THE DETECTION AND DETERMINATION OF SOME TRACE ELEMENT IMPURITIES IN TECHNETIUM-99m GENERATOR ELUATES

by

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A Thesis Submitted to the Faculty of the

DEPARTMENT OF NUCLEAR ENGINEERING

In Partial Fulfillment of the Requirements
For the Degree of

MASTER OF SCIENCE

In the Graduate College

THE UNIVERSITY OF ARIZONA

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STATEMENT BY AUTHOR

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ACKNOWLEDGMENTS

The author would like to express his appreciation to Dr. F. Eric Haskin, Dr. Morton E. Wacks, Dr. George W. Nelson, Dr. Roy G. Post, Dr. Robert E. O'Mara and Mr. Jack N. Hall, Rph., for their advice and help along the course of this work.

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ABSTRACT

Eluates from irradiation and fission produced ^{99m}Tc generators used in nuclear medicine applications were analyzed for possible trace radionuclide and stable isotope impurities. The radionuclides ^{134}Cs, ^{60}Co, ^{131}I, ^{99}Mo, ^{92m}Nb, ^{86}Rb and ^{103}Ru, were detected and quantitatively measured. The samples were also analyzed for stable impurities by neutron activation analysis; only Br and Cu were detected due to large interferences from the Na and Cl present in the normal saline eluting solution. Cesium-134 eluted from the generator column, although present in low activities, was broad scale contaminant detected in 49 of 50 samples analyzed in this work. Using the Ge(Li) detection system, ^{60}Co was detected in most (eleven of twelve) irradiation-produced generator eluates analyzed but was absent in all fission-produced generator eluates tested, thus, from this work, indicating the possible use of this radionuclide as a tentative check of generator type. The initial activities of ^{99}Mo in two commercial fission-produced generator eluates analyzed, (16.04 ± .046 μCi/ml) and 10.59 ± .030 μCi/ml), were in excess of criteria for radionuclide contaminants established by the United States Atomic Energy Commission.

CHAPTER 1

INTRODUCTION

Technetium-99m is the daughter product of ^{99}Mo by beta decay and has been used for a number of investigative purposes by the nuclear medicine community in the last ten years. The short half life (6 hours) coupled with the low energy photon (140 keV) emitted in this isomeric transition and the absence of concomitant β^- emission allows this radionuclide to be used for clinical investigations while producing only a relatively small patient radiation dose, Technetium-99m is eluted from the generator with a physiological saline solution as the pertechnetate ion (TcO_4^-) which is very similar to the iodide (I^-) ion insofar as biological transport mechanisms are concerned.[1,2] It is rapidly distributed into the extracellular space and is trapped specifically by the thyroid gland, salivary glands, and the stomach. It does not cross the blood-brain barrier appreciably, and this together with its favorable radiological properties makes it very useful also for brain scanning.

Technetium-99m in the sulphur colliod form is removed from the blood by the reticuloendothelial system, thus permitting scanning of the bone marrow, liver and spleen. Placental imaging is also accomplished by either labeled ^{99m}Tc human serium albumin, (^{99m}Tc-HSA), or ^{99m}Tc eluate directly. Kidney imaging has been accomplished by using ^{99m}Tc labeled diethylenetriamine pentaacetic acid (DTPA), and preliminary work

has been done involving lung imaging with ^{99m}Tc labeled macro-aggregated albumin (^{99m}Tc-MAA). Extended explanations of the medical uses of this radionuclide are beyond the scope of this paper, but may be found in the literature.

Several papers have been published regarding the activity levels of contaminants in ^{99m}Tc eluates from both irradiation (n,γ) and fission produced ^{99}Mo. In 1963, Weiss and Hillman[3], reported the predominant contaminants of fission produced ^{99m}Tc generators to be ^{132}Te and ^{132}I. Smith[4], in 1964 using fission produced ^{99m}Tc generators, reported ^{99}Mo, ^{103}Ru, and ^{131}I in eluates with respective typical activities of .05μCi, .003μCi and .0002μCi per millicurie of ^{99m}Tc at the time of elution. In 1969 Crosby[5], using irradiation produced ^{99m}Tc generators in the pertechnetate ($^{99}TcO_4$) form and a 2" x 2" NaI(Tl) detection system with a 400 channel analyzer, determined ^{186}Re contamination with typical levels of .1% of the total administered dose to the patient.

In 1971 Wood and Bowen[6], using generators produced by an unspecified process and using a 2" x 2" NaI(Tl) detection system with a 400 channel analyzer, qualitatively determined ^{95}Zr and ^{124}Sb from one distributor's eluates. Muller and Steinnes[7], in 1971, using generators from five European distributors and a 20 cm^3 Ge(Li) detector with a 2000 channel analyzer detected "small" amounts of ^{60}Co, ^{86}Rb, ^{110m}Ag, ^{131}I, ^{131}Ba, ^{134}Cs, and ^{239}Np in at least one of the eluates analyzed. Using flame spectroscopy for aluminum determination in solution and neutron activation analysis for particulate filter trapped aluminum, Muller and Steinnes[7] also reported between $\leq$ .5 ppm and 92 ppm Al in solution, and

between $\leq$ .10 ppm and 3.8 ppm Al in the filter for these same eluates. General Electric, the commercial manufacturer of irradiation produced ^{99}Mo in the United States, supplied a list of radionuclide contaminants in ^{99}Mo Target Lot Number 15, which as of January 1973, was the current lot in use[8]. The results of their analysis are presented in Table 1. Aronson[9], listed the contaminants found in General Electric Target Lot Number 6. (Table II). Lewis[10], in 1971, described details of the separation and purification of fission produced ^{99}Mo. Also presented was an assay of a typical ^{99}Mo preparation, shown in Table III. In 1971 Webber, Cragin, and Victery[11], determined aluminum concentrations in five distributor's eluates using the aluminon colorimetric procedure, and reported between $\leq$ .2 ppm and 44.8 ppm Al in the eluates analyzed.

In 1971 Palmer, Hall and Tyson[12], determined aluminum concentrations in eluates from 65 ^{99m}Tc generators, and reported between .051μCi/mCi ^{99m}Tc and 40.69 μCi/mCi ^{99m}Tc at the time of eluation.

The purpose of this study was to analyze both irradiation and fission produced ^{99m}Tc generator eluates, and quantitatively to determine when possible the activity of radionuclide and stable isotope contaminants present in these samples. An attempt was also made to correlate the data to determine the method of production of ^{99m}Tc generators resulting in eluates containing the lowest impurity levels.

Table I Radiopurity Analysis of General Electric Lot Number 15 Four Days After Removal of Target from Reactor.[8]

Isotope	Assay(mCi/ml)	% Isotope/^{99}Mo
^{99}Mo	296	-----
^{92m}Nb	1.1	.37
^{187}W	.022	.007
^{95}Nb	.02	.007
^{86}Rb	.016	.005
^{124}Sb	.005	.002
^{134}Cs	.004	.001
^{65}Zn	.0003	.0001
^{60}Co	.00008	.00003
^{188}Re	.0002	.00008
^{186}Re	.0009	.00035

Table II Contaminants in General Electric Target Lot Number 6.[9]

Isotope	Assay(mCi/ml)
Nb-92m	1.5
Nb-95	.02
W-187	.05
Cs-134	.002
Sb-124	.003
Rb-86	.004
Zn-65	.0002
Co-60	.00007

Table III Typical Radiopurity Analysis of Union Carbide Fission Molybdenum Lot.[10]

Isotope	Assay(mCi/ml)
^{99}Mo	200
^{131}I	.01
^{103}Ru	.0001
^{132}Te	$\leq$ .00014*
^{95}Zr	$\leq$ .00022*
^{95}Nb	$\leq$ .00002*
gross alpha	$\leq$ 1000 dpm/ml*

* detection limit

CHAPTER 2

EQUIPMENT AND SUPPLIES

The generators employed in this study were manufactured in the United States and used ^{99}Mo produced by two basic methods. The first method utilizes ^{99}Mo produced by neutron irradiation of a molybdenum target via the (n,γ) reaction. This ^{99}Mo is produced by General Electric, Nuclear Energy Division, Vallecitos Nuclear Center and supplied in polybottles as sodium molydate to the four major commercial vendors of ^{99m}Tc generators in this country: Abbott, Mallinckrodt, New England Nuclear (NEN), and Squibb. These vendors then transfer the solution, after possible final processing, (company properietary information), to an alumina (Al_2O_3) column in which form they are then marketed to the nuclear medicine community. (At this time, only three of the four vendors produce their own generators; Abbott uses columns produced by Mallinckrodt).

Description of the Generator

Schematic representation of a commerical ^{99m}Tc generator is presented in Fig. 1. The entire system is packaged in a small cylindrial metal can, the contents being secured with polystrene inserts. The generator column is constructed of a molded plastic column depending upon manufacturing between 2" and 4" long and between 1/2" and 1 1/2" in diameter containing between 5 and 10 grams of Al_2O_3, which has the ^{99}Mo adsorbed on it. A lead shield surrounds the column which is positioned

upright in the container. Typically an inverted vial containing sterile physiological saline is first connected to the system via a dual hypodermic needle at the top of the container. A similarly inverted empty collection vial whose inside is under a partial vacuum is then connected to the system by a hypodermic needle as shown in Fig. 1. The partial vacuum in the collection vial causes saline to flow to the column while air is being drawn through a particulate filter designed to eliminate external contamination of the solution. The solution flows through the column, eluting ^{99m}Tc from the Al_2O_3, passes through a millipore filter that is designed to remove particulate alumina (Al_2O_3) from the solution and is then drawn into the collection vial. By first removing the collection vial, then the saline vial from the system, the elution is stopped and the introduction of air into the collection vial is avoided. The system may then be stored for the next elution which follows the same procedure.

The other method for the production of ^{99}Mo involves its separation from the fission products of ^{235}U, and is used by primarly in the United States by Union Carbide, Isotope Sales Division. Details for the processing and purification of fission produced ^{99}Mo at Union Carbide, as well as the method of placing the radionuclide on an alumina column for the user, are given by Lewis[10].

