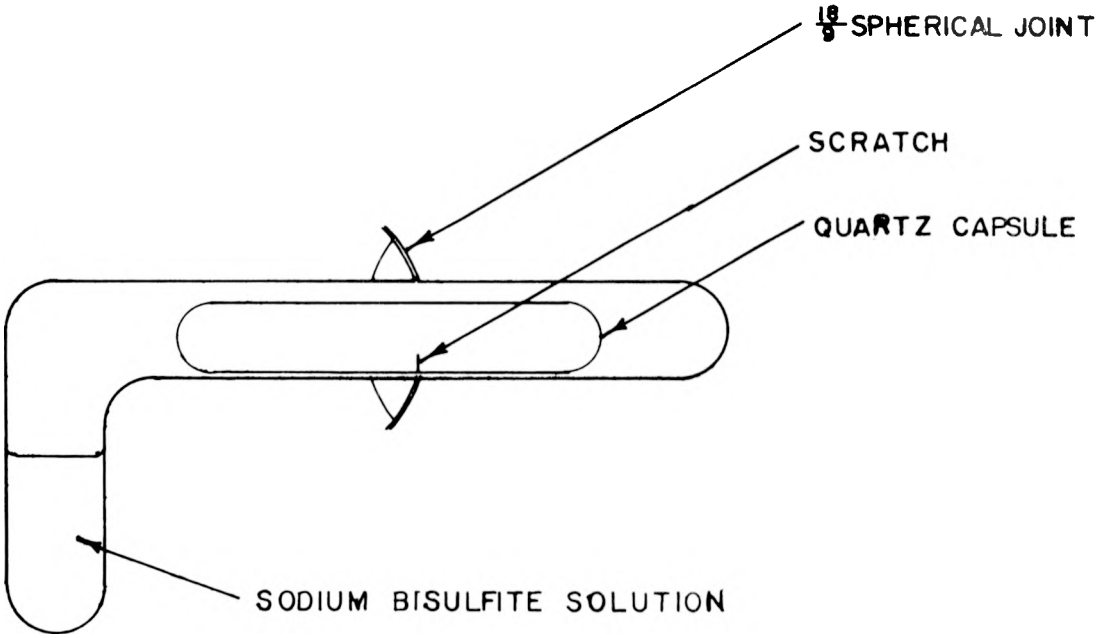

FIGURE 2 CAPSULE-OPENING APPARATUS

Industry Services

Use of nuclear technology applied to research and engineering problems such as quality control, wear rates, corrosion, product integrity, process tracing, etc. Applicable to many industries.

Reactor Technology

Applied nuclear chemistry for engineering testing of reactor concepts.

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Radioactivity tracing studies for the pharmaceutical, cosmetic, food, chemical, packaging, and other pertinent industries.

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Tritium and C^{14} determinations.
Deuterium measurements.
Isotope dilution.
Leukopenic assays.
Reticulo-endothelial studies.
Product sterilization.
Enzyme activity studies.
Biosynthesis.

Products

Accelerator-produced radioisotopes, virtually chemically pure. Laboratory standards and custom sources. Selected reactor-produced radioisotopes. Neutron dosimeters, standard and custom. Custom labeled compounds.

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