To the Graduate Council:

I am submitting herewith a thesis written by Dairin Wade Malkemus entitled "Bi-213 Vapor Phase Generator". I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Chemical Engineering.

Jack S. Watson, Major Professor

We have read this thesis and recommend its acceptance:

Accepted for the Council:

Associate Vice Chancellor and
Dean of The Graduate School

BI-213 VAPOR PHASE GENERATOR

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Dairin Wade Malkemus

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Abstract

Bi-213 is a radioactive isotope being evaluated for a variety of cancer therapies. Tissue-specific monoclonal antibodies are used to deliver the isotope to the cancer site, where alpha particles generated during the radioactive decay kill the cancerous cells. Bi-213 has many characteristics that are advantageous for alpha emitting isotopes, namely; a high ratio of alpha emissions relative to beta and gamma emissions, chemical characteristics suitable for attachment to monoclonal antibodies, and a relatively short half-life. What is currently lacking is a reliable, hospital–ready separations process for the preparation of Bi-213 from its parent isotope Ac-225. Current ion exchange processes are subject to radiolysis, which limits the capacity and shelf-life of the generator.

This study investigated the use of a high temperature vacuum process to produce Bi-213 from an Ac-225 generator. A prototype filament apparatus was tested using Ac-225 in the activity range of 10-20 μCi; yields up to 85% were achieved with a one-hour operation. A process window for both temperature and time was determined, such that contamination from the Ac-225 parent material was kept below 0.03%.

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1. Introduction

Recent studies and ideas in nuclear medicine offer the potential for treatment of a wide range of the most dangerous cancer cases, those in which cancer cells are transported from the original cancer sites to other sites throughout the body (metastases). This thesis explores an alternative process to separate the individual isotopes that are required for one such treatment.

Beta emitting radioisotopes have been studied for use in treating several types of cancers. Some isotopes, such as I-131 and Sr-89, naturally concentrate in target organs (thyroid and bone respectively). Rhenium-188 is being studied as a possible treatment for pain in metastatic bone cancers (1). Work investigating this isotope for treatment of breast and prostate cancers is also underway (2). Others, such as Holmium-166, have been successfully combined with monoclonal antibodies for use in beta therapy; the antibody targets the specific type of cancer cell and carries the isotope to it (3). Ionizing radiation from these isotopes then kills the cells near it.

As promising as many of the beta emitters are, they have limitations. Beta particles have a relatively long range and penetrating power; treatment of the smallest metastatic cancers is not feasible due to irradiation of surrounding healthy cells. Alpha particles, by contrast, have a shorter range, depositing their energy over a much shorter distance (8-10 cell diameters). This quality improves the cancer-killing efficiency roughly a thousand fold compared to beta-isotope therapies (4).

The use of alpha emitting isotopes in nuclear medicine is new and has been limited to animal tests and clinical trials. There are few alpha emitting isotopes available that are suitable for

nuclear medicine because of the need for a short half-life, emission of little or no gamma or beta radiation (as close to pure alpha emitters as possible), and a relatively short decay chain to a stable daughter (to eliminate unwanted or escaping radioactive daughter isotopes).

Because of the short half-lives of the isotopes used in nuclear medicine, the isotope is produced (usually by radioactive decay) and separated in the hospitals using a "generator". A longer-lived parent isotope is contained within the generator apparatus, and the shorter-lived daughter isotope, the one used for the treatment, is periodically "milked" from the generator, usually in very close proximity to the room used to administer the treatment itself. This requires that the separation equipment be relatively simple, operable by semi-trained staff, relatively stable, and safe.

Alpha-emitting radiotherapy using Bi-212 has been developed in recent years. Although its decay chain yields a number of alpha particle emissions, it also has a high energy gamma ray emission (2.2 MeV) from the Tl-208 daughter; in addition to being an undesirable radiation source for the patient, it also requires radiation shielding during all phases of production (5).

Bi-213 is an isotope that is showing promise. It lacks high energy gamma emissions, and its Po-213 daughter has a high energy alpha emission (8 MeV), making it a more desirable isotope for alpha therapy. The current methods used for separation of Bi-213 from its parent isotope Ac-225 involve ion exchange processes. Similar methods have been used successfully for other radionuclides; however, the high energy alpha emissions tend to break down the ion exchange resins rapidly, limiting the useful life for the resin. This radiolysis effect increases with the level of radioactivity used, making scale-up difficult. A hospital generator based on this process would require more highly trained staff than practical, and the resin would have a limited

lifetime, requiring frequent replacement.

A separations process is needed that will produce useful quantities of Bi-213, with a longer lifetime than ion exchange processes and the capacity for scale-up to larger systems. This is needed to accelerate research in this area, as well as for eventual use in treatment facilities.

This thesis investigates an alternate approach to the production and separation of Bi-213. The approach is based upon the higher volatility of the daughter isotopes of Fr-221 and Bi-213 compared to the parent Ac-225; under controlled temperatures and pressures the daughters can be volatilized while leaving the Ac-225 as a solid. This approach allows the Bi-213 to be collected where condensed, and it would then be dissolved and attached to monoclonal antibodies for injection into the patients.

2. Background

Alpha radioisotopes are expected to play an ever increasing role in nuclear medicine, especially in the developing treatments for blood-borne cancers (4, 6). In these treatments the isotopes are attached to antibodies which specifically target the cancer cell, where the resulting radiation kills these cells. Those isotopes with primarily alpha emissions are proving to be superior to isotopes with beta or gamma emitting properties for this purpose (7). The characteristics desired for such isotopes are:

1) a high ratio of alpha emissions to beta and gamma emissions, as the short range alphas are better absorbed by the targeted cells and have a minimum effect on non-targeted, healthy tissues;

2) a method to chemically attach the isotopes to the antibodies and a high affinity for the antibodies, to keep the isotopes from breaking free and decaying in non-targeted cells; and

3) a relatively short half life, to further minimize the spread of the emissions to non-targeted cells.

Bi-213 is one of the most recent isotopes being investigated.

Other isotopes have been considered for alpha therapies as well. As shown in an excerpt from the Chart of the Nuclides in Figure A-1, Bi-212 is formed from the decay of Ra-224, with Rn-220 as an intermediate species. Some work has been done by others to separate these isotopes by taking advantage of the volatility of intermediate isotopes (5). In the apparatus described, Th-228 is bound in a solid chemical form in a filter packet. The intermediate radon is a gas at standard temperature and pressure and diffuses out of the filter, where it further decays to Pb-212 and Bi-212. The solid bismuth and lead deposit on the walls of a collection bottle and are subsequently washed off and collected. Some mention was made of the use of vacuum systems to assist the process.

Note that the use of Bi-213 results in significantly fewer gamma emissions than the Bi-212 decay chain, making Bi-213 more desirable for nuclear medicine work. Bi-213 is formed as part of the decay chain of U-233 (Figure A-2) and Th-229, from Ac-225, by way of Fr-221 and At-217. One source of the Th-229 being utilized is derived from stockpiles of U-233 being stored at Oak Ridge National Laboratory. Another method to produce Th-229 involves neutron irradiation of Ra-226 with a high neutron flux (8); uranium mill tailings from former uranium mill sites can provide a ready source for Ra-226 (9).

Elemental Ac-225 is a solid at Standard Temperature and Pressure; At and Fr are normally not gases at STP, but are expected to volatilize under higher temperature and lower pressure. (Figure A-3) In a system under vacuum and high temperature, the evolving Fr and At could be expected to separate from the Ac as a vapor phase. The "recoil effect" associated with the formation of these species is expected to result in their production as ionized species, which may improve the motility. At sufficiently high temperatures, Bi can be expected to volatilize as well. Some studies have been done to produce volatile Fr-221 from Ac-225 (10). The effective flux yield of Fr-221 was reported to be 15%. Emphasis in these studies was on the isolation of Fr-221 for measurement of atomic properties; no attention was given to the production of Bi-213.
The immediate use for this process is as an alternative method for generating Bi-213 for clinical trials and further research on the preparation of the actual monoclonal antibodies (treatment drugs). Eventually this will lead to a generator suitable for use in hospitals without the need for highly trained personnel.

Current ion exchange methods being used for research involve loading the Ac-225 parent material in acid reagent, typically nitric acid or hydrochloric acid of about 1 M concentration,

then passing the reagent through a column of organic cation resin of about 1 mL bed volume (Figure A-4). The Ac material is held on the resin. The Bi-213 is then eluted off in a different reagent, such as 0.1 M hydroiodic acid. Careful monitoring of eluted fractions is necessary to ensure a clean separation, as the elution characteristics can vary with reagent strength, age of the resin, resin batch, and the inevitable radiolysis of the resin. Volumes of reagents used must be minimized as an aid to the labeling process, further complicating the ion exchange separation. The parent Ac-225 often cannot be stored on the column and must be eluted at the end of the process, to minimize radiation damage to the resin. This introduces a risk of loss of the material as well as an increased risk of radiological contamination. All of these factors combine to make a hospital generator based on ion-exchange a difficult operation, requiring highly skilled personnel, and involving some hazards since the Ac-225 must be eluted from the resin frequently.

A generator based on the volatile separation process, by contrast, would require a receiving vial to be attached to the apparatus, then the vacuum pump and filament current to be activated. After a specified run time, the filament current would be shut off, the pump turned off and the system vented, and the receiver vial removed. The Bi-213 would be dissolved with the required reagent and the "standard" labeling process would begin.

The primary advantage of the thermal vaporization process would be the capacity to process larger quantities of isotopes than is currently feasible with ion exchange processes. The same apparatus could handle different quantities of the isotopes; thus, different users (hospitals) could use the same type of apparatus loaded with different quantities of Ac-225. This process appears to be a promising competitor to the ion exchange methods used in current clinical trials.

3. Theory/Mathematical Models

Ingrowth of Bi-213

To better describe the behavior of the process, it is necessary to define the expected "ingrowth" of Bi-213 from the parent Ac-225. As shown in Figure A-2, Ac-225 undergoes radioactive decay, to Fr-221, which in turn decays to At-217, and that decays to Bi-213. Since the half life of the parent Ac-225 is considerably longer than that of its daughters, the growth and decay of these isotopes results in a condition known as "transient radioactive equilibrium"; the activity of the daughters will increase until they are in "equilibrium" with the activity of the parent isotope, and the rate of decay of each isotope are equal. A plot of the "ingrowth" of Fr-221 and Bi-213 from the decay of the parent Ac-225 is shown in Figure A-5. This provides a boundary condition for determining the theoretical yield of the process. For instance, if this Bi-213 production process was run with 100% yield of Bi-213 (temporarily depleting Bi-213 from the Ac-225 source), then run again after 1 hour, the maximum theoretical yield would be 55% of the "equilibrium" activity of Bi; after 3 hours, you could achieve up to 92% yield.