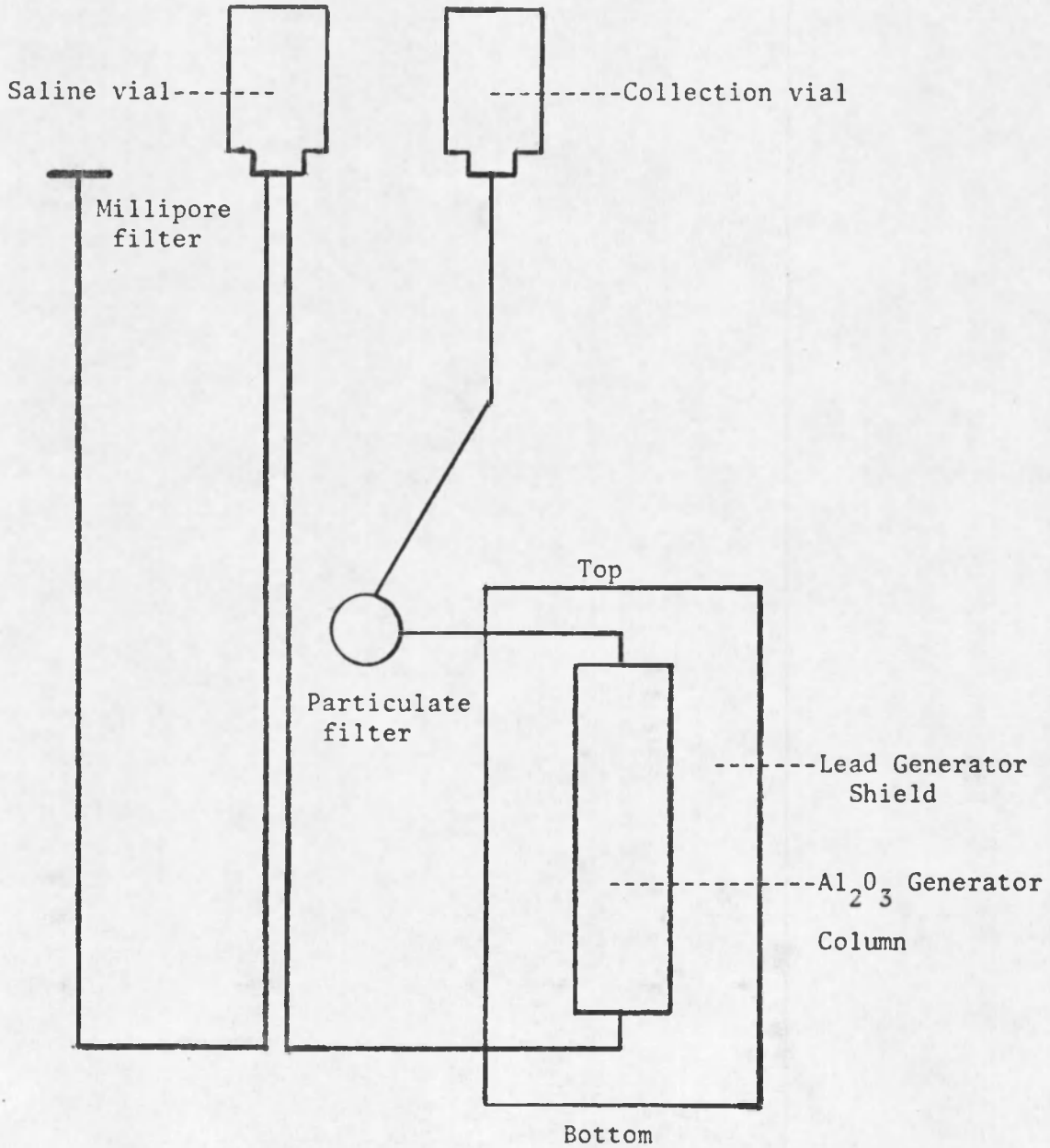

Fig. 1 Schematic Representation of A ^{99m}Tc Generator

The largest number of eluates analyzed in this work were from NEN, because their generators are obtained weekly by the Nuclear Medicine Division, Department of Radiology, University of Arizona. It was very difficult to procure samples from certain distributors of ^{99m}Tc generators due to reluctance of the suppliers and users to furnish eluate samples or discarded generators. Samples from fission produced generators were particularly difficult to procure as such generators are not used extensively at this time by members of the nuclear medicine community in the state of Arizona.

Detection Systems

The Ge(Li) detection system of the Department of Nuclear Engineering was used for high resolution spectrum analysis of samples believed to contain multiple radionuclides with gamma ray peaks of closely neighboring energies. A diagram of this detection system is presented in Fig. 2. The Ge(Li) detector used had an active volume of 41 cm^3, and was manufactured by Nuclear Diodes (Model LGC 3.05-2.9). The preamplifier connected to the Ge(Li) detector was manufactured by Nuclear Diodes (Model 101A). The detector high voltage power supply was made in the Department of Nuclear Engineering electrical shop, and was operated at -1600 volts. The main shaping amplifier and stretcher was manufactured by Tennelec (Model 250A). The analog to digital converter was manufactured by Northern Scientific (Model 623). The multichannel analyzer capacity was provided by a 4069 channel analyzer manufactured by Northern Scientific (Model 636). The computer interface used was manufactured by Northern Scienfitic (Model 440). The on-line computer

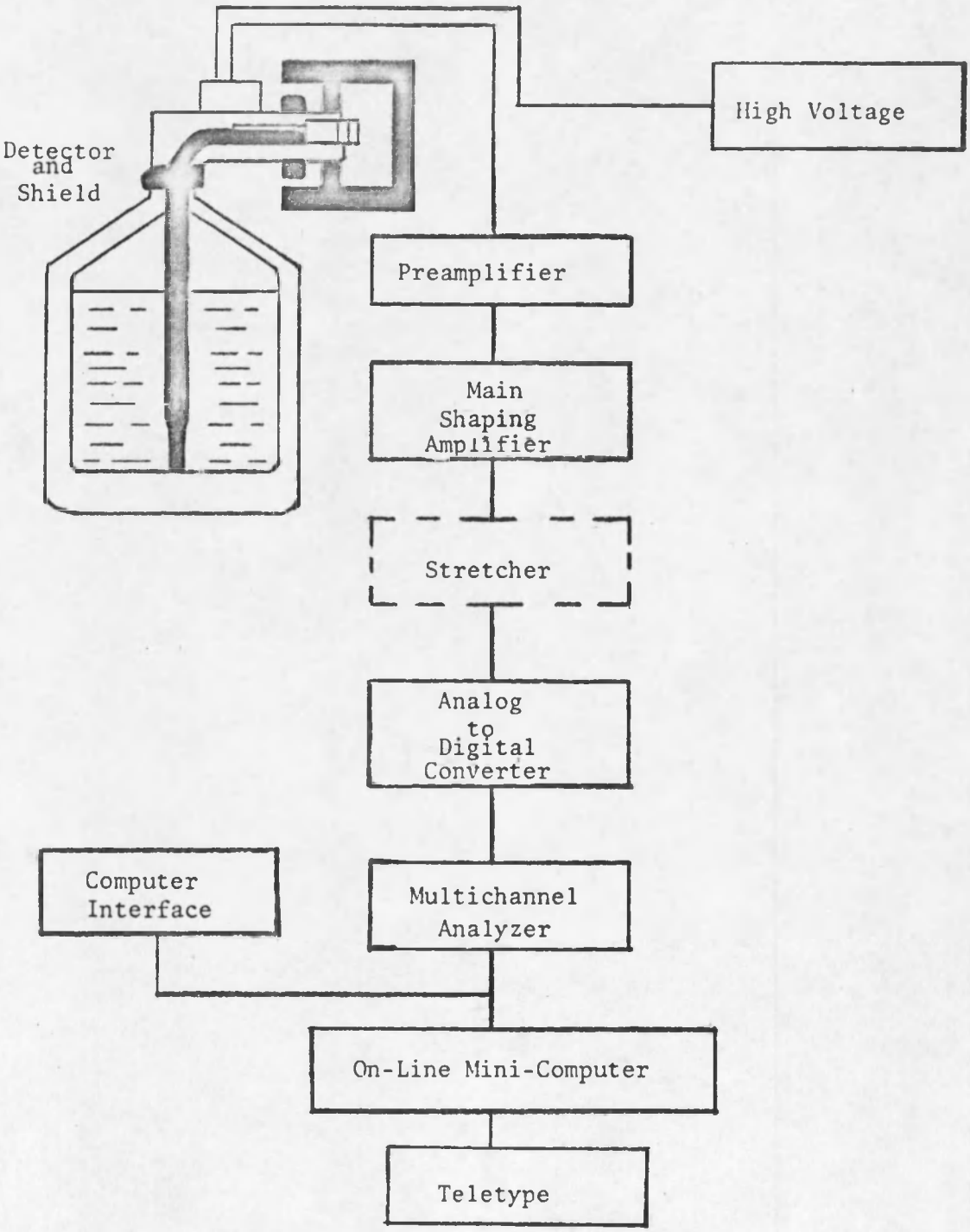

Fig. 2 Ge(Li) Detection System

was maunfactured by Data General (Model Nova 1200). Readout was provided by a Teletype unit.

The NaI(Tl) detector was part of a low level counting system[13] for the determination of radionuclide in low quantities by a significant reduction of the background of the system through special shielding precautions. The detection system, as shown in Fig. 3 utilized a 3" x 3" Harshaw NaI(Tl) detector crystal. The photomultiplier tube was a ten stage, head-on type manufactured by RCA (Model 8054). A .032 inch one-piece self-contained aluminum jacket enclosed the crystal and the photomultiplier tube. The preamplifier used by Nuclear Chicago (Model 20701). The high voltage was supplied by a Fluke high voltage power supply with a recommended operating voltage of +1100 volts for the photomultiplier. The delay line amplifier was manufactured by Ortec (Model 460). The remaining equipment in the system was identical to that used in the Ge(Li) detection system, as previously described.

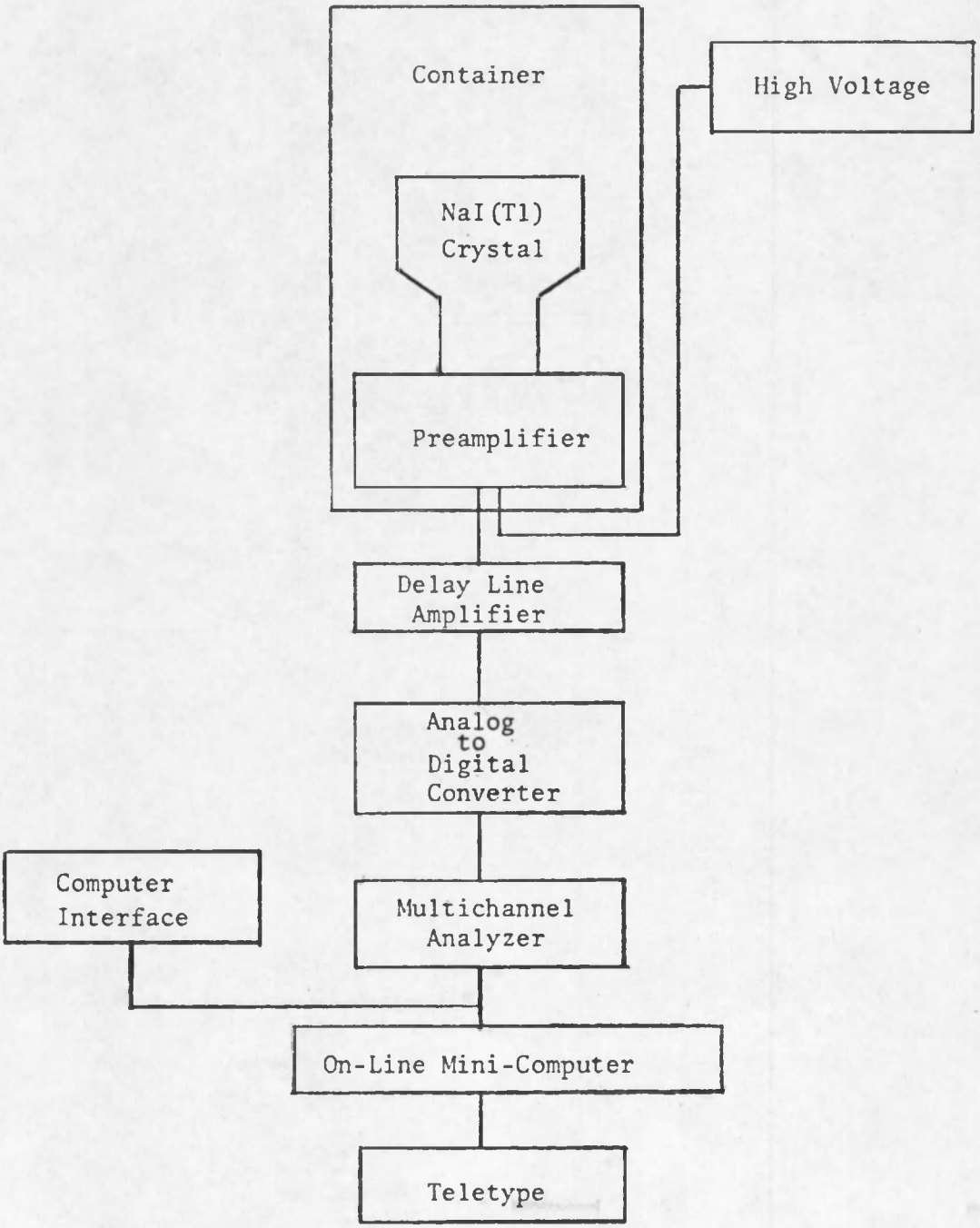

Fig. 3 NaI(Tl) Detection System

CHAPTER 3

EXPERIMENTAL PROCEDURES

Similar techniques were used with the NaI(Tl) and Ge(Li) detection systems. Peak height analyses, aided by an on-line minicomputer, were also identical with both systems. Counting geometries were approximated with both detection systems to match both the physical shape of the calibration sources and the spatial distance from the sample to the center of the detector.

