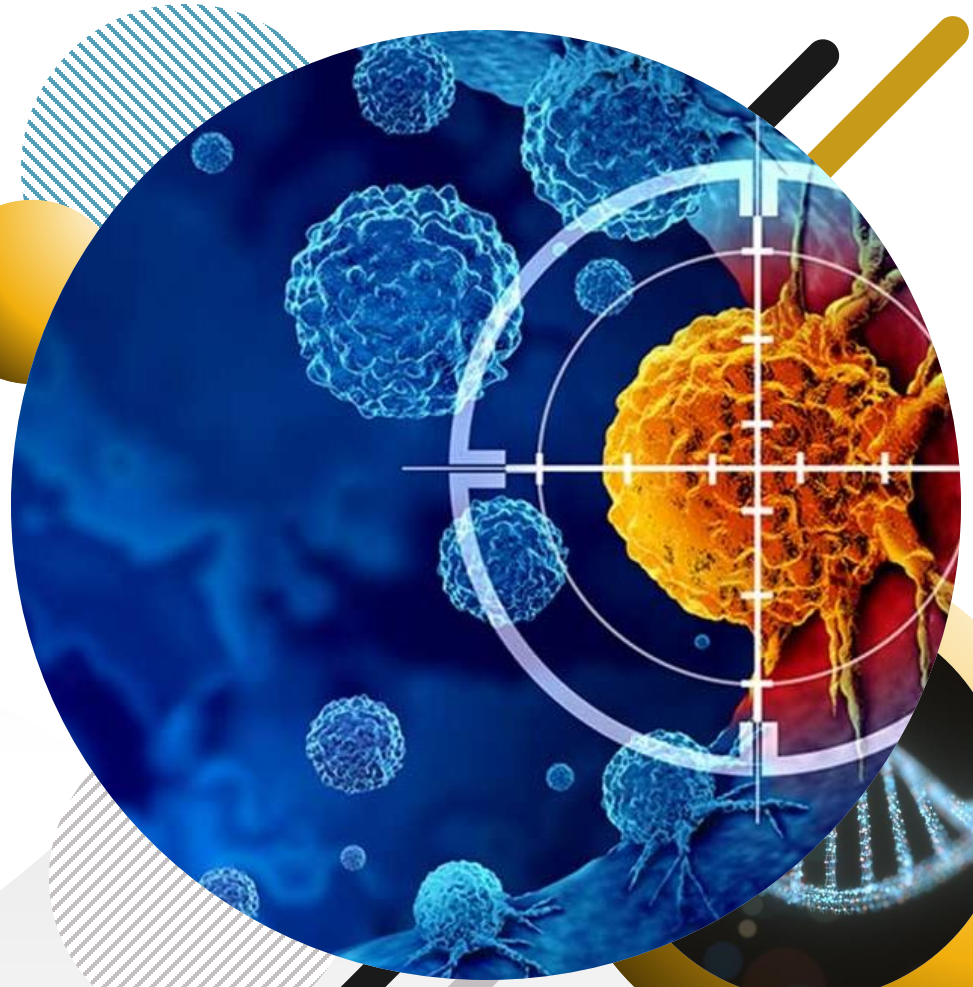
Nucleus RadioPharma

Radioprotection and Safety in a Complex Environment



Mirion Connect, 2025
Shaun Kelley MHP, CHP, CHMM
Director, Radiation Safety/Corporate RSO

1 Sept 2024

Radiopharmaceutical Industry Overview

Data from a leading 2024 marketing report showing the number of therapeutic radiopharmaceuticals planned to make it to market by 2030.

Radionuclides	#Products in Development
177Lu	32
90Y	12
131I	11
225Ac	10
212Pb	5
188Re	5
227Th	4
117mSn	3
211At	3
67Cu	2
224Ra	2
213Bi	1
64Cu	1
186Re	1
153Sm	1
152Tb	1
Grand Total	94