Gamma spectroscopy calculations

The amounts of each isotope present in the receiver and source filament were measured by gamma-ray spectroscopy. To accurately measure the activity of an isotope, it must have a gamma emission in the energy range for the gamma detector crystal, and sufficient "intensity" (percentage of radioactive decays of the isotope which lead to that gamma emission). As shown in Table 1, Bi-213 has a detectable gamma emission at 440 keV; Fr-221 has a gamma emission at 217 keV. The parent Ac-225 has a weak gamma emission (only 0.45% intensity), but the amount of Ac can be verified using the Fr and/or Bi peak; a 30 minute delay is sufficient for the Fr activity to approach "transient equilibrium" with the Ac present. Thus, the activity of pure Fr in

the receiver will gradually decay with a half-life of 4.8 minutes; any residual Fr activity present after a few hours can be assumed to be in equilibrium with an equal activity of Ac. The samples are positioned in a shielded chamber, for which the efficiency has been determined using calibrated gamma standards, so the amount of each isotope present can be determined, in the receiver and source, both before and after each run.

Table 1: Gamma Emissions for Isotopes

Isotope	Gamma Energy	Intensity	Gamma Detector Efficiency
Ra-225	40 keV	30.0%	9.335 E-08
Ac-225	188 keV	0.45%	1.270 E-07
Fr-221	217 keV	11.6%	1.522 E-07
Bi-213	440 keV	26.1%	3.044 E-07

The gamma spectroscopy system yields output in the form of counts per second for each gamma peak. This must be converted to level of activity for the isotope, using the efficiency of the counter for each peak (previously determined for a particular geometry in relation to the detector using the calibrated gamma standards) and the intensity of the gamma emissions, by way of the following formula:

$$A = \frac{(CPS) * Eff}{I} * K$$

Where

A= Activity of the isotope (μCi)
CPS= Counts per second for a particular peak or gamma energy range (detector data)
Eff = Efficiency of the detector for that gamma energy
I = Intensity of gamma emission
K= Conversion factor for disintegrations per second to μCi

Yields and Decay

The activities of Ra, Ac, Fr, and Bi were all measured with the gamma counter, for both receiver and source, before and after the run. The "actual yield" was calculated from the amount of Bi-213 measured in the receiver shortly after the run, compared to the amount of Bi-213 indicated in the source before the run.

The formula used for calculating Bi-213 "Actual Measured Yield" is as follows:

$$Y_{act} = \frac{A_A - A_B}{A_S}$$

Where:
Y_{act} = Bi-213 "Actual Measured Yield"
A_A = Measured Bi-213 Activity in Receiver after run
A_B = Measured Bi-213 Activity in Receiver before run
A_S = Measured Bi-213 Activity in Source before run

There is a variable delay of approximately 5-10 minutes between the filament shutoff and the counting process. Bi-213 has a half-life of 45 minutes, so there is naturally a small loss of Bi product, as illustrated in Figure A-6. An "extrapolated yield" was calculated based on the expected Bi activity at filament shutoff, accounting for this decay.

The formula used for calculating Bi-213 "Extrapolated Yield" is as follows:

$$Y_{extp} = \frac{A_E - A_B}{A_S}$$

Where:
Y_{extp} = Bi-213 "Extrapolated Yield"
A_E = Extrapolated Bi-213 Activity in Receiver after run
A_B = Measured Bi-213 Activity in Receiver before run
A_S = Measured Bi-213 Activity in Source before run

The "extrapolated Bi-213 activity" was defined as follows:

$$A_E = A_A * e^{k(T-T_o)}$$

Where:
A_E = Extrapolated Bi-213 Activity in Receiver after run
A_A = Measured Bi-213 Activity in Receiver before run
k = decay constant for Bi-213
T = time at start of gamma activity count
T_o = time at filament shutoff

Note that the above formula is simply the reverse of the radioactive decay function for Bi-213.

As mentioned previously, the Ac-225 counting efficiency is not good, and Ac could not be detected directly at the low levels of contamination expected for a successful product; the amount of Fr and Bi measured several hours later gave a more accurate measurement of the amount of Ac that was present at these low levels. The "Ac Transfer Percent" figure was based on the amount of Ac in the receiver, as indicated by Fr-221 and Bi-213 activity in the receiver the day after the run. At that point all "free" Fr-221 and Bi-213 should have decayed; any remaining activity can be considered to be in "transient equilibrium" with trace amounts of Ac-225. It is calculated in a similar fashion to the Bi-213 yield above, as illustrated in the following formula:

$$Ac_T = \frac{Ac_A - Ac_B}{Ac_S}$$

Where:
Ac_T = "Ac Transfer Percent"
Ac_A = Measured Ac-225 or Fr-221 or Bi-213 Activity in Receiver after run the day after
Ac_B = Measured Ac-225 or Bi-213 Activity in Receiver before run ("residual")
Ac_S = Measured Bi-213 Activity in Source before run

4. Experimental Apparatus/Methodology

The final version of the experimental apparatus used in this study is shown in Figures A-7 and A-8. The primary components are a filament (90% platinum/10% rhodium) and a Pyrex receiver glass, with a valving system connected to a vacuum pump, and a voltage controller for the filament . The Ac source is first prepared by dissolving the Ac-225 in about 50-100 μL of 0.1 M hydrochloric acid solution, then applying it to the filament using a pipette. The filament is allowed to air dry for several hours. Between 10-20 μCi of Ac is deposited in this manner (presumably as an Ac chloride compound), and the Ac "charge", with a half -life of 10 days, provides a useful amount of material for 2-3 weeks before a new source is required.

Three earlier devices were tested before the final version was selected. Despite the expectation that a temperature between 400-500 C would be adequate for the separation, yields with these earlier devices were low. The first device (Figure A-9) used a stainless steel pipe, heated by conduction with heater wraps, and achieved yields of 1-2% with temperatures up to 400 C. The second device (Figure A-10) used a smaller platinum paddle, also heated by conduction; this device achieved temperatures up to 900 C and yields up to 10%; it appeared higher temperatures could achieve more satisfactory yields. A third device used a filament from a standard halogen bulb with the same setup as the final device. This device achieved the desired temperatures, with yields of 60% of Bi-213 and 0.1% Ac-225 parent material; however, the filament vaporized and degraded rapidly and was unsuitable for long-term use.

The final version of the process is a batch operation. The receiver and source are counted using gamma spectroscopy to measure the activity of the isotopes present prior to the run (it was

necessary to reuse the receivers, so it was important to know how much, if any, material was left from previous runs). The apparatus is assembled, then put under a vacuum (from 50-250 millitorr.) Current is applied to the filament at a controlled voltage (power) and held for a specified period of time. An infrared pyrometer is used to monitor the temperature of the filament during the runs (Capintec RatioScope 20, calibrated range 1000-2000 C, 1% measurement error as reported by the manufacturer). At the conclusion of the run, the filament current is shut off, and the apparatus is allowed to cool for a few minutes. The system is vented to air, and the apparatus is disassembled. The receiver glass and source filament are counted separately to determine the activity of each isotope present.

Little or no deposit is visible on the receiver. The actual physical amount of Bi-213 product is much too small to detect, other than by its radioactivity, by way of the gamma spectroscopy methods described earlier. Any visible deposit is attributed to contaminants and is not desirable.

5. Results

Table 2 shows the data for a typical run.

Table 2: Typical Run Results

Bi Generator Run- Platinum Rhodium Filament #1 8/18/98 (A)				
Conditions:	Temp (C):	1313		
	Pressure (mtorr):	87-270		
	time:	pump down time + 1 hr		
	Ac (μCi)	Fr (μCi)	Bi (μCi)	Ra (μCi)
Source Before Run	17.20	16.87	18.81	0.24
Receiver Before Run	0.00	0.00	0.00	4.46E-03
Source After Run	13.90	15.02	7.85	0.09
Receiver After Run	0.00	2.83	15.66	0.00

Actual Measured Yield of Bi
83.26%

Extrapolated Yield
91.51%

Actinium Transfer Percent
0.00%

Radium Contamination
0.02%

Summarized data for the runs can be found in Table A-2 and Table A-3 in the Appendix.

See Figure 1 for the correlation of temperature with Bi yield. Temperatures from 1300 °C to 1500 °C gave good results. The correlation of Bi yield with temperature closely follows the literature data given for Bi vapor pressures and the boiling point (Figure A-3).