Because of the differences in size and shape between the detection components of the two systems, standards and samples were analyzed in a manner designed to eliminate major geometry variations as much as possible. With the NaI(Tl) detector the crystal and preamplifier formed an upright cylinder with the bottom of the vial perpendicular to the axis of the detector, as shown in Fig. 4A. Samples were placed on the top of the crystal and on the center of its surface. The eluate samples were transferred to evacuated, calibrated volume injection vials, (6 ml and 25 ml), and were counted inside a 250 ml polypropylene beaker to eliminate possible direct contamination of the detector. (A background count of this beaker in position of the crystal later revealed that no detectable amount of radioactive contamination was present.) One ml samples were analyzed inside sealed 1 1/2 ml polyethylene vials and positioned on the NaI(Tl) crystal with the aid of a plexiglass holder positioned in the same manner as standards, as shown in Fig. 4B.

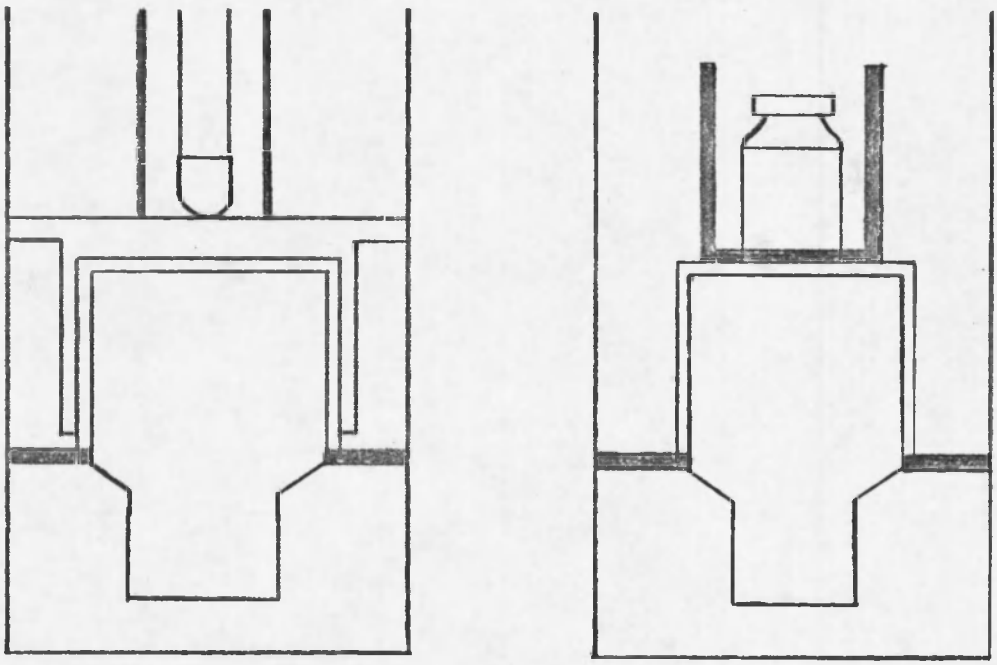

Fig. 4 NaI(Tl) Standard and Sample Counting Configuration

With the Ge(Li) detection system the axis of the detector was parallel to both the bottom of the counting vial, and to the bottom of the tip of the calibration standards, as shown in Figs. 5A and 5B respectively. Calibrated volumes of 6 ml and 25 ml were used for counting and were placed atop a one-inch thick piece of fiberboard to maintain the sample geometry. Calibrated standards were taped in place at the same height and position to simulate the spatial geometry of the counting sample vials. Background analysis of the fiberboard holder with the Ge(Li) detection system revealed no detectable activity transferred from the vials to the counting environment.

The ^{99m}Tc generators were eluted in the same manner as if the eluates were to be used for human injection, i.e., via standard procedures as recommended by the manufacturing using sterile physiological saline (.9% NaCl). The generators were eluted with 20 ml of saline on Monday, Tuesday, and Wednesday. By Thursday, the fourth day of the five day elution period, the column had been sufficiently depleted in activity, due to the 67 hour half life of the parent ^{99}Mo to necessitate a revised elution procedure. This procedure consisted of eluting with a 3 ml volume of saline followed by three (3) 6 ml volumes of saline each. The 3 ml eluate and the first of the 6 ml eluates were discarded because of low ^{99m}Tc activity. The remaining two (2) 6 ml eluates were then used for patient administration. This same procedure was also followed for the Friday elution which was the fifth and final day of the generators use. Due to health physics considerations, the generator column was stored for at least sixty days before being discarded.

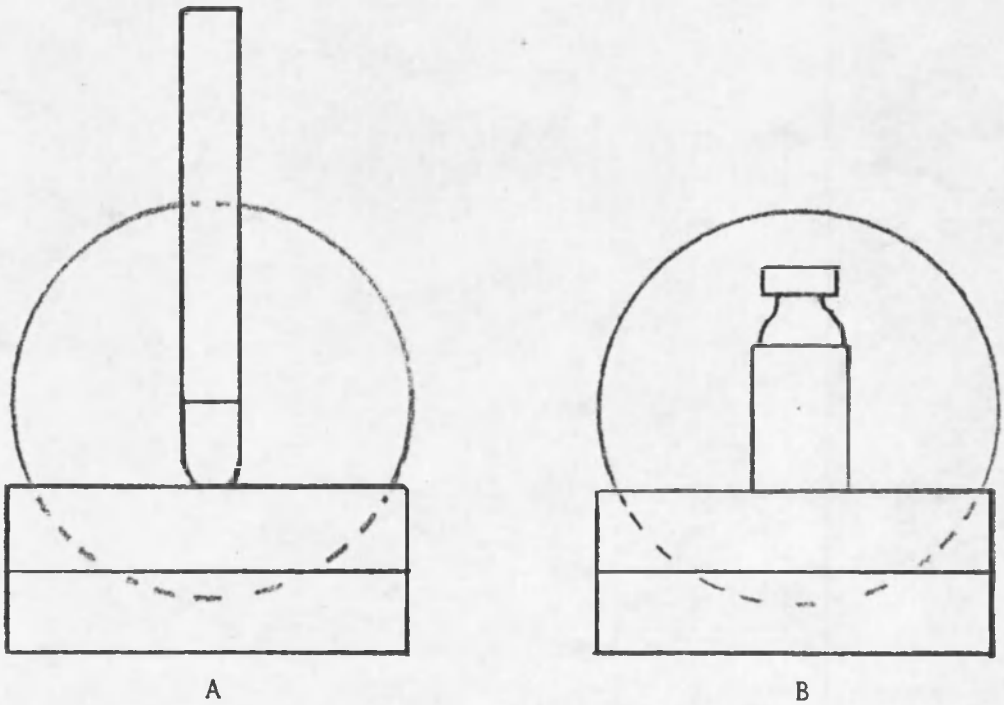

Fig. 5 Ge(Li) Standard and Sample Counting Configuration

The so-called "initial" activities of ^{99m}Tc generators analyzed varied between 50 mCi and 300 mCi. These generators are calibrated with the stated "initial" activity for a Friday elution. Thus, because of 67 hour half life of the ^{99}Mo the Monday elution may be 270% of the Friday elution, or up to 800 mCi in activity. Elution yields are typically 80%, i.e., if 300 mCi of ^{99m}Tc is present on the column, then approximately 240 mCi of ^{99m}Tc will be present in the eluate.

Holding times of at least one week before analysis were necessary because of the significant analyzer dead time introduced by high ^{99m}Tc activity present in the eluates. Because of the duration of this holding time, radionuclides with short half lives possibly present in the sample might not have been detected at the time of counting although present at the time of elution. Dilution of an aliguot of eluate could have been used as a method of reducing this factor and thus allowing the possible detection of these radionuclides.

With both detection systems the appropriate counting facilities were readied, samples or standards were positioned in place, and the systems were set to predetermined count time and activated for this count time. Gamma ray spectra taken from the multichannel analyzer at the end of the count were reduced by an on-line mini-computer in preparation for further calculations.

The standards used for computional purposes and for calibration of the computer multichannel-analyzer systems were produced by Baird Atomic Inc. These standards were in holders manufactured from plexiglass and had an overall length of five inches and a diameter of one-half inch.

The active tip was positioned on the center line of the standard holder and located one-quarter inch from one end.

Each set of standards had been calibrated by the manufacturer with the date of calibration and initial activity in microcuries recorded. These standards were positioned in front of the detectors to approximate the center sample position as close as possible.

The on-line mini-computer was used for initial calculations throughout. Peak area, centroid, and resolution were all calculated through a computer routine entitled "A PX", devised and programmmed by Mr. Robert Arbaugh, graduate student, Department of Nuclear Engineering, University of Arizona. The "A PX" routine is a machine language program to reduce complex gamma ray spectra derived from a Ge(Li) detector and can also be used for NaI(Tl) spectra analyses with an acceptable amount of introduced error. A brief explanation of the data acquisition and reduction follows.

Characteristics of peaks were determined by one of several computer-stored routines. The spectra obtained were displayed on the cathode ray tube of the multichannel analyzer. The regions of interest of the spectra were intensified in the memory for better observation and marking for later computer recognition. These intensified peaks were then transferred to the on-line mini-computer for mathematical analysis. The "A PX" routine began computation by taking five channels on each side of a particular intensified peak, and calculating an average number of counts for these channels, to be used as the average background under the peak channel. The net counts obtained for each channel was thus equal to the gross counts minus the background counts.

The centroid of the peak was calculated by summing the net counts in each channel times the channel number divided by the sum of the nets counts. This procedure was carried out for each peak in the intensified region, (points one to n), with the results printed out as the centroid of the peak by the teletypewriter.

The area of a peak was calculated by taking the net counts in each channel and summing over the peak channels, (points one to n). The area of each peak was then printed out by the routine on the teletypewriter.

The full width at half maximum, or the resolution of the peak was determined by using standard gaussian equations; knowing the peak area and the peak height. The resolution may be equated to the area times the square root of π divided by two divided by the peak height. This procedure was carried out for each intensified peak, with the results printed out by the teletypewriter.

An energy calibration table was stored in the computer memory and used to correlate centroid values to energy values by linear interpolation between points; thus with a calculated centroid value from the "A PX" routine, an equivalent peak energy was also determined and printed out by the teletypewriter.

CHAPTER 4

COMPUTATIONS

The energy and activity of an unknown radionuclide were obtained by comparison with calibrated standards of known activity and gamma ray energies using the "A PX" routine. Peak areas for each standard were determined and the activity of the standards at the time of investigation was calculated from the initial activity and the elapsed time from calibration to count by Eq. (4-1).

$$A = A_o e^{-\lambda t} \qquad (4.1)$$

The symbols used in Eq. (4.1) have the following definitions:

A = the activity at the time of investigation;

A_o = the initial activitiy at time, $t = 0$;

λ = the decay constant, equal to $.693/T_{1/2}$ where $T_{1/2}$ is the half life of the radionuclide;

t = the time from calibration ($t = 0$) to count.