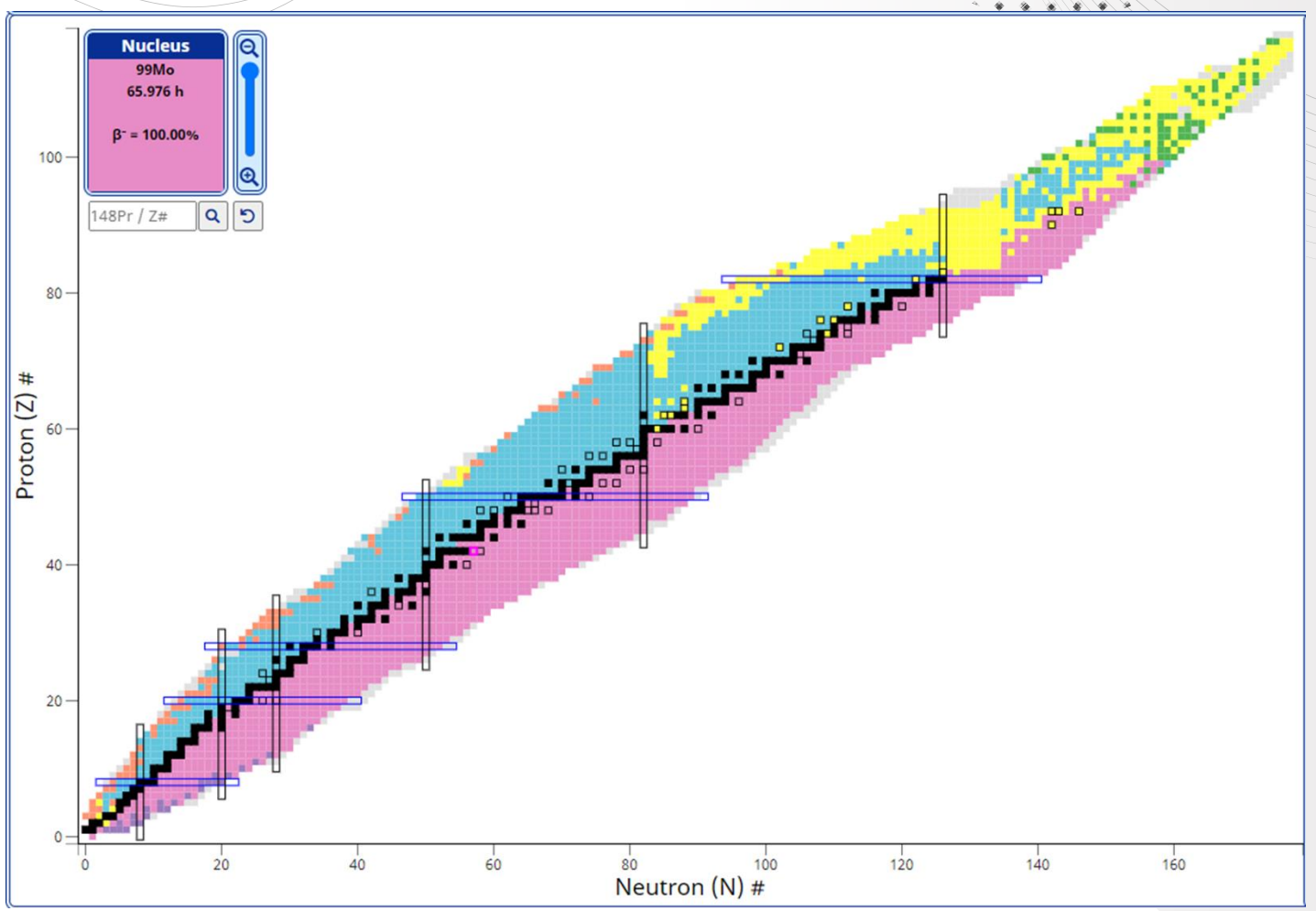
Ref: MEDraysintell NM Report 2024; Late Stage 1, 2 and 3 drug development

Nucleus
RadioPharma

Evaluating Nuclide Properties

Key Nuclide Properties to Evaluate

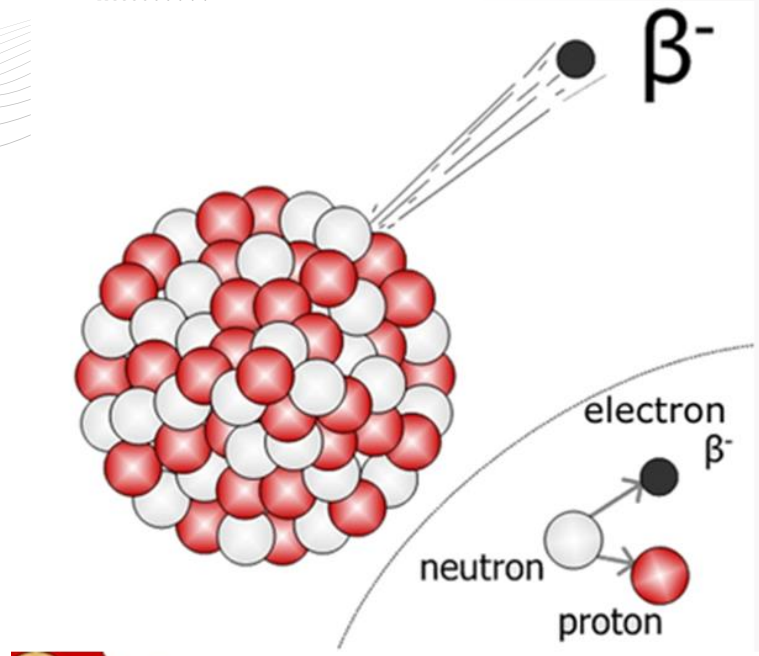
- Decay Mode
  - (α,β,γ)
- Particle Energy
- Half-life
- Chemical/physical properties