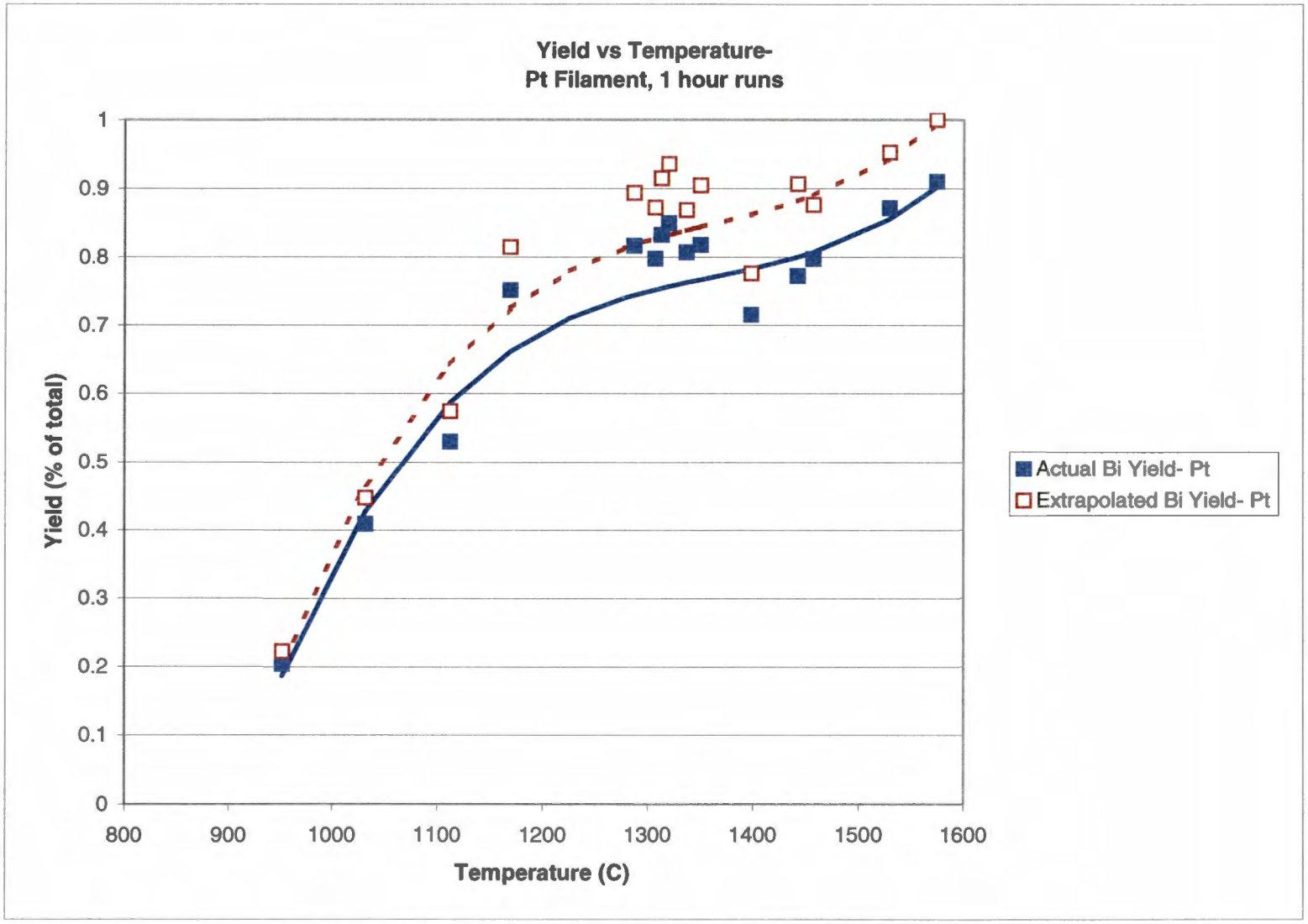

Figure 1: Correlation of Bi-213 Yield with Temperature

A run time of 60 minutes was sufficient for a steady-state yield (Figure 2); longer times did not increase the yield significantly. It should be noted that 60% of Bi-213 was transferred in a minute. This indicates that direct volatile transfer of Bi-213 is the major mode of transport (as opposed to Fr-221 transferring then decaying to Bi-213); if Fr transfer were the sole transfer mechanism, it would take at least an hour for ingrowth of 55-60% of Bi-213 (Figure A-5).

Note that small residual amounts of Ra-225 were detected in the receivers. Small variable amounts of Fr-221 and Bi-213 were detected on the receivers after time was allowed for the product to decay, indicating the presence of Ac-225. Although some question remains as to whether this activity was due entirely to the Ra-225 deposited during the runs, or if Ac-225 transferred directly, Ra and Ac transfers are less than 0.03%, for the temperature range of 1300-1500 °C. Greater amounts of Ra and Ac were found to transfer at a higher temperature of 1575 °C. Degradation of the platinum filament prohibited the use of higher temperatures for the experiments.

The yield of Fr-221 was more difficult to determine; due to the low levels of activity (μCi) used. Gamma counts of 5 minutes were required; since Fr-221 has a half-life of 4.8 minutes, the Fr decayed as it was being counted. A computer model was used to calculate the amount of Fr present for a representative run (Figure A-11). A value for the Fr yield of 65% was estimated. The pressure was measured, although it was not possible to control with a great degree of accuracy. No correlation of yield with pressure was observed; pressure variation is assumed to neither hinder nor enhance the yield over the range tested.

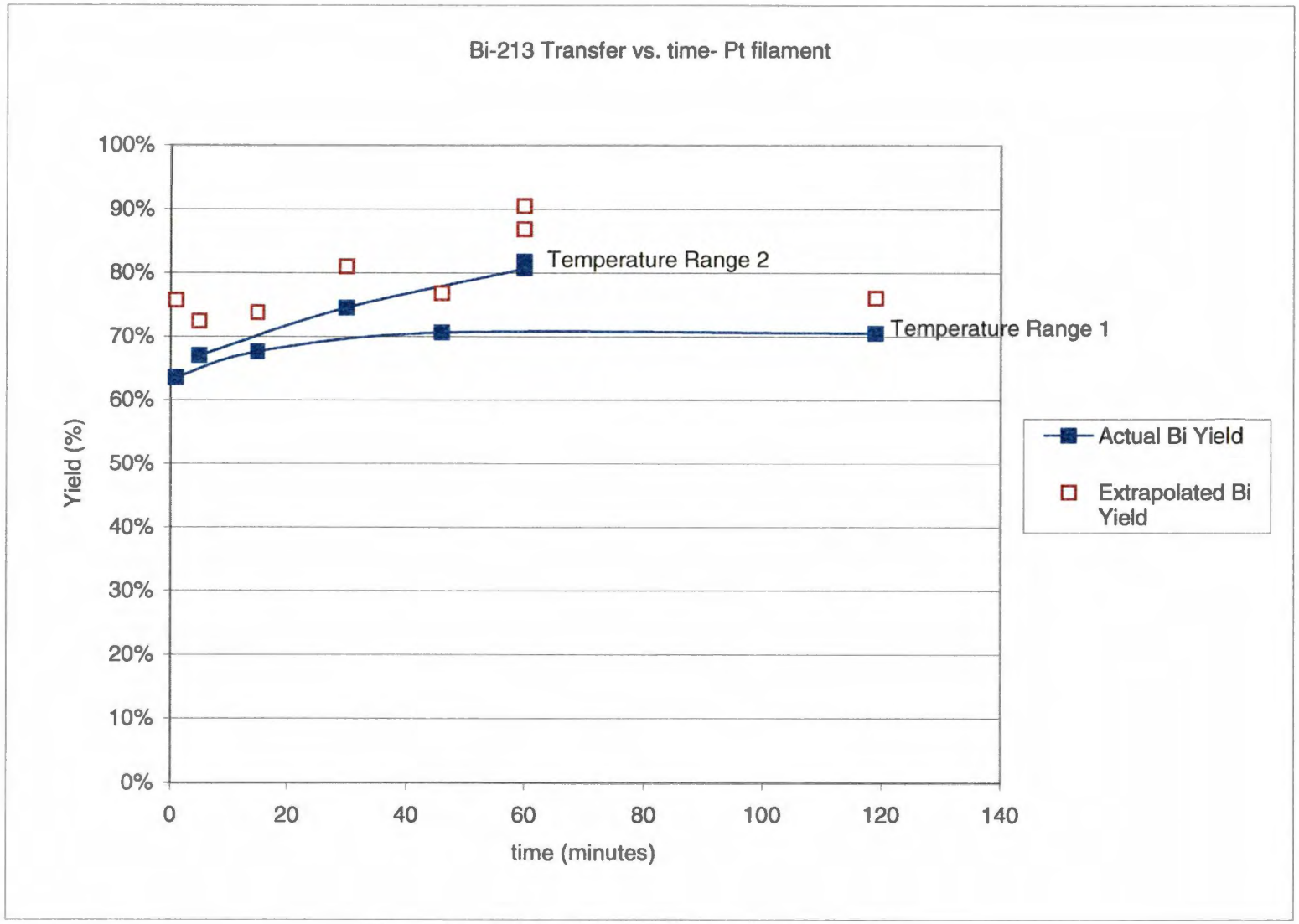

Figure 2: Correlation of Bi-213 Yield with Time

6. Conclusions

An apparatus has been tested that can be used to separate Bi-213 (and Fr-225) from Ac-225 parent material, with a yield of over 85% for Bi-213, 65% for Fr-225, and with negligible (<0.03 %) transfer of Ac-225 and Ra-225. The amount of material used in this experiment ranged from 10-20 mCi. Direct volatile transfer of Bi-213 is the major mode of transport; Fr-221 also transported, although with a slightly lower yield.

The important parameters were determined to be temperature and collection time. The "process window", or that range of conditions for which the desirable product is maximized and undesirable species are minimized, was bounded by a temperature range of 1300-1500 °C and a collection time of 60-100 minutes.

Although a vacuum is believed to be necessary to reduce possible oxidation/degradation effects on the filament, no effects on yields from pressure variation were observed over the region tested. Future work should examine the effects of ambient oxygen and pressure more closely, since only pressures between 50 and 250 mtorr were tested during this study.

This thermal vaporization process appears to be a promising competitor to the ion exchange methods used in current clinical trials.