The product of the activity of the standard (A, Eq. (4.1)) and the absolute intensity, (A.I.) which is defined as the number of photons emitted per 100 disintegrations of parent nuclide, of the gamma ray under observation, gave the number of gammas of that energy emitted per second. The efficiency of the system for a particular energy gamma ray was then calculated by dividing the area obtained from the "A PX" computation by the calculated gamma activity. The results of the several

standards were plotted as system efficiency versus gamma ray energy. A separate efficiency calibration was required for each detection system and counting configuration employed because of inherent differences in the detector efficiency and counting geometry of the Ge(Li) and NaI(Tl) systems. Typical efficiencies for the Ge(Li) and NaI(Tl) detectors are presented in Figs. 6 and 7 respectively; (the counting geometries employed in obtaining the data for these graphs are those shown in Figs. 4A and 5A.

Knowing the system efficiency for the particular gamma ray energy in question, the specific activity of the radionuclide under investigation may then be calculated.

$$A_{sp} = \frac{C}{(V)(A.I.)(\eta)(t_{count})(37,000)} \qquad (4.2)$$

The symbols used in Eq. (4.2) have the following definitions:

A_{sp} = the specific activity (activity/cc) of the sample at the time of investigation, in μCi, equivalent to A, Eq. (4.1);

C = the net sample count;

V = the sample volume, in ml.

A.I. = the absolute intensity of a particular gamma ray energy of a radionuclide;

η = the system efficiency for a particular gamma ray energy;

t_{count} = total count time in seconds;

37,000 = the conversion factor between dps and μCi.

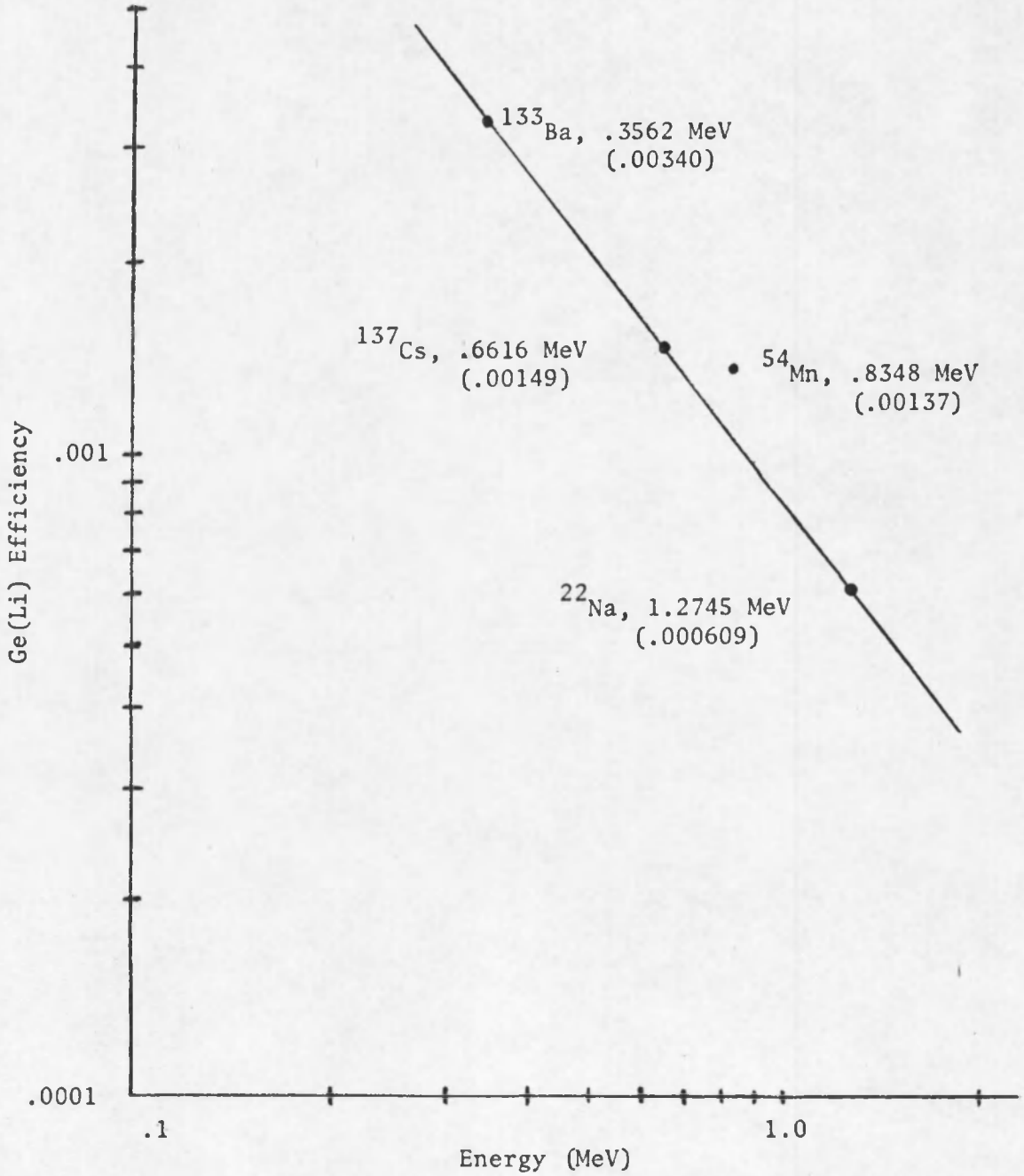

Fig. 6 Ge(Li) Efficiency Versus Gamma Ray Energy

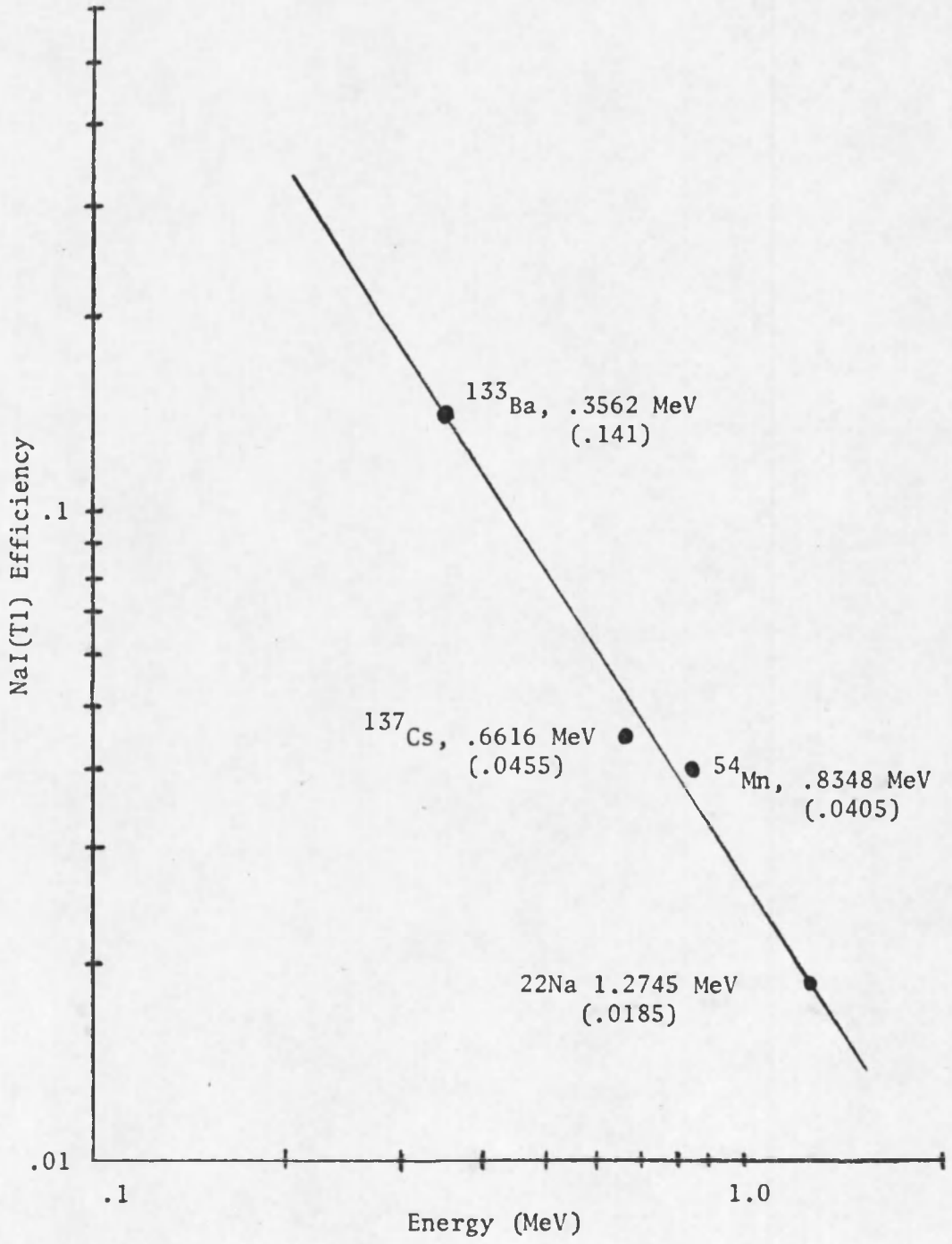

Fig. 7 NaI(Tl) Efficiency Versus Gamma Ray Energy

The initial specific activity of a radionuclide at the time of elution was then calculated by substituting the value of A_{sp} determined by Eq. (4.2) into Eq. (4.1) as A and calculating A_o.

Some gamma ray peaks of interest also occured in the background spectra, (i.e., ^{134}Cs). In such instances, the net count, C, used in Eq. (4.2) was the difference between the "A PX" computed net counts of the two spectra.

In the event that a particular radionuclide peak is not detected in a sample spectrum, a method for the determination of a maximum activity level possibly present without detection is necessary to allow accurate quantitative evaluations. The relationship used here[14] to determine the maximum activity level which might be present before detection of the gamma ray peak is possible is

$$\text{m.a.l.} = 20\sqrt{b}$$

where b is the maximum background value of the spectrum where the peak under investigation would lie if present. The value of b for this peak was determined by plotting b versus centroid location for existing peaks in the spectrum followed by linear interpolation to find the value of b at the channel location of interest, with the location of the centroid of the peak under investigation being determined from previous Ge(Li) spectra where it was present.

CHAPTER 5

RESULTS

Twenty-nine, 1 ml samples were obtained from irradiation produced ^{99m}Tc generators from four distributors and analyzed with the NaI(Tl) detection system for possible gamma ray emitting contaminants. Samples eluted from each generator were also compared on a day-to-day basis if possible to determine if elution number dependent relationships existed for the activity of contaminants eluted from the generator. Using the NaI(Tl) detection system, only ^{134}Cs was found in these samples; however analyzing a composite eluate from this group with the Ge(Li) detection system also indicated the presence of ^{60}Co in low concentrations. The calculation of ^{134}Cs activity levels using equations and techniques previously discussed, gave the results reported in Table IV. Cesium-134 activities of these eluates varied from .000013 μCi/ml to .0046 μCi/ml using both the .605 MeV peak and .797 MeV peak for analysis. In all tables presented in this chapter where there is more than one sample represented in each category the standard deviation reported is of the mean.

In four series of first and second day eluates from irradiation-produced generators analyzed with the NaI(Tl) detection system, ^{134}Cs activity increased on the second day of the five day series in all four cases. In four series of samples eluted from identical irradiation-produced generators from the third to fifth day of the elution week,

Table IV Cesium-134 (.605 MeV Peak and .797 MeV Peak) Initial Activities (nCi/ml) in Irradiation-Produced Commercial Technetium-99m Generator Eluates with NaI(Tl) Analysis.