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Appendix

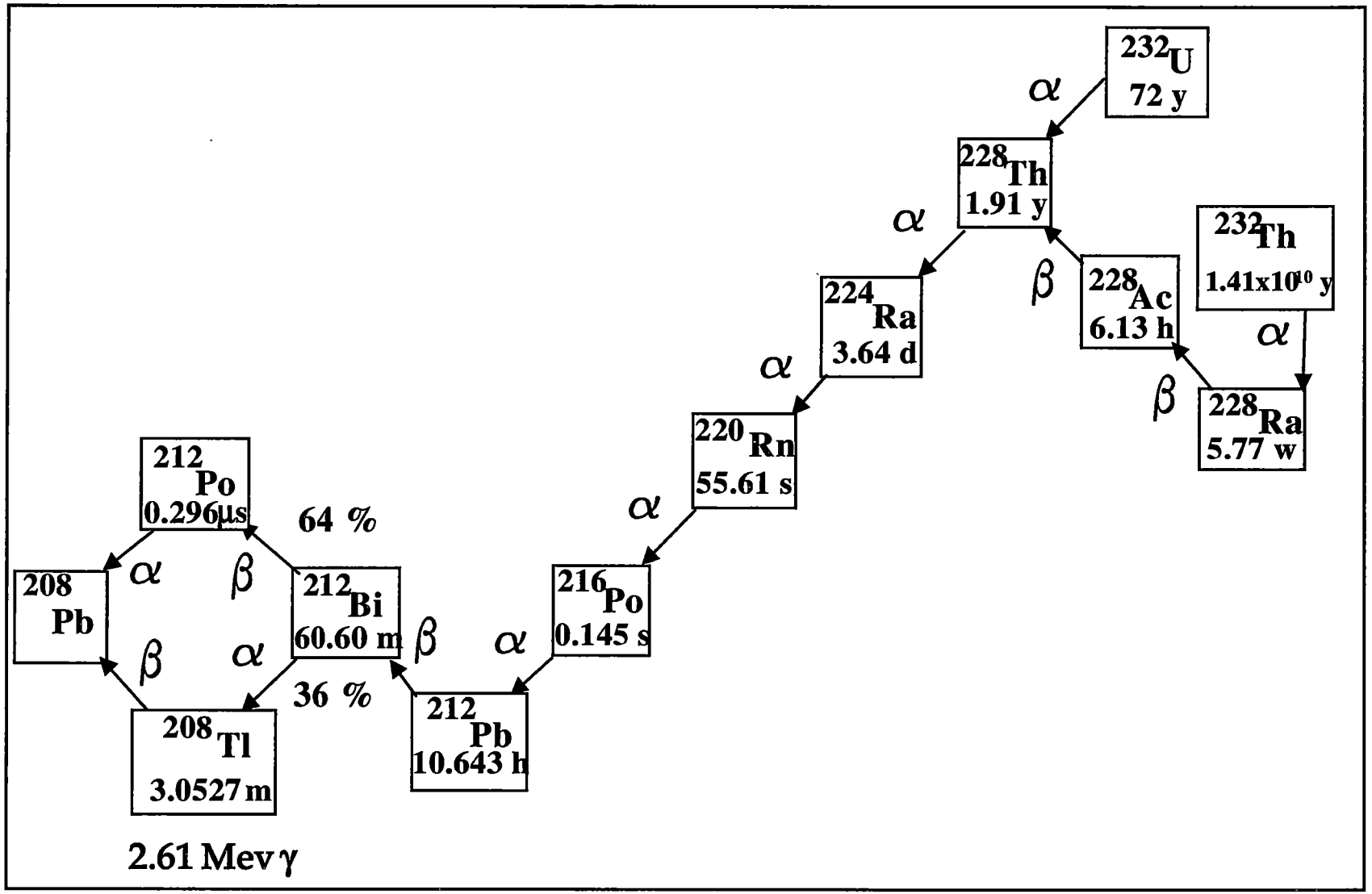

Figure A-1: U-232 Decay Chain

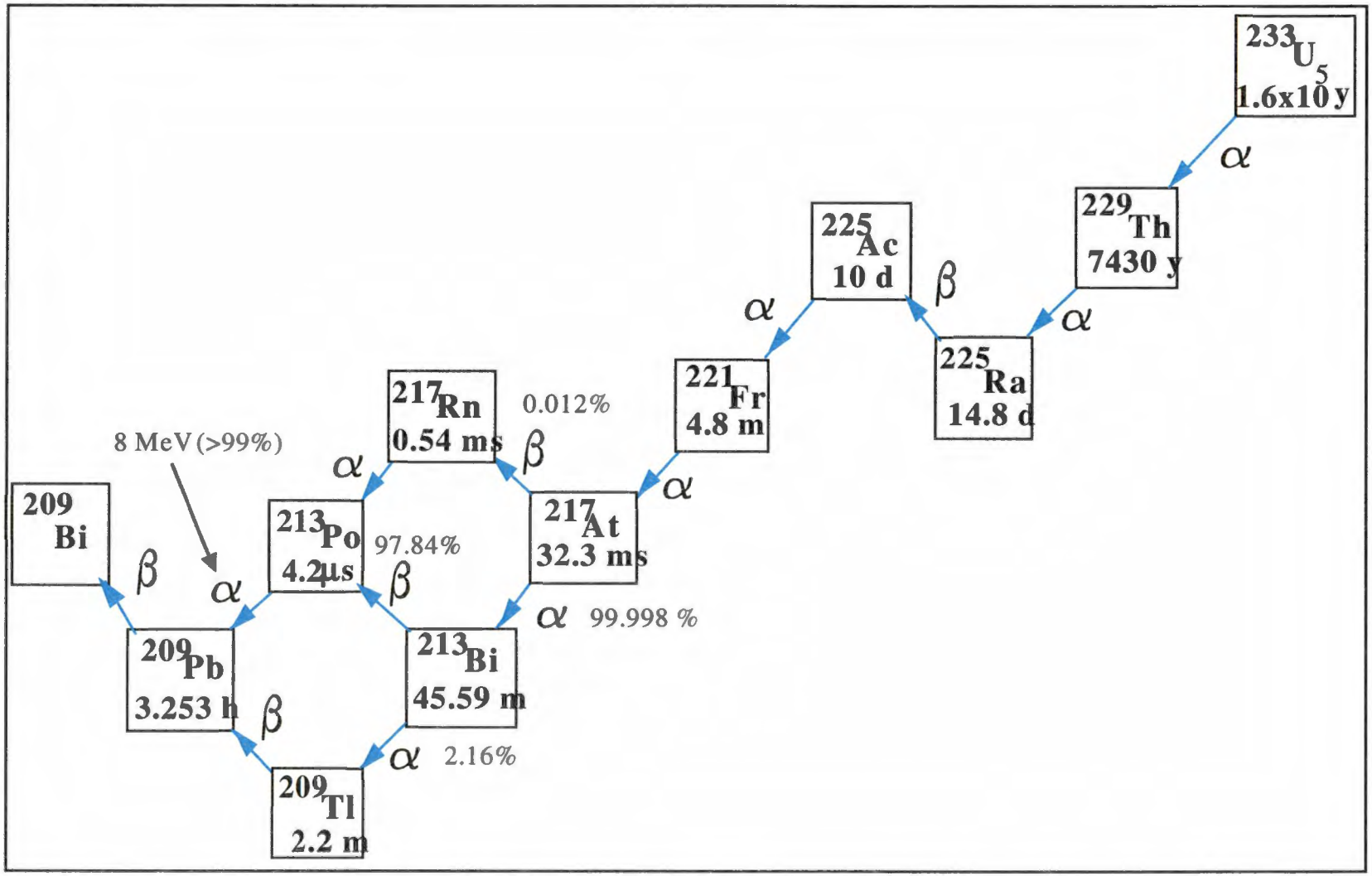

Figure A-2: U-233 Decay Chain

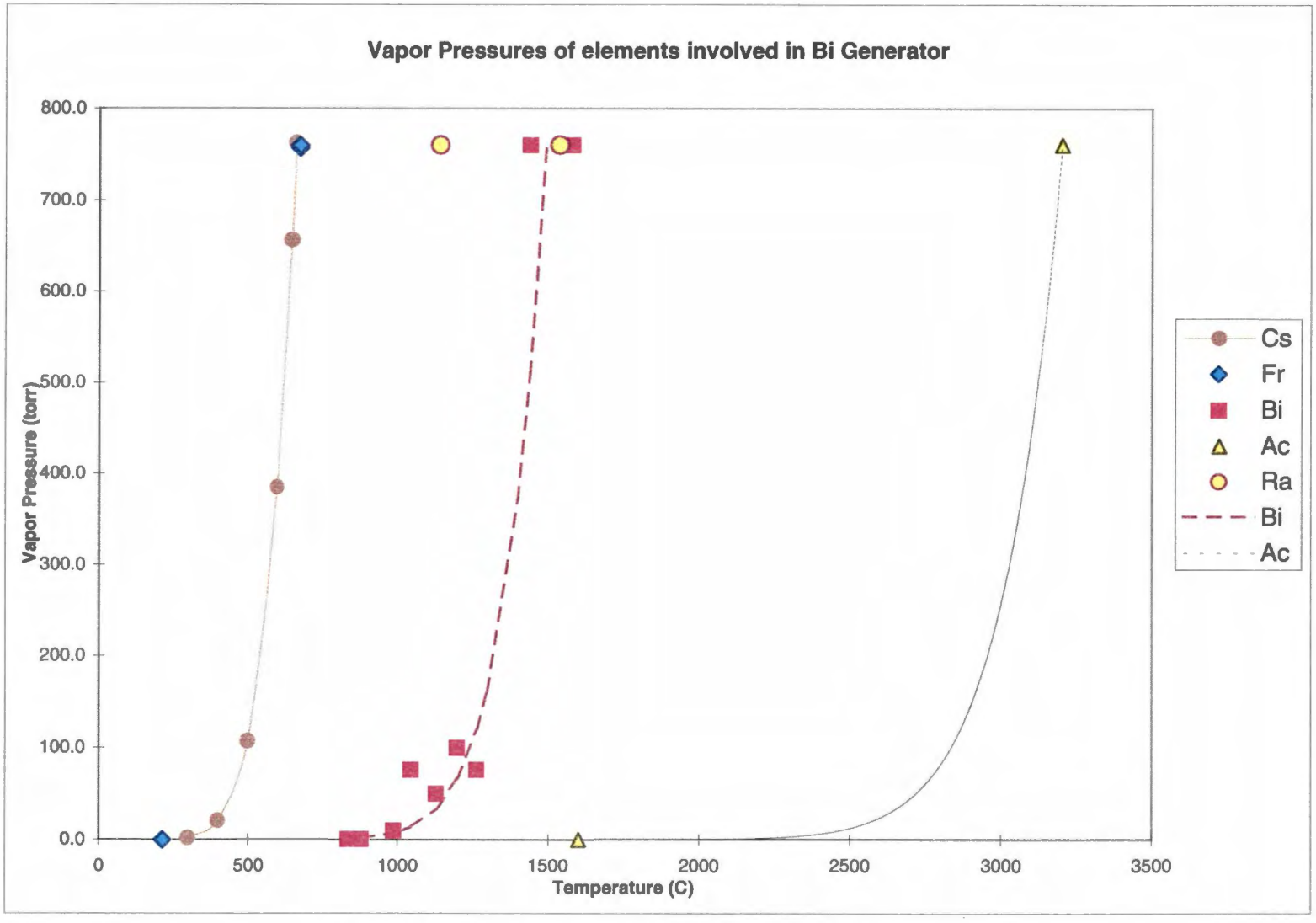

Figure A-3: Vapor Pressures and Boiling Points of Isotopes

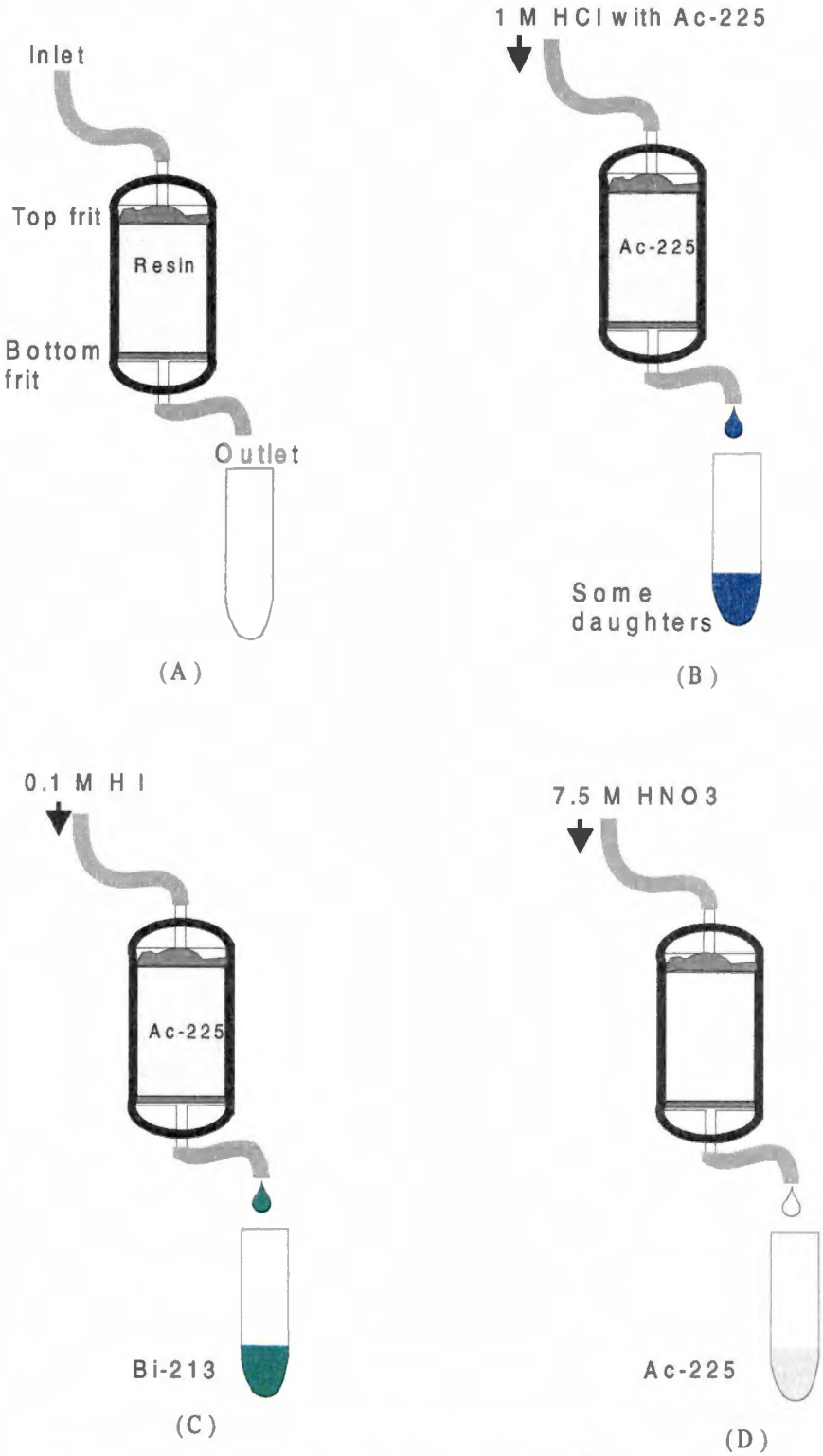

Figure A-4: Current Ion-Exchange Separation Process:
A) Parts of Column; B) Loading Ac-225 Source;
C) Milking of Bi-213 Product; D) Eluting Ac-225 from Column

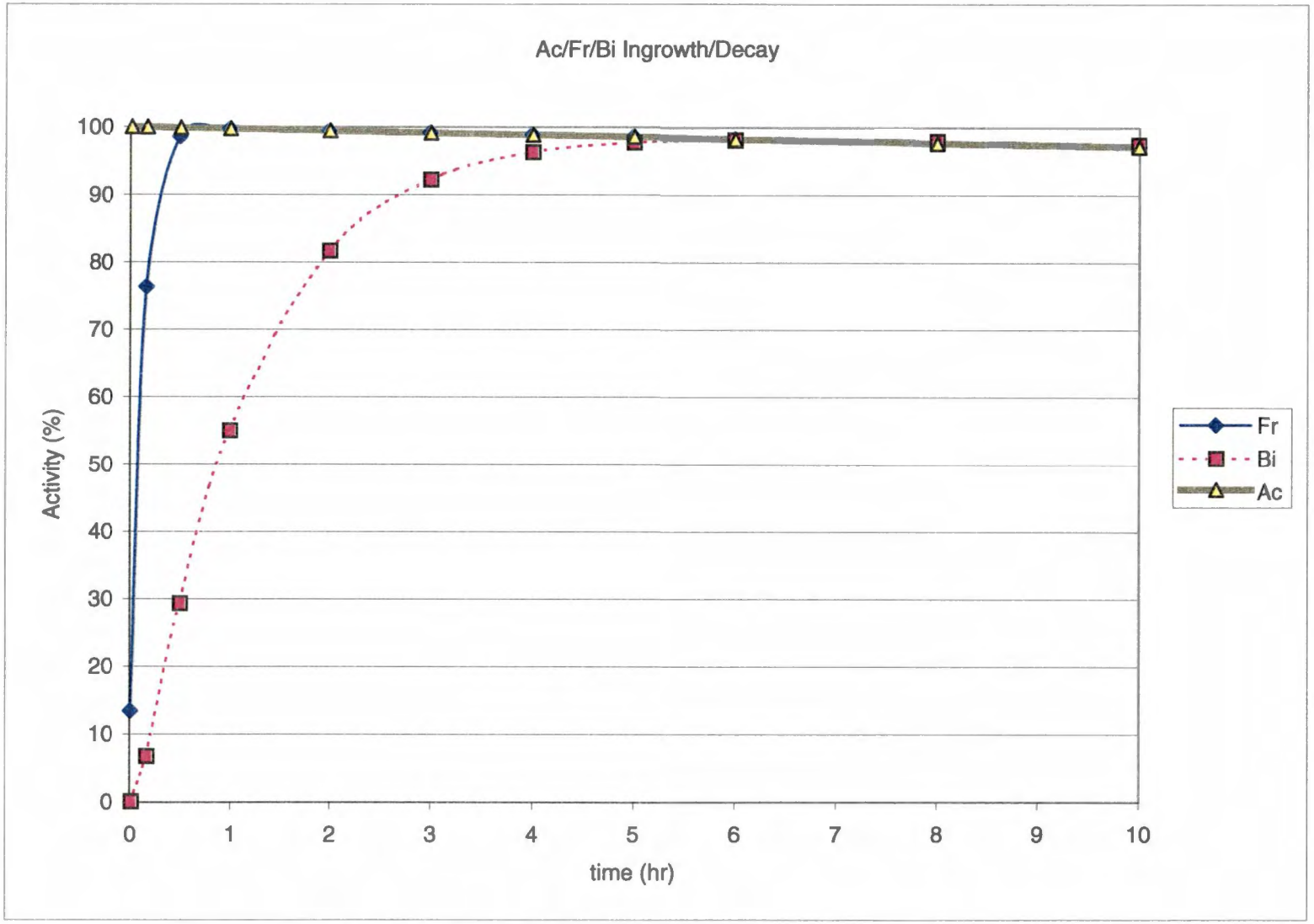

Figure A-5: Calculated Ingrowth/Decay of Bi-213 from Ac-225

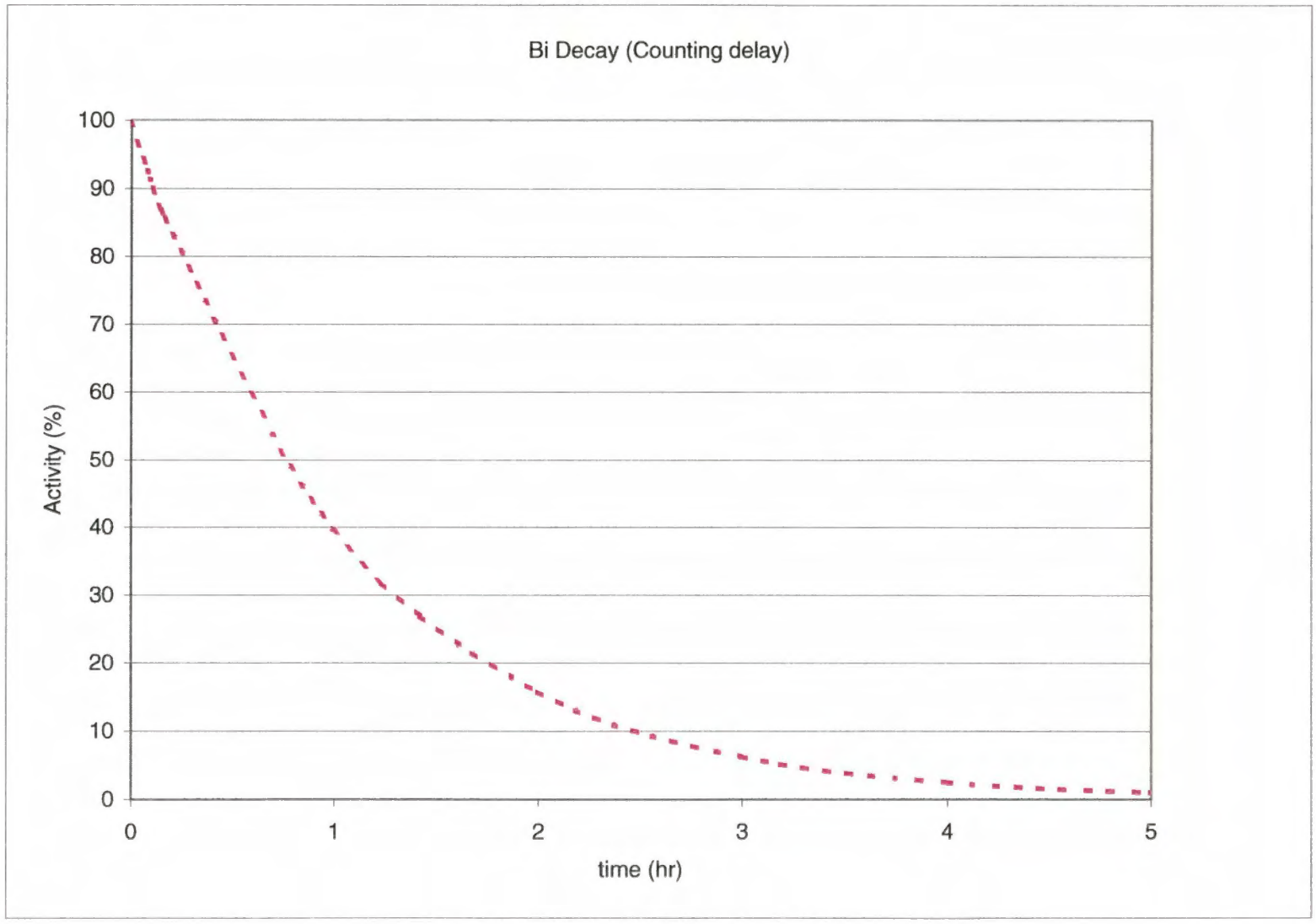

Figure A-6: Decay of Bi-213 After a Run

A-1. Detailed Description of Apparatus

A diagram of the separation apparatus is shown in Figure A-7 and A-8. The separation cell is the heart of the apparatus, composed of a filament and receiver glass.

The filament is constructed from 90% Pt /10% Rh wire, 0.0100 inches thick, wrapped in 2 mm diameter coils, approximately 15 coils in a 1 cm long filament; the filament has been welded to metal contacts and copper electrical wire, and the base imbedded in a 19/22 straight taper glass fitting (male) using OmegaBond-400 cement. RTV sealant was used around the outer end to improve the vacuum seal.

This filament assembly is connected to the receiver glass by the 19/22 straight taper glass fitting. The receiver glass (Pyrex glass) was constructed from two glass adapters, both female straight glass taper, one 19/22 taper, connected to the filament assembly, the other 14/35 straight taper, connected to the vacuum system. The receiver is approximately 7 cm long and 2.5 cm diameter, with walls 2 mm thick.

The cell is connected to the vacuum system, with a pressure transducer, valves for air vent and vacuum control, liquid nitrogen cold trap, and vacuum pump. A voltage controller is connected to the wires from the filament, to control the voltage between 0-10V; an infrared pyrometer measures the temperature during the runs (Capintec RatioScope 20, calibrated range 1000-2000 C, 1% measurement error as reported by the manufacturer).