Manufacturer (*)	Day 1 Elution(#) Mean Activity	Day 2 Elution Mean Activity	Day 3 Elution Mean Activity	Day 4 Elution Mean Activity	Day 5 Elution Mean Activity
Abbott (1)	nsa$^{\Phi}$	nsa	nsa	4.52 (1)	.23 (1)
Mallinckrodt (1)	.57^{+} (1)	.49 (1)	nsa	nsa	.50 (1)
NEN (12)	1.09 ± 1.36 (8)	1.46 ± 1.33 (5)	1.25 (1)	nsa	.55±.37(3)
Squibb (5)	1.27 ± .81 (2)	2.28 ± 2.24 (2)	.34 (1)	.27 ± .055 (2)	nsa

(*) total number of generators of each manufacturer analyzed

(#) total number of samples of each distributor analyzed per day of elution

Φ no samples analyzed for day of elution

$+$ standard deviations are expressed in nCi/ml

^{134}Cs activity decreased from the initial eluate to the final eluate in three of the cases analyzed. These results are presented in bar graph form in Fig. 8 where ^{134}Cs initial activity is plotted versus day of week elution for samples taken from the same generators of the four distributors.

Twelve irradiation-produced generator eluates from these generators and nine fission-produced generator eluates from two distributors were analyzed with the Ge(Li) detection system for gamma ray emitting radionuclide contaminants. Six radionuclides were detected in irradiation-produced generators eluates, and five radionuclides were detected in commercial and non-commercial fission-produced generators eluates, as shown in Table V. When a particular radionuclides was absent from a distributor's series of sample spectra, maximum activity of undetected levels were calculated as previously described and reported in Table V.

Large ^{99}Mo activity levels were detected in two of the four commercial fission-produced generator eluates, (16.04 μCi/ml and 10.59 μCi/ml) for a Thursday and Friday (4th day and 5th day) elution of the same generators, as analyzed with the Ge(Li) detection system. A comparison of AEC limits[15] of contaminants and maximum detected levels of contaminants reported in this work of ^{99m}Tc generation eluates are presented in Table VI. These can be compared by assuming an average patient dose of 20 mCi ^{99m}Tc in 1.5 ml volume.

One series of samples eluted from an irradiation-produced generator of five consecutive days was analyzed for gamma ray emitting radionuclides using the Ge(Li) detection system, and is reported in

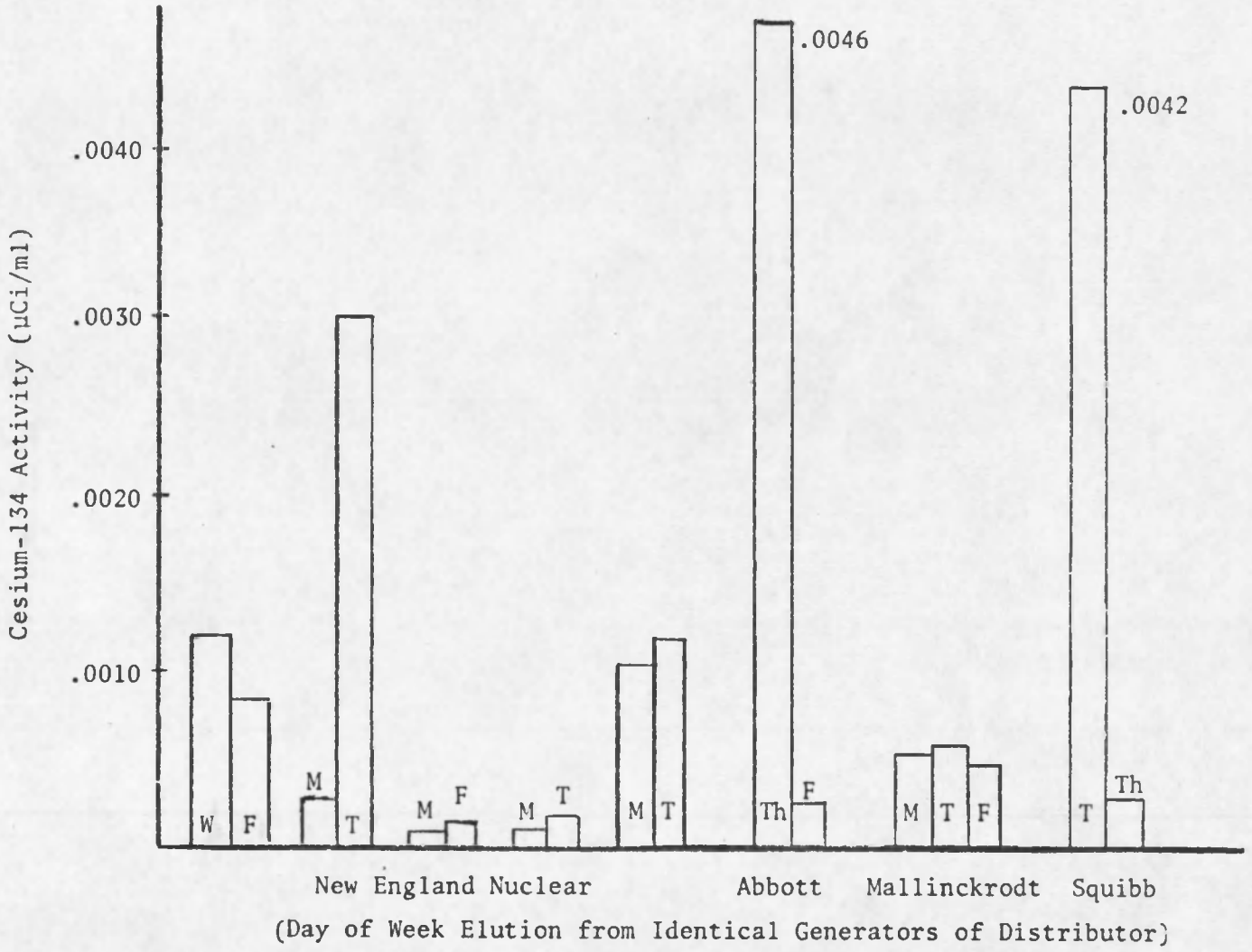

Fig. 8 Cesium-134 Activity Versus Day of Week Elution

Table V Mean Initial Activities (nCi/ml) of Radionuclides in Irradiation and Fission-Produced Commercial and Non-Commercial Technetium-99m Generator Eluates with Ge(Li) Analysis.

Manufacturer(*)	^{134}Cs (#)	$^{60}Co^{+}$	^{131}I	^{99}Mo	^{92m}Nb	^{86}Rb	^{103}Ru
Mallinckrodt(3)	.029±.015(3)$^{\nabla}$	.023±.012(3)	≤.019(3)	≤.42(3)	≤ .025(3)	≤.36(3)	≤.020(3
NEN (6)	2.98±1.76(6)	.028±.018(6)	.073±.025(4)	≤.86(6)	≤ .76(6)	1.30(1)	.94±.064(6)
Squibb(n,γ) (3)	1.07±.41(3)	.023±.013(2)	≤.030(3)	.38(1)	≤ .070(3)	≤1.14(3)	.016(1)
Squibb (F) (4)	.013±.013(3)*	≤.039(4)	≤.019(4)	13,310 ± 3850	≤ .035(4)	≤.45(4)	.27±.25(3)
Union Carbide(5)	.070±.029(5)*	≤.042(5)	.83(1)	3.17(1)	.14±.22(4)	≤.48(5)	1.16±.57(5)

(*) total number of eluates of each distributor analyzed

(#) total number of eluates of each distributor analyzed in which radionuclide was present

≤ Calculated maximum activity possible

* only .797 MeV peak used for analysis

\+ only 1.332 MeV peak used for analysis

∇ standard deviations are expressed in nCi/ml

Table VI AEC Legal Limits[15] and Maximum Detected Levels of Contaminants Present in Technetium-99m Generator Eluates Analyzed.

Mode of Production	Criteria	Aluminum	^{131}I	^{99}Mo	^{103}Ru	Gross Gamma Activity
	A.E.C.[18]	10 ppm	.05μCi/mCi ^{99m}Tc	5μCi (total or 1μCi/mCi ^{99m}Tc	.05μCi/ mCi ^{99m}Tc	.1μCi/ mCi ^{99m}Tc
Fission ^{99}Mo	Highest Detected Activity or Concentration	≤ .1ppm	.00083μCi/ml	16.04μCi/ml	.00019 μCi/ml	16.40 μCi/ml
	A.E.C[18]	20 ppm	----------	5μCi (total) or 1μCi/mCi ^{99m}Tc	------	.5μCi/ mCi ^{99m}Tc
Irradiation ^{99}Mo	Highest Detected Activity or Concentration (this work)	≤ .1 ppm	.00011μCi/ml	.00038μCi/ml	.00011 μCi/ml	.0040 μCi/ml

in Table VII. Of the five radionuclides detected in these eluates, all but ^{60}Co roughly followed a pattern of activity versus elution day. Cesium-134 increased in activity in each consecutive sample, with ^{103}Ru following a similar pattern for the first four of five days. Rubidium-86 decreased in activity below the detectable level after the first eluate sample, and ^{131}I decreased in activity in the first four of five samples analyzed.

Although not currently intended for patient administration, eluates from a non-commercial fission-produced generator were analyzed for possible gamma ray emitting radionuclide contaminants. A series of samples were eluted on five consecutive days from this generator and analyzed with the Ge(Li) detection system, as reported in Table VIII. The ^{99}Mo used in this generator was supplied by Union Carbide, and transferred to an alumina column by Mr. Jack Hall of the Division of Nuclear Medicine, Department of Radiology, University of Arizona. Iodine-131 decreased below the detectable level after the first eluate sample, and ^{92m}Nb decreased in activity in the second through the fifth samples, as shown in Table VIII. Both ^{134}Cs and ^{103}Ru increased in activity with the first through third eluate samples and decreased in activity in the fourth and fifth samples.

Neutron Activation Analysis

Because of the reported presence of aluminum in ^{99m}Tc generator eluates, the concern of its toxicity to the patient, and its possible interference with labeled technetium compounds, the determination of

Table VII Initial Activities (μCi/ml) of Radionuclides in Consecutive Irradiation-Produced Generator Eluates with Ge(Li) Analysis, New England Nuclear Lot No. 7312-3-57.

Elution Day of Week	Cesium-134	Cobalt-60	Iodine-131	Rubidium-86	Ruthenium-103
Monday (H)	.0010	.000039	.00011	.0013	.000018
Tuesday (I)	.0016	.00016	.000074	nd*	.000050
Wednesday (J)	.0022	.000092	.000056	nd	.000064
Thursday (K)	.0030	.00016	nd	nd	.00013
Friday (L)	.0038	.000057	.000057	nd	.00011

* nd: not detected.

Table VIII Initial Activities (μCi/ml) of Radionuclides in Consecutive Fission-Produced Generator Eluates with Ge(Li) Analysis, Union Carbide Lot No. Non-Commercial.

Day of Elution	Cesium-134*	Iodine-131	Molybdenum-99	Niobium-92m	Ruthenium-103
4-9-73 (A)	.000050	.00083	nd[Φ]	nd	.00027
4-10-73 (B)	.000067	nd	.0032	.00047	.0011
4-12-73 (C)	.00011	nd	nd	.000035	.0017
4-13-73 (D)	.000092	nd	nd	.000025	.0017
4-16-73 (E)	.000035	nd	nd	.000016	.0011

[Φ]nd: not detected

* .797 MeV peak used for analysis

this element via neutron activation analysis was undertaken with several irradiation and commercial fission-produced generator eluates.