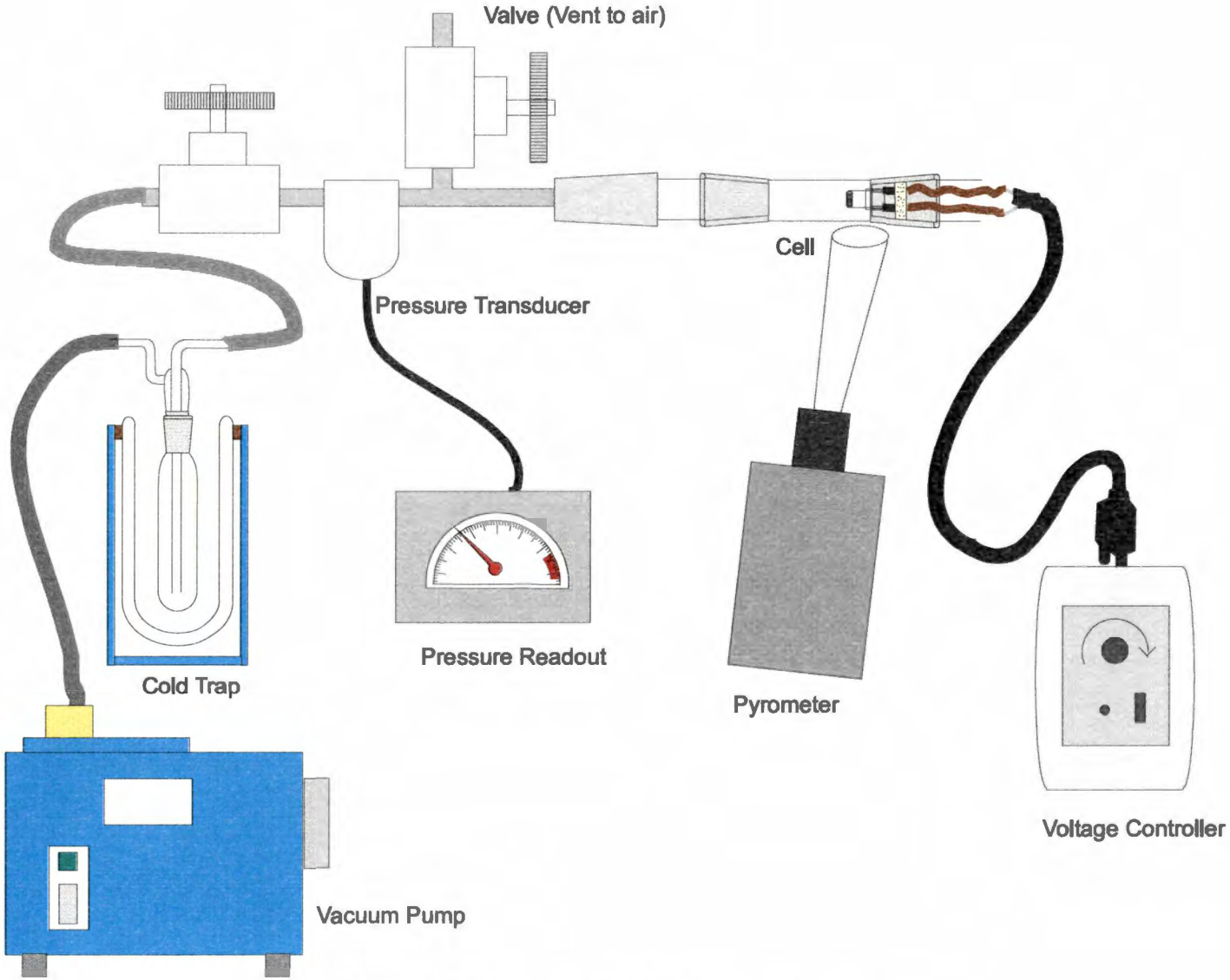

Figure A-7: Diagram of Bi-213 Generator Apparatus

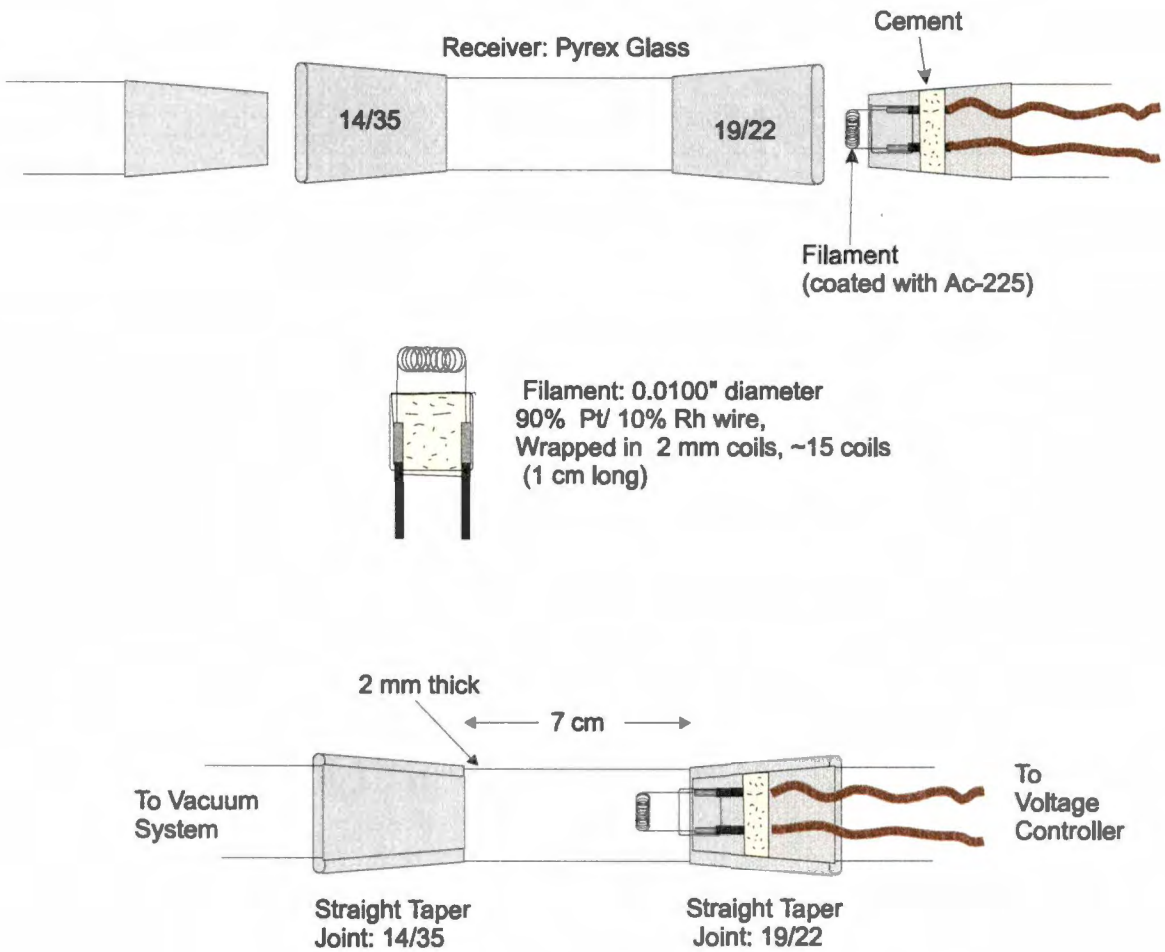

Figure A-8: Diagram of Bi-213 Generator Cell

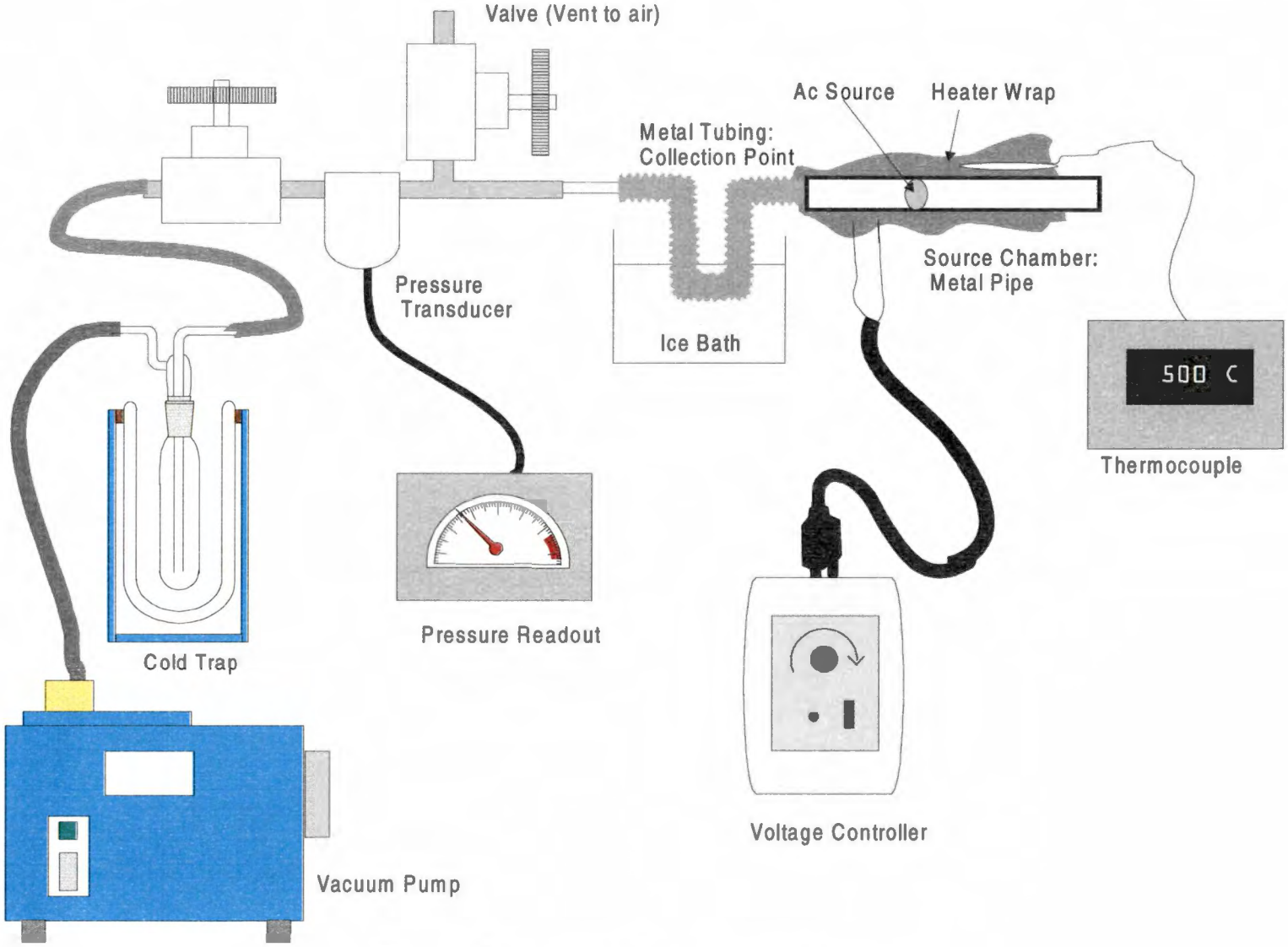

Figure A-9: Diagram of First Generation Apparatus

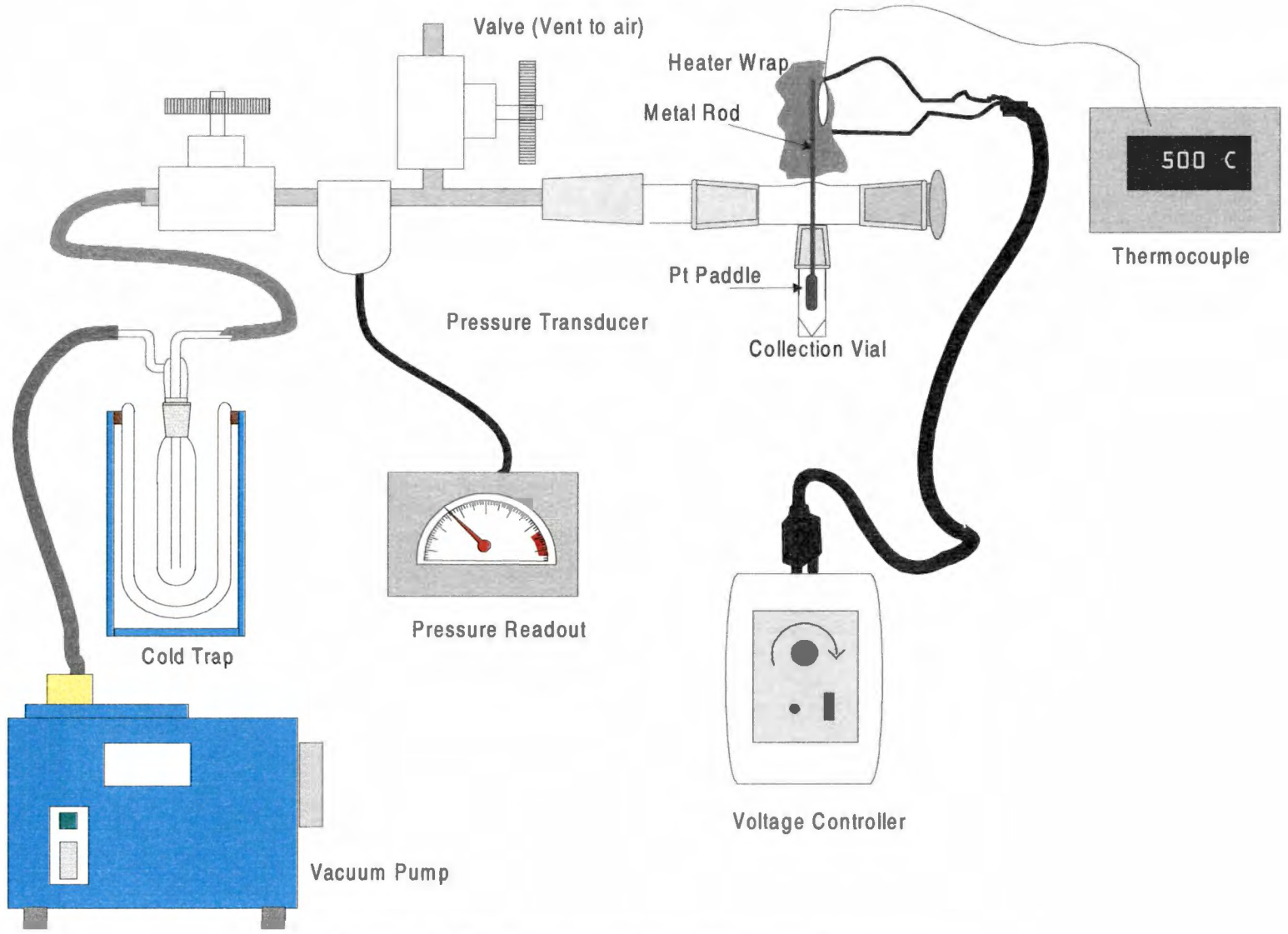

Figure A-10: Diagram of Second Generation Apparatus

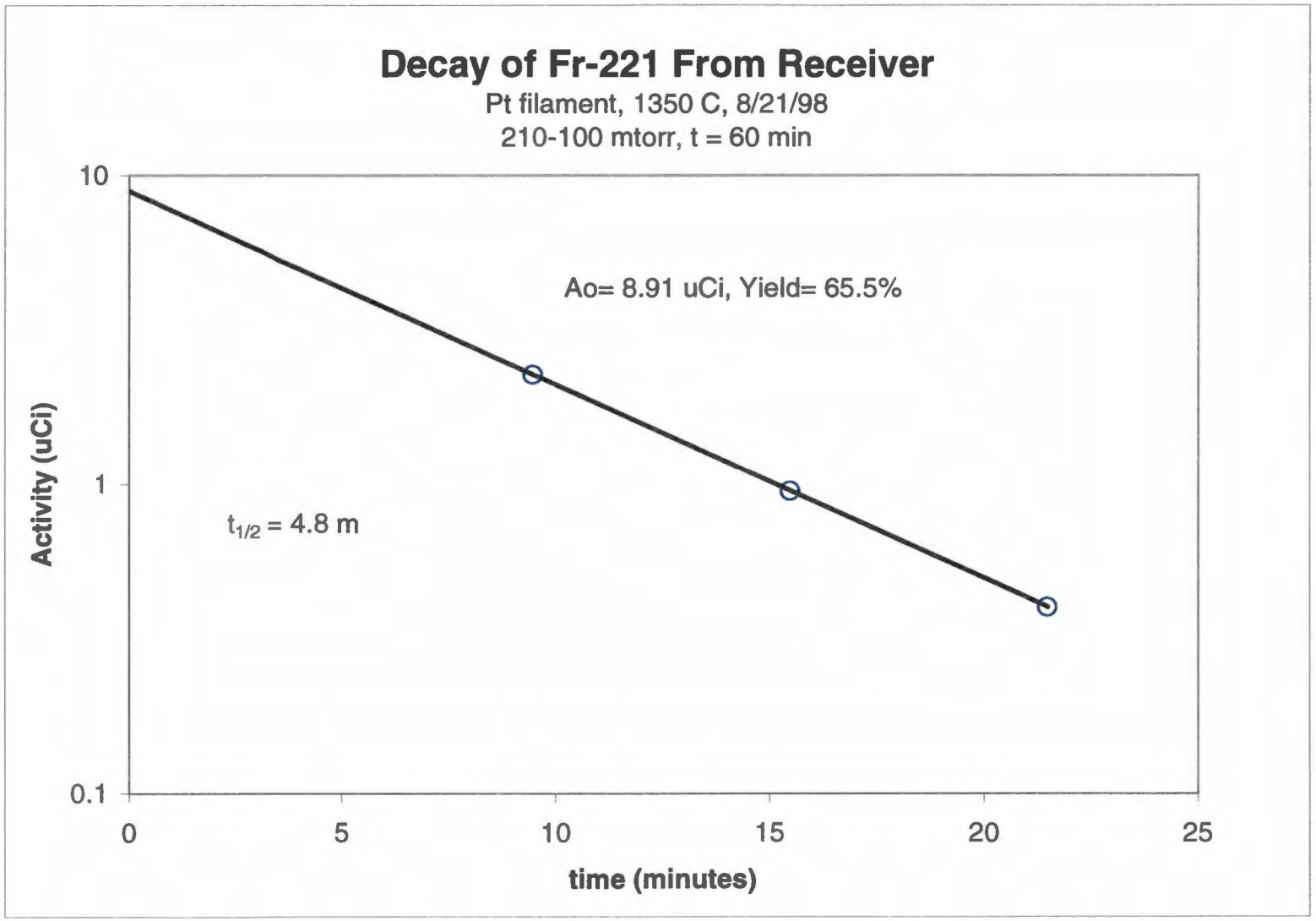

Figure A-11: Determination of Fr-221 Yield

Table A-1 : Typical Run Results - Detailed

Bi Generator Run- Platinum Rhodium Filament #1				
8/18/98				
Conditions:	Temp (C)=	1313		
	P(mtorr) =	87-270		
	time	pump down time + 1 hr		
Initial count of filament (before run)				
time	Ac (μCi)	Fr (μCi)	Bi (μCi)	Ra (μCi)
8/18/98 9:14	17.20	16.87	18.81	0.24
Receiver glass before run				
time	Ac (μCi)	Fr (μCi)	Bi (μCi)	Ra (μCi)
8/18/98 8:55	0.00	0.00	0.00	4.46E-03
Source after run	Note ingrowth of Bi			
time	Ac (μCi)	Fr (μCi)	Bi (μCi)	Ra (μCi)
8/18/98 14:30	13.90	15.02	7.85	0.09
8/18/98 14:37	15.10	15.02	9.06	0.09
8/19/98 14:52	15.00	15.66	17.73	0.23
Receiver glass after run				
time	Ac (μCi)	Fr (μCi)	Bi (μCi)	Ra (μCi)
8/18/98 14:05	*shutoff*			
8/18/98 14:12	0.00	2.83	15.66	0.00
8/18/98 14:18	0.00	1.16	14.02	0.00
8/18/98 14:24	0.00	0.47	12.30	0.00
8/19/98 14:44	0.00	3.73E-03	3.52E-03	3.70E-03
		ingrowth from residual Ra		
Actual Measured Yield of Bi				
83.26%				
Extrapolated Yield				
91.51%				
Actinium Transfer Percent				
0.00%				

Table A-2: Process Summary Data, Variation with Temperature*

Run #	Voltage	Temperature (C)	Actual Bi Yield	Extrapolated Bi Yield	Ac Transfer	Ra Contamination
8/17/1998 (B)	4.5 V	1320	84.98%	93.57%	0.00%	0.00%
8/18/1998 (A)	4.5 V	1313	83.26%	91.51%	0.00%	0.02%
8/19/1998 (A)	4.5 V	1307	79.79%	87.24%	0.00%	0.02%
8/21/1998 (A)	4.5 V	1350	81.77%	90.49%	0.00%	0.02%
8/22/1998 (A)	4.0 V	1287	81.65%	89.37%	0.01%	0.02%
8/24/1998 (A)	3.5 V	1169	75.17%	81.48%	0.01%	0.02%
8/24/1998 (B)	3.0 V	1112	53.02%	57.44%	0.01%	0.00%
8/25/1998 (A)	2.7 V	1032	40.94%	44.73%	0.01%	0.02%
8/26/1998 (A)	2.5 V	953	20.46%	22.26%	0.00%	0.02%
8/26/1998 (B)	5.0 V	1398	71.54%	77.65%	0.02%	0.00%
8/27/1998 (A)	5.5 V	1457	79.75%	87.65%	0.02%	0.02%
8/27/1998 (B)	5.5 V	1442	77.24%	90.65%	0.01%	0.01%
8/28/1998 (A)	6.0 V	1529	87.17%	95.27%	0.03%	0.03%