Eleven irradiation-produced generator eluates from four distributors, (two from Abbott, three from Mallinckrodt, four from NEN, and two from Squibb), and one empty vial, (blank), were irradiated with a neutron flux of approximately 10^{12} n/cm^2-sec for 120 seconds, held for 120 seconds, and counted with the Ge(Li) system for 128 seconds. One eluate from one distributor (NEN) was irradiated with the same flux for 10 minutes and counted for 128 seconds after a 120 second decay period. The radionuclides detected in these eluates and the blank were ^{24}Na, ^{38}Cl, ^{19}O and ^{23}Ne. Sodium-24 and ^{38}Cl were produced by the (n,γ) reaction with ^{18}O, and ^{23}Ne was produced by the (n,p) reaction with ^{23}Na. Absolute intensities, half lives and γ ray energy used in analysis of the data in this paper are presented in Table IX.

To observe any radionuclides that might be produced by a fast neutron reaction, three eluates from one distributor (NEN) were then irradiated in the Fast (neutron) Irradiation Facility (FIR) along with an empty vial, normal saline blank, and distilled water blank. As in the previous case, only ^{24}Na, ^{38}Cl, ^{19}O, and ^{23}Ne were detected using the Ge(Li) system.

The eluate (21ml) from one distributor's irradiation produced generator (Squibb) was evaporated on aluminum foil and together with an aluminum foil blank, irradiated for 4-1/2 hours with a neutron flux of approximately 10^{12}n/cm^2-sec. Both samples were analyzed after 11 days with the Ge(Li) system for possible radionuclide contaminants. Bromine-82, ^{24}Na, ^{60}Cs and ^{134}Cs were dectected on the evaporated aluminum foil

Table IX Absolute Intensities, Half Lives and γ Ray Energies of Detected Radionuclides.[16]

Radionculide	AI	$T_{1/2}$	γ Ray Energy (MeV)
^{134}Cs	.875	2.06yr	.605
	.988	2.06yr	.797
^{60}Co	1.000	5.2 yr	1.3325
^{131}I	.790	8.03d	.3645
^{99}Mo	.137	66.7hr	.7397
^{92m}Nb	1.000	10.1d	.934
^{86}Rb	.088	18.7d	1.0788
^{103}Ru	.890	39.5d	.497
^{66}Cu	.0895	5.10m	1.0392
^{23}Ne	.33	38.0s	.439*
^{24}Na	1.000	15.0hr	1.3684
^{38}Cl	.470	37.3m	2.1676
^{19}O	.979	29.15	.1974
^{82}Br	.835	35.3hr	.7765

* All information on this line is from reference 17.

sample, but were absent from the blank. Sodium-24 was produced predominantly by the (n,γ) reaction with the sodium of the physiological saline eluting solution, while ^{134}Cs and ^{60}Co were eluted from the generator column. Bromine-82 was produced from the (n,γ) reaction with stable ^{81}Br which was probably introduced into the eluate vial from the generator column matrix.

One ml samples from four commercial fission-generator (Squibb) eluates and an empty vial, (blank), were sealed in polyethylene vials and irradiated in a neutron flux of approximately 10^{12} n/cm^2-sec, held for 30 seconds, and counted for 128 seconds. The five radionuclides detected in these eluates with the Ge(Li) system were ^{24}Na, ^{38}Cl, ^{19}O, ^{23}Ne and ^{66}Cu; with the origin of the first four isotopes being previously described. Copper-66 was detected and found to vary in three of the four samples analyzed and was produced from the (n,γ) reaction with stable ^{65}Cu.

Although aluminum was not detected in any of the samples analyzed by neutron activation analysis, the maximum concentration of this element possibly present was calculated to be $\leq$ .1 ppm in all cases.

Statistical Counting Analysis

An attempt was made to estimate errors in the results due to statistical fluctuations in the counting data. The standard deviations of the net counts N used in Eq. (4.2) were calculated using the valid assumption that all raw counting data was Poisson distributed.[18] Using this assumption the standard deviations or errors in the data may be approximated as the square root of the number of counts. The error in

N may then be obtained by standard propagation of error techniques. For example, for an isolated peak as shown in Fig. 9 the net counts N are given by

$$N = G - B \tag{5-1}$$

where G is the gross counts under the peak and B is the background counts. The error in N (one standard deviation σ_N) is thus given by

$$\sigma_N = \sqrt{\sigma_G^2 + \sigma_B^2}$$

$$\sigma_N = \sqrt{G + B} \tag{5-2}$$

Although N was calculated using the "A PX" routine only estimates of B and hence G could be provided. B was approximated by

$$B = xb \tag{5-3}$$

where

b = the "A PX" output for the number of background counts in the channel with the maximum number of net counts, and was taken to be an approximate number of B counts per channel;

x = the channel width of the prak under analysis, determined from the "A PX" program.

Using Eqs. (5-1), (5-2), and (5-3), we obtain

$$\sigma_n = \sqrt{N + 2 \times b} \tag{5-4}$$

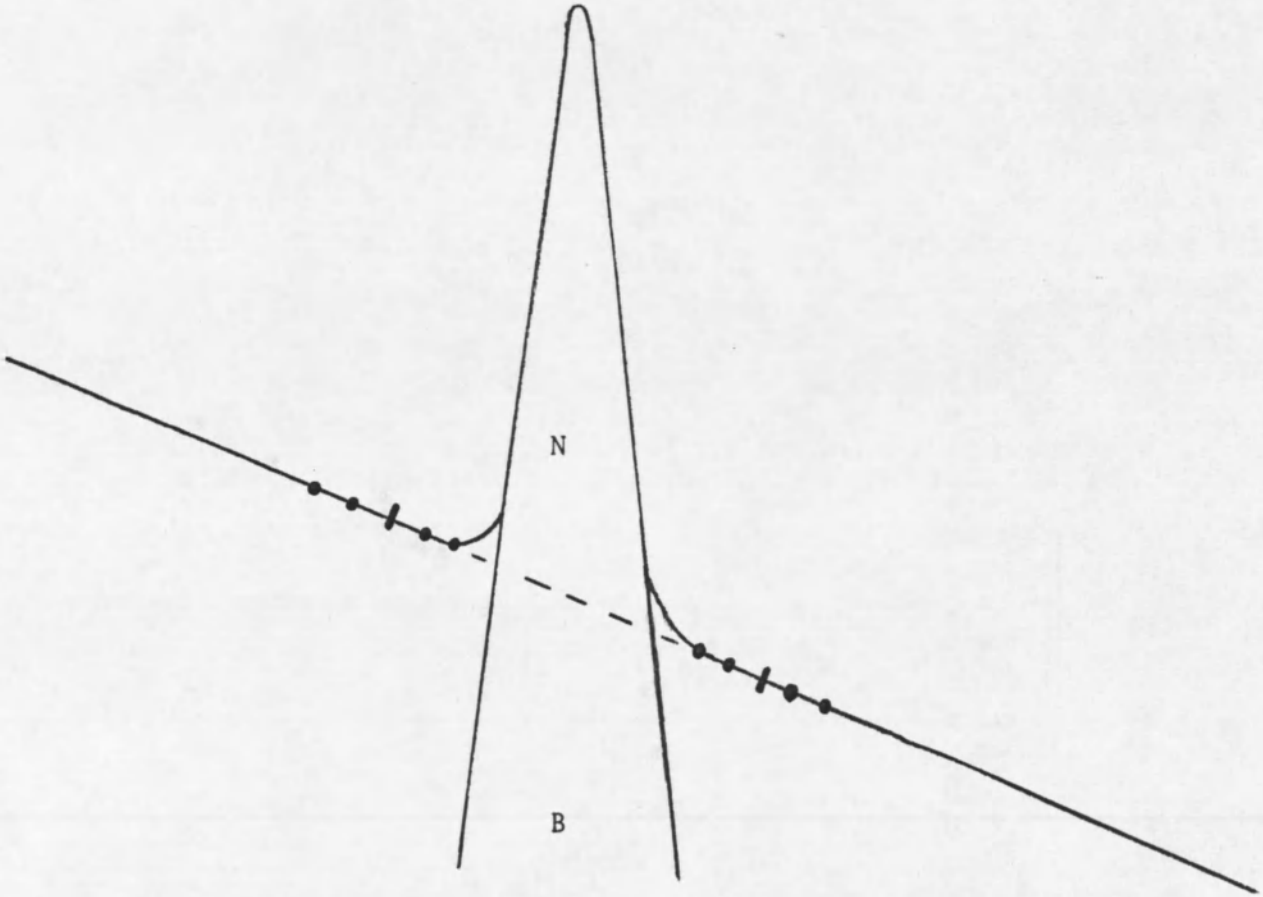

Fig. 9 Isolated Gamma Ray Peak with "A PX" Analysis

In those instances where sample peaks were interfered with by background peaks

$$N_N = N_{sample} - N_{background} \tag{5-5}$$

$$\sigma_n = \sqrt{\sigma^2_{n(sample)} + \sigma^2_{n(background)}} \tag{5-6}$$

$$= \sqrt{N_N + 2[X_{(S)}{}^b{}_{(S)} - X_{(bkg)}{}^b{}_{(bkg)}]} \tag{5-7}$$

A per cent statistical variation may then be calculated by

$$Y_N = (\sigma_N/N_N) \quad 100 \tag{5-8}$$

where Y_N is the per cent statistical variation for variables previously defined. Tabulated values of Y_j for the Ge(Li) peaks analyzed in this work are presented in the Appendix.

When radionuclides are present in a spectra that emit multiple γ rays, such as ^{134}Cs, the standard deviation of the corresponding peaks is given by

$$Y_T = \sqrt{\left(\frac{\sigma_{N_1}}{N_1}\right)^2 + \left(\frac{\sigma_{N_2}}{N_2}\right)^2 + \ldots + \left(\frac{\sigma_{N_j}}{N_j}\right)^2} \tag{5-9}$$

where

$$\sigma_{N_1} = \sqrt{N_1 + [2 \times b]_1}$$

$$\sigma_{N_2} = \sqrt{N_2 + [2 \times b]_2}$$

and

$$\sigma_{N_j} = \sqrt{N_j + [2 \times b]_j}$$

both σ_{N_1} and σ_{N_2} being given by Eq. (5-4)

The per cent statistical variation is then defined to be

$$Y_{NT} = Y_T \quad (100) \tag{5-10}$$

where σ_{N_T} is previously defined.

In those instances where multiple peaks of a radionuclide were interferred with by background peaks

$$Y_T = \sqrt{\left(\frac{\sigma_{N_1}}{N_1}\right)^2 + \left(\frac{\sigma_{N_2}}{N_2}\right)^2 + \cdots + \left(\frac{\sigma_{N_j}}{N_j}\right)^2} \tag{5-11}$$

where

$$\sigma_{N_1} = \sqrt{(N_1 - N_{(bkg)1}) + 2[xb]_1}$$

$$\sigma_{N_2} = \sqrt{(N_2 - N_{(bkg)2}) + 2[xb]_2}$$

and

$$\sigma_{N_j} = \sqrt{(N_j - N_{(bkg)j}) + 2[xb]_j}$$

The per cent statistical variation is then defined to be

$$Y_T = Y_T \ (100) \qquad (5\text{-}12)$$

where σ_T is previously defined.

Gamma ray spectral interferences that could introduce errors in the activity calculations in at least one of the radionuclides present were identified in three cases. The first case involved the interference of the 1.168 MeV peak of ^{134}Cs (absolute intensity of .0202)[16] in the calculation of the 1.172 MeV peak of ^{60}Co (absolute intensity of 1.00)[16]. A routine to substract the area of the 1.168 MeV ^{134}Cs peak from the total area of this detected peak was developed and yielded the area of the 1.172 MeV ^{60}Co peak, which then allowed the calculation of the ^{60}CO activity in the sample. The area of the 1.168 MeV ^{134}Cs peak was calculated by determining the average activity of the .605 MeV and .797 MeV ^{134}Cs peaks, and then by using Eq. (4-2) as modified below to find the area under the full energy peak.

$$\text{Area} = (C_{peak}(\text{average})(V)(\text{A.I.})(\eta)(t_{count})(37{,}000)$$

The variables in this equation have been previously defined. The 1.168 MeV ^{134}Cs peak area was then substracted from the total peak area; the remaining area being the 1.172 MeV ^{60}Co peak. Cobalt-60 activity was then calculated by using Eq. (4-2) for both the 1.172 MeV peak and the interference free 1.332 MeV peak. These values could then be compared to observe the statistical variation between the calculated activities of the two energy peaks.

The second possible case of spectral interference involved the .610 MeV peak of ^{103}Ru (absolute intensity of .0555)[16] interfering with the .605 MeV peak of ^{134}Cs (absolute intensity of .988)[16]. This interference would become a factor if the ^{103}Ru activity was much greater than that of the ^{134}Cs present, as was true of the commercial and non-commercial fission-produced generator eluates analyzed. Calculation of the ^{134}Cs activity by using the .797 MeV peak following a ^{134}Cs background subtraction routine showed a mean ratio in five eluates of the .605 MeV peak activity to the .797 MeV peak activity to be 1.06.

Apparently the "A PX" routine's straight line method of isolating peaks from the background continuum and the high resolution of the Ge(Li) system lessened the effect of possible interference.

The third possible case of spectral interference involved the .366 MeV peak of ^{99}Mo (absolute intensity of .0163)[16] interferring with the .3645 MeV peak of ^{131}I (absolute intensity of .790)[16]. The only possible cases of this interference observed involved two commercial fission generator eluates with high ^{99}Mo activity. A very large ^{99}Mo activity present in the eluate will overshadow the .3645 MeV peak of ^{131}I if the activity of this radionuclide is small. The largest initial ^{131}I activity detected was approximately .00010 μCi/ml, considerably smaller than the ^{99}Mo activity in two samples in question, (16.04μCi/ml and 10.59μCi/ml). A separation of either iodine or molybdenum from the eluate with the analysis of this subsequent solution, however, would allow a radiochemical determination of possible ^{131}I present in the solution.

Calculation of initial activities can be impeded by large inaccuracies introduced from basic equations coupled with long holding times for radionuclides with short half lives. Such a possible error should always be considered when evaluating activities of radionuclides with short half lives.

Error Analysis

Because of the low activity levels of the radionuclides under observation, several sources of errors were encountered in addition to those related to the statistical nature of radioactive decay. Due to the construction amd material of the low-level NaI(Tl) counting facility there should be an absence of all contaminants in the background environment that would interfere with the spectra of the radionuclides analyzed. Utilizing counting times of up to 48 hours, the only interfering radionuclide that was detected in the background of the Ge(Li) detection system was ^{134}Cs. Background subtraction routines were employed when analyzing samples with low ^{134}Cs activity with the Ge(Li) system to eliminate possible errors that would produce elevated count rates.

Some error was introduced because of the inability to match standard-sample geometries exactly except on a repetitive basis. As previously discussed, standards were placed before the detectors in a manner to approximate as closely as possible the geometry of the samples that would be counted.

Errors introduced into the count time and sample spectrum by the detection system were considered unlikely and minimal. Exact count times were provided after each analysis by the multichannel analyzer, and except for severe electrical transients, the system was relatively free from environmental effects except for a day-night background variation which could be influenced by factors such as fluorescent lighting, traffic, electrical equipment operation and changing temperature. Spectra obtained with the Ge(Li) system and output with the "A PX" routine that have been influenced by the preceding factors may have a three to four KeV drift day to day from the same standards and calibration tables. From observation, this energy calibration shift did not cause a significant variation in the area of replicate spectra.

The importance of experimental errors introduced by geometrical, instrumental and environmental variations can be evaluated from replicate spectra of eluate samples. Variations in areas of identical peaks in these replicate spectra which are significantly greater than that attributable to the statistical process of radioactive decay can be considered to be experimental in nature. Replicate spectra of an eluate sample that show variations in the background, B, and an energy calibration shift may be due to instrumental or environmental effects previously discussed. Errors due to geometrical effects between replicate spectra will produce variations in the net count, N.

The results of two eluates samples analyzed in replicate are presented in Tables X and XI. Ruthenium-103 produced almost identical values of N and Y_n in the replicate count of sample 1. The large percent

Table X Replicate Spectra Analysis of A Fission-Produced Generator Eluate.*

	^{134}Cs		^{137}Cs	^{60}Co	^{92m}Nb	^{103}Ru
Gamma Ray Energy (MeV)	.605	.797	.6616	1.3325	.934	.497
N_1	349.1975	211.2992	1539.099	------	55.7988	11392.38
σ_1/N_1	.2355	.2555	------	------	.8282	.0122
N_2	741.7975	281.7995	1493.999	------	23.7988	11217.38
σ_2/N_2	.7028	.1739	------	------	1.867	.0120
*$\Delta N(1\rightarrow2)$	+112.4%	+33.4%	-2.9%	------	-56.9%	-1.5%
Y_N or Y_T	Y(.605) = 25.7% Y(.797) = 30.9%		-----	------	$Y_{N(1)}$ = 82.8% $Y_N(2)$ = 186.7%	$Y_{N(1)}$ = 1.2% $Y_{N(2)}$ = 1.2%

*Union Carbide(E), Fission-Produced ^{99}Mo, Eluted 4/16/73, 5.0 ml
Count 1, 32768 Seconds, 4/20/73
Count 2, 32768 Seconds, 4/22/73

Table XI Replicate Spectra Analysis of An Irradiation-Produced Generator Eluate.*

	^{134}Cs		^{137}Cs	^{60}Co	^{92m}Nb	^{103}Ru
N_1	428.5272	168.5386	1601.3086	119.9576	-----	------
σ_1/N_1	.2046	.3427	-------	.2607	-----	------
N_2	157.7988	175.7988	1527.2990	104.0002	-----	------
σ_2/N_2	.4978	.2955	------	.3062	-----	-------
$^{*}\Delta N_{(1\rightarrow 2)}$	-63.2%	+4.3%	-4.6%	-13.3%	-----	--------
Y_N or Y_T	Y(.605) = 53.8% Y(.797) = 45.3%		------	$Y_{N(1)}$ = 26.1% $Y_{N(2)}$ = 30.6%	-----	--------

*Mallinckrodt(G), Irradiation Produced ^{99}Mo, Eluted 2/12/73, 6.0 ml
Count 1, 32768 Seconds, 4/28/73
Count 2, 32768 Seconds, 5/9/73

statistical variation in both counts of ^{92m}Nb in sample 1 is to be expected due to the low number of net counts in each peak. The large percentage variation in the net counts of the .605 MeV ^{134}Cs peaks in sample 1 was due to improper peak boundaries entered into the computer memory during the intensification routine. Cesium-137 contamination in the counting environment background produced similar values of N in both replicate spectra.

It is apparent from Tables X and XI that geometrical, and environmental effects were kept to a minimum, at least in those replicate sample spectra analyzed, and the largest source of variation was introduced by the statistical nature of the radioactive decay process.

It is expected that large variations in samples from distributor to distributor and day to day sampling as compared to the statistical variation expected on the basis of counting statistics are attributable to generator to generator differences and variations in sampling beyond the control of the experimental planning in this work.

Errors that affected the efficiency of the detection systems, and that were introduced into the calculations indirectly were considered. Geometrical variations, as previously discussed, yield errors in the efficiency versus energy graph. This will then produce a direct error in the determination of the system's efficiency, as will the inaccuracy of the corresponding graph.

Errors that were introduced into the calculations were considered to be the most basic in nature and subject to the most direct evaluation. Peak areas from the "A PX" routine may have had different resolutions

due to incorrect intensification or significantly large dead times from high sample activity. Volume measurements of liquid eluates were considered accurate as calibrated syringes and volumetric pipets were used throughout. Absolute intensities have been tabulated by several authors but disagreements occur between these sources. One example of this variation is the .797 MeV peak of ^{134}Cs with listed absolute intensities from .875[16] to .99[17]. Errors encountered in the calibration of system efficiency have been previously presented.

CHAPTER 6

DISCUSSION

Eluate contamination was produced by two basic modes; radionuclides transferred from the irradiation target or fissioned uranium with the ^{99}Mo to the generator and those introduced by contamination of the elution and counting environments. Seven radionuclide contaminants were detected in the various eluate solutions analyzed (Table V). With irradiation-produced generators, the presence of ^{60}Co, ^{134}Cs, ^{99}Mo, ^{92m}Nb, and ^{86}Rb in eluates was probably due to contamination of the target material, as reported by the manufacturer[8].

Iodine-131 and ^{103}Ru were detected in irradiation-produced generator eluates, as well as in fission-produced generator eluates. Iodine-131 may be produced by either a (n,γ) interaction with ^{130}Te producing ^{131}Te which undergoes beta decay to form ^{131}I or by the fission reaction. Tellurium may be present in the molybdenum target material due to its presence in molybdenum bearing ore.

Iodine-131 was detected in one non-commercial fission eluate analyzed. Iodine-131 contamination of the target material at the processing center or at the distributor's generator production center is possible, as is contamination of the sample at the site of elution. Ruthenium-103 may be produced by both the (n,γ) interaction with ^{102}Ru (31.6% natural abundance) or the fission reaction with uranium.

The Ge(Li) and NaI(Tl) detection system as well as some facilities at the Division of Nuclear Medicine, Department of Radiology, University of Arizona, were analyzed for ^{131}I contamination as this radionuclide was used in the latter for diagnostic patient incestigation. Background determinations were performed using the Ge(Li) system with no ^{131}I being detected. Evacuated vials, the same as used in eluate transfer and spatially located in the same position to the ^{131}I sources as the sample vials, were filled with physiological saline solution, and analyzed for ^{131}I contamination. The .3645 MeV peak of ^{131}I was not detected in the background determinations. The maximum calculated ^{131}I present in the Ge(Li) system was .00013μCi, (.000022μCi/ml for a 6 ml counting vial), approximately 2-1/2 times greater than the lowest detected ^{131}I activity in any irradiation-produced generator eluate (Table V). The source for this contamination was thus probably either the target material processing center or the distributor's generator production center.

Ruthenium-103 was detected in both irradiation and fission produced generator eluates. It was not used for diagnostic patient investigation at the Division of Nuclear Medicine, Department of Radiology, University of Arizona, nor was it produced or used in the environment of the Ge(Li) or NaI(Tl) counting facilities. Ruthenium-103 can be produced by both irradiation and fission reactions. Because of its presence with other noble metals in molybdenum ore it is a possible molybdenum target material contaminant.

Niobium-92m was detected in non-commercial fission-produced eluates but was absent from both commercial fission-produced eluates and irradiation-produced eluates analyzed. It is not directly produced by the fission process, but can be indirectly produced by an (n, 2n) reaction with ^{93}Nb, a stable fission-produced isotope and present in 100% abundance in natural niobium. Using computer calculated fission spectra[19], in atoms per 100 atoms fissioned, for a one day thermal fission and one day cooling period, and for a 15 day thermal fission and one day cooling period, there are 6.70×10^{-7} and 6.49×10^{-7} atoms per 100 atoms fission-produced. The small fission yield for ^{93}Nb coupled with the undoubtedly small thermal cross section for the (n,2n) reaction indicates a very low probability for the production of ^{92m}Nb by this compound reaction. (This assumes that there is no detectable quantity of ^{93}Nb present in the enriched (93%) ^{235}U target material.) Niobium-93 might, however, be present in the aluminum alloyed with this target material, allowing the (n, 2n) reaction to proceed directly: a process that is theoretically possible. The presence of ^{99m}Nb in the eluate solutions may also have been due to contamination in one of the two processing stages of generator production previously mentioned.