8/29/1998 (A)	6.5 V	1574	91.04%	100.00%	0.22%	0.43%
8/31/1998 (B)	4.5 V	1337	80.73%	86.88%	0.03%	0.01%

Table A-3: Process Summary Data, Variation with Time*

Run #	Voltage	Temperature (C)	Time (minutes)	Actual Bi Yield	Extrapolated Bi Yield	Ac Transfer	Ra
9/1/1998 (A)	4.5 V	1344	5	67.04%	72.42%	0.00%	0.00%
9/2/98	4.5 V	1326	30	74.55%	81.01%	0.03%	0.03%
8/31/1998 (B)	4.5 V	1337	60	80.73%	86.88%	0.01%	0.01%
8/21/1998 (A)	4.5 V	1350	60	81.77%	90.49%	0.00%	0.00%
8/20/1998 (A)	4.5 V	1226	1	63.60%	75.73%	0.02%	0.02%
9/1/1998 (B)	4.5 V	1278	15	67.65%	73.76%	0.00%	0.00%
9/3/98	4.5 V	1308	46	70.63%	76.79%	0.00%	0.00%
9/4/98	4.5 V	1297	119	70.55%	76.04%	0.00%	0.00%

* data recorded in Oak Ridge National Laboratory Lab Book #B000400, and printouts from gamma spectroscopy system.

	A	B	C	D	E	F	G
1	Bi Generator Run- Filament			Platinum Rhodium Filament #1			
2	8/18/98						
3	Conditions:	Temp (F)=	1313.00	C			
4		P(mtorr) =	270-87	mtorr range			
5		Cl source	pump down time + 1 hr				
6							
7	Initial count of filament (before run)						
8	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)		
9	8/18/98 9:14	17.20	16.87	18.81	0.24		
10							
11							
12	Receiver glass before run						
13	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)		
14	8/18/98 8:55	0.00	0.00	0.00	4.46E-03		
15							
16							
17	Source after run	Note ingrowth of Bi					
18	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)		
19	8/18/98 14:30	13.90	15.02	7.85	0.09		
20	8/18/98 14:37	15.10	15.02	9.06	0.09		
21	8/19/98 14:52	15.00	15.66	17.73	0.23		
22							
23	Receiver glass after run						
24	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)	Fr (decay)	Bi (decay)
25	8/18/98 14:05	*theoretical shutoff*				8.21	17.21
26	8/18/98 14:12	0.00	2.83	15.66	0.00	2.83	15.66
27	8/18/98 14:18	0.00	1.16	14.02	0.00	0.92	14.17
28	8/18/98 14:24	0.00	0.47	12.30	0.00	0.32	12.90
29	8/19/98 14:44	0.00	3.73E-03	3.52E-03	3.70E-03	0.00	0.00
30			ingrowth from residual Ra				
31							
32	Actual Measured Yield of Bi			Ac decay constant=		0.069314718	day^{-1}
33	83.26%			Fr decay constant=		249.532985	day^{-1}
34				Bi decay constant=		22.18070978	day^{-1}
35	Extrapolated Yield						
36	91.51%						
37							
38	Actinium Transfer Percent						
39	0.00%						

Figure A-12: Sample Data (Excel Spreadsheet)

	A	B	C	D	E	F	G