The presence of ^{99}Mo in both irradiation and fission-produced generator eluates is understandable as this radionuclide is the parent isotope of ^{99m}Tc. The activity of this radionuclide in the eluate solution was kept to a minimum by proper elution of the generator column.

Cesium-134 was also detected in fission-produced generator eluates. It may be produced directly by the fission process or by an (n-γ) reaction with ^{133}Cs which is also produced by the fission reaction.

Using computer calculated fission spectra[19], for a one day thermal fission and one day cooling period, and for a fifteen day thermal fission and one day cooling period, there were 2.43×10^{-4} and 2.45×10^{-4} atoms of ^{134}Cs produced per 100 atoms fissioned. The production of ^{133}Cs by thermal fission would be 0.48 and 3.54 atoms per 100 atoms fissioned respectively. The ^{134}Cs produced by both these reactions would be sufficient to account for its activity detected in both the irradiation and fission-produced eluates analyzed, and their consequent eluates.

The exact mechanism for the elution of some of the radionuclides detected in the samples analyzed are unknown. Due to the amphoteric nature of alumina, anions are strongly adsorbed in an acid medium and citions are strongly adsorbed in a basic medium[20]. Molybdenum-99 is loaded on the column in the anionic form as the doubly charged molybdate anion and ^{99m}Tc is eluted from the column as the singly charged pertechnetate anion thus indicating the use of an acid medium for column loading. Elution pH values are held between 4.5 and 7.4 to decrease bulk cation and anion desorption. The affinity of cations for the adsorption medium increases with charge density (increased valence with constant ionic radius and decreased ionic radius with constant valence).[21] Anions follow this same pattern, thus explaning the elution of ^{131}I as IO_3^- along with ^{99m}Tc as TcO_4^- in a near neutral pH medium. Cations such as $^{134}Cs^+$ would also be expected to desorb more readily than ones such as $^{103}Ru^{+4}$.

Due to complicating factors such as initial column preparation, i.e., batch loading or chomatographic band loading, no simple conclusions can be made for the desorption of these cations from the column. More information would be needed regarding the method of sample loading on the alumina, the pH of the loading medium on the column, intermediate purification and preparation procedures of the ^{99}Mo solution by the distributor, and preparation procedures of the alumina used in the column in order to be able to draw further conclusions about the desorption of these ions from the column.

CHAPTER 7

CONCLUSIONS AND RECOMMENDATIONS

Cesium-134 appeared to be a widespread qualitative contaminant in both the irradiation and the fission-produced generator eluates analyzed. Although it was not present at high activity levels, it was found in all but one of the fifty samples analyzed. This radionuclide appeared to increase in activity in consecutive eluates taken from an identical generator (a phenomena that is most likely related to its adsorption properties to the alumina column).

Ruthenium-103 was detected in eight of nine fission-produced eluates analyzed and seven of twelve irradiation-produced eluates analyzed. The presence of ^{103}Ru in most of the irradiation-produced eluates analyzed necessitates review of the qualitative use of this radionuclide in an eluate sample to indicate that the eluate origin is from a fission-produced generator. Quantitatively, the activity of ^{103}Ru in fission-produced eluates analyzed was greater than that in irradiation-produced eluates analyzed, but not so significantly different as to allow the identification of the generator origin based on this observation alone. At best, this method offers a tentative identification and should not be used alone if accurate determination is necessary.

Cobalt-60 was detected in eleven of twelve eluates analyzed from irradiation-produced generators, but was not detected in any eluates

analyzed from fission-produced generators. The low activity of ^{60}Co detected in the eluates analyzed would not present a health hazard for patient administration. If these eluates were not a typical in nature, then the use of ^{60}Co as a tentative origin tag for irradiation-produced generators is possible. It should be pointed out, however, that the activities detected were small, and only long counting times coupled with a high resolution detector system should be used with this method if meaningful results are to be expected.

Iodine-131 was detected in four of twelve irradiation-produced eluates analyzed and one of nine fission-produced generator eluates analyzed. The activity levels determined were low enough to be neglected as a potential health hazard in these eluates analyzed, but monitoring of eluates for this radionuclide should be continuously utilized. Long holding times in some cases before counting coupled with the relatively short half life of this isotope may have allowed enough radioactive decay to occur so that any ^{131}I present would be below the detection limit of the counting system employed.

Rubidium-86 was detected in only one of twelve irradiation-produced generator eluates analyzed and in one of the nine fission-produced generator eluates analyzed, indicating that this radionuclide was not a significant contaminant in the eluates analyzed in this work.

Niobium-92m was not detected in any of the twelve irradiation produced generator eluates analyzed, or in any of the four commercial-produced fission generator eluates analyzed, but was detected in four of the five non-commercial fission produced generator eluates analyzed.

Because of its high energy gamma ray emission and short half life, the administration of an eluate with high activitivies of this radionculide should be avoided.

Molybdenum-99 was detected in one of twelve irradiation-produced generator eluates analyzed, two of four commercial fission-produced generator eluates analyzed, and one of five non-commercial fission produced generator eluates analyzed. Because of the short half life of ^{99}Mo and its associated high energy beta particles and gamma rays this radionuclide is a health hazard in high activities due to its large radiation dose to the patient. A maximum of 5μCi of ^{99}Mo at the time of administration in the total injected eluate volume is permitted by the United States Atomic Energy Commision[15]. Two commercial fission-produced generator eluates from the same generator had ^{99}Mo activities significantly greater than this maximum permissible level permitted by the A.E.C. . Any administration of such an eluate solution to the patient should be strictly avoided. Again, as in the case of ^{131}I, a long holding time coupled with the short half life of this radionuclide before counting might have allowed enough to decay and thus the ^{99}Mo present would be below the detection limit of the system employed.

Using neutron activation analysis as a tool for the possible activation and consequent detection of some stable trace elements that might be present in the eluates, only bromine was detected in one of the twelve irradiation-produced generator eluates analyzed, and only copper was detected in any (three of four) of the commercial fission-produced generator eluates analyzed. The detection of additional stable nuclides

present was hampered when using neutron activation analysis because of the large interferences introduced by the saline eluting solution.

Contaminants in General Electric target material also seemed to vary considerable between target lots. Comparing activity levels in General Electric Target Lot Number 15 (Table I) to those determined for General Electric Target Lot Number 6 (Table II) shows a considerable quantitative difference for several radionuclides. These analyses indicate not only the difference in the number of radionuclides present in these target lots, but also in the activity of those radionuclides present in both lots which it is presumed would be reflected in eluates from generators produced from these lots of target material.

Results presented here contain inaccurracy due to procedures and the random nature of radioactive decay processess in addition to the much larger variations of eluate radionclide inaccuracies from lot-to-lot and generator-to-generator differences. Any attempt to analyze eluate solutions for some of the radionuclides determined in this work with an insensitive detection system should be discouraged to avoid large statistical uncertainties resulting from the low total counts and relatively large background correction.

An attempt was made in this study to accumulate data that would indicate which of the two ^{99}Tc generator production sources, irradiation or fission, would produce eluates least contaminated by radionuclides and stable isotopes. Because of the reluctance of the users and distributor of the commercial fission-produced generator to provide samples for analysis in this work, the planned study of eluates of this origin was severely impeded. Of the twelve irradiations-produced eluates

analyzed, only ^{134}Cs and ^{60}Co were detected in the majority of these samples, and in the four commercial fission-produced eluates analyzed, only ^{134}Cs was detected in the majority of the samples analyzed. Stable nuclide contamination determination was servely hindered by interference from activity induced in the saline used as the eluate but, was found in one of the twelve irradiation-produced eluates analyzed, and in three of the four commercial fission-produced eluates analyzed, both having only one stable nuclide detected instrumentally as a contaminant and non-toxic in the low concentration present.

Eluates of commercial fission-produced generator origin analyzed in this work contained fewer different radionuclides as contaminants than did samples of irradiation-produced generator origin eluates analyzed, but the recommendations of one particular type of generator from this data would not be possible without a more detailed systematic investigation on a larger number of samples obtained on a programmed basis from a larger number of generators.

The large standard deviations present in multiple samples in Tables IV and V are due to factors in addition to the statistics of radioactive decay, geometrical and environmental effects; such as day to day variations in the eluate compositions, generator to generator, lot to lot, and distributor to distributor variations in the generator compositions. Eluates supplied for analysis were on a random sample basis with little or no control over the samples analyzed. In some cases up to five samples were available from generator, in others, however, only one sample from a generator was available for analysis.

Samples eluted from generators of the same lot and distributor but from different generators were unavailable for this work. To analyze differences on a lot to lot and day of week basis for future work a scheduled elution program should be employed. Three generators from each of three different lots of the same distributor could be eluted on a five day elution week basis, analyzed with results reported, thus providing information on day of week and lot to lot differences. Three additional generators of the same lot and distributor could also be eluted and analyzed in a similar manner, furnishing information on day of week and generator to generator differences within a lot. If a combined type of program was employed for generators with both fission and irradiation produced parent molybdenum, then information regarding day of week, generator to generator, and lot to lot differences could be gathered to help establish a "best type" of generator production method.

APPENDIX A

PER CENT STATISTICAL VARIATION

Table A-1. Per Cent Statistical Vatiation in Eluates Samples without Background Interference.

Distributor	$^{60}Co^{\#}$	^{134}Cs	^{131}I	^{99}Mo	^{92m}Nb	^{103}Ru
Squibb $^{\Delta}$	----	21.5+	----	----	----	3.8
Squibb	----	47.5	----	----	----	----
Squibb	----	34.5	----	.29	----	22.6
Squibb	----	----	----	.28	----	----
Union Carbide(A)	----	18.2*	10.6	----	----	4.1
Union Carbide(B)	----	14.2	----	11.6	3.9	1.3
Union Carbide(C)	----	8.1	----	----	50.1	.97
Union Carbide(D)	----	10.6	----	----	60.6	.98
Union Carbide(E)	----	24.1	----	----	82.8	1.2
Mallinckrodt$^{\Phi}$	60.9	68.4°	----	----	----	----
Mallinckrodt(G)	26.1	39.9	----	----	----	----
Mallinckrodt	32.3	23.3	----	----	----	----

Δ all samples of this distributor from fission-produced generators

Φ all samples of this distributor from irradiation-produced generators

\# 1.332 MeV peak used for analysis

* .605 MeV peak used for analysis of this series

\+ .797 MeV peak used for analysis of this series

$\circ$ .605 MeV peak and .797 MeV peak used for analysis of this series

Table A-2. Per Cent Statistical Variation of Spectral Peaks in Eluate Samples with Background Interference.

Distributor+	^{60}Cs #	^{134}Cs *	^{131}I	^{99}Mo	^{86}Rb	^{103}Ru
NEN	7.4	.26	----	----	----	2.6
NEN(H)	22.9	1.9	19.1	----	20.1	75.1
NEN(I)	5.4	1.2	15.6	----	----	13.1
NEN(J)	9.3	1.2	25.7	----	----	16.5
NEN(K)	7.4	1.0	----	----	----	8.5
NEN(L)	12.9	.90	31.0	----	----	11.1
Squibb	----	1.8	----	----	----	----
Squibb	32.5	1.7	----	34.3	----	29.4
Squibb	22.5	1.3	----	-----	----	----

1.332 MeV peak used for analysis

* .605 MeV peak and .797 MeV peak used for analysis

+ all samples in this section were from irradiation-produced generators

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