1	Bi Generator Run- Filament			Platinum Rhodium Filament #1			
2	8/18/98						
3	Conditions:	Temp (F)=	1313.00	C			
4		P(mtorr) =	270-87	mtorr range			
5		Cl source	pump down time + 1 hr				
6							
7	Initial count of filament (before run)						
8	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)		
9	8/18/98 9:14	17.20	16.87	18.81	0.24		
10							
11							
12	Receiver glass before run						
13	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)		
14	8/18/98 8:55	0.00	0.00	0.00	4.46E-03		
15							
16							
17	Source after run	Note ingrowth of Bi					
18	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)		
19	8/18/98 14:30	13.90	15.02	7.85	0.09		
20	8/18/98 14:37	15.10	15.02	9.06	0.09		
21	8/19/98 14:52	15.00	15.66	17.73	0.23		
22							
23	Receiver glass after run						
24	time	Ac (uCi)	Fr (uCi)	Bi (uCi)	Ra (uCi)	Fr (decay)	Bi (decay)
25	8/18/98 14:05	*theoretical shutoff*				=F26*EXP(F33*(A26-A25))	=G26*EXP(F34*(A26-A25))
26	8/18/98 14:12	0.00	2.83	15.66	0.00	=C26	=D26
27	8/18/98 14:18	0.00	1.16	14.02	0.00	=F26*EXP(-F33*(A27-A26))	=G26*EXP(-F34*(A27-A26))
28	8/18/98 14:24	0.00	0.47	12.30	0.00	=F27*EXP(-F33*(A28-A27))	=G27*EXP(-F34*(A28-A27))
29	8/19/98 14:44	0.00	3.73E-03	3.52E-03	3.70E-03	=F28*EXP(-F33*(A29-A28))	=G28*EXP(-F34*(A29-A28))
30			ingrowth from residual Ra				
31							
32	Actual Measured Yield of Bi			Ac decay constant=		0.069314718	day^{-1}
33	=(D26-D14)/D9			Fr decay constant=		249.532985	day^{-1}
34				Bi decay constant=		22.18070978	day^{-1}
35	Extrapolated Yield						
36	=G25/D9						
37							
38	Actinium Transfer Percent						
39	=(B29-B14)/B9						

Figure A-13: Sample Data Showing Calculations (Excel Spreadsheet)

Vita

Dairin Malkemus was born in New Castle, Indiana, on October 30th, 1964. He graduated with a Bachelor of Science degree in Chemical Engineering from Purdue University in May, 1988. In 1993, he began the Master's degree program in Chemical Engineering at the University of Tennessee.

From 1986 to 1990, he worked in the semiconductor industry at IBM and chemical process development and manufacturing. He has been employed as an engineer at Oak Ridge National Laboratory since 1991, involved in cleanup operations at various radioisotope facilities, and more recently, in radioisotope process development.