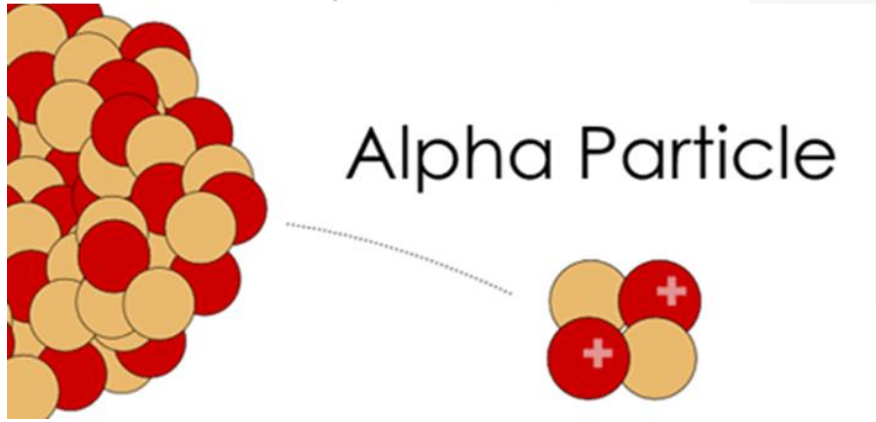


Decay Mode

What does this nuclide emit?

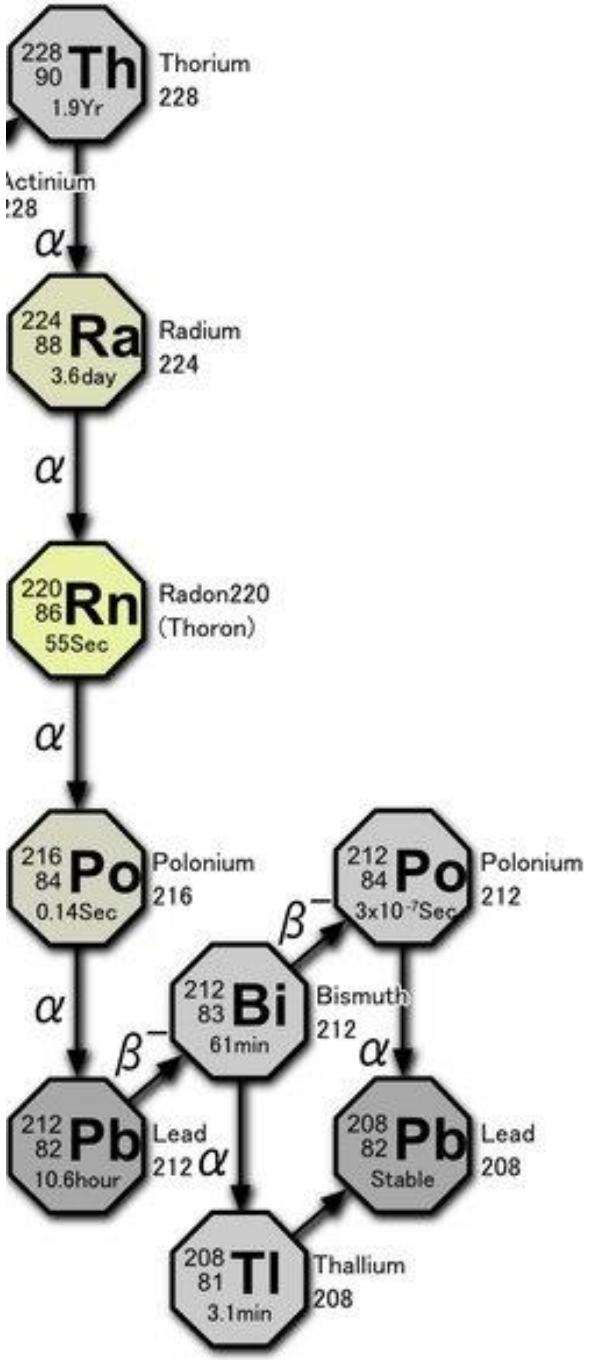
- What depends on decay mode?
  - Hazard
  - Shielding
  - Instrumentation
- Account for all emissions
  - Most nuclides emit more than one.
  - Just because it's an alpha emitter doesn't mean it may not need shielding.
- Are there radioactive progeny?
  - Progeny may have different emission types
  - Must account for them all





Th-228 decay presents many radiological health risks:

- Radon-220 (α emission) is an inhalation hazard
- Several high energy α particles are produced in the decay chain
- Skin contamination can cause high β- dose exposure
- Thallium-208 decay produces high-energy γ photon (2.6 MeV)



Particle Energy

- What depends on energy?
  - Hazard
  - Shielding
  - Instrumentation
- Account for all emissions - again
  - High energy low abundance gammas can bite you on shielding.
- Are there radioactive progeny? - again
  - Progeny may have different emission energies
  - Many references do not account for progeny
    - See TVL for Pb-212 vs. Tl-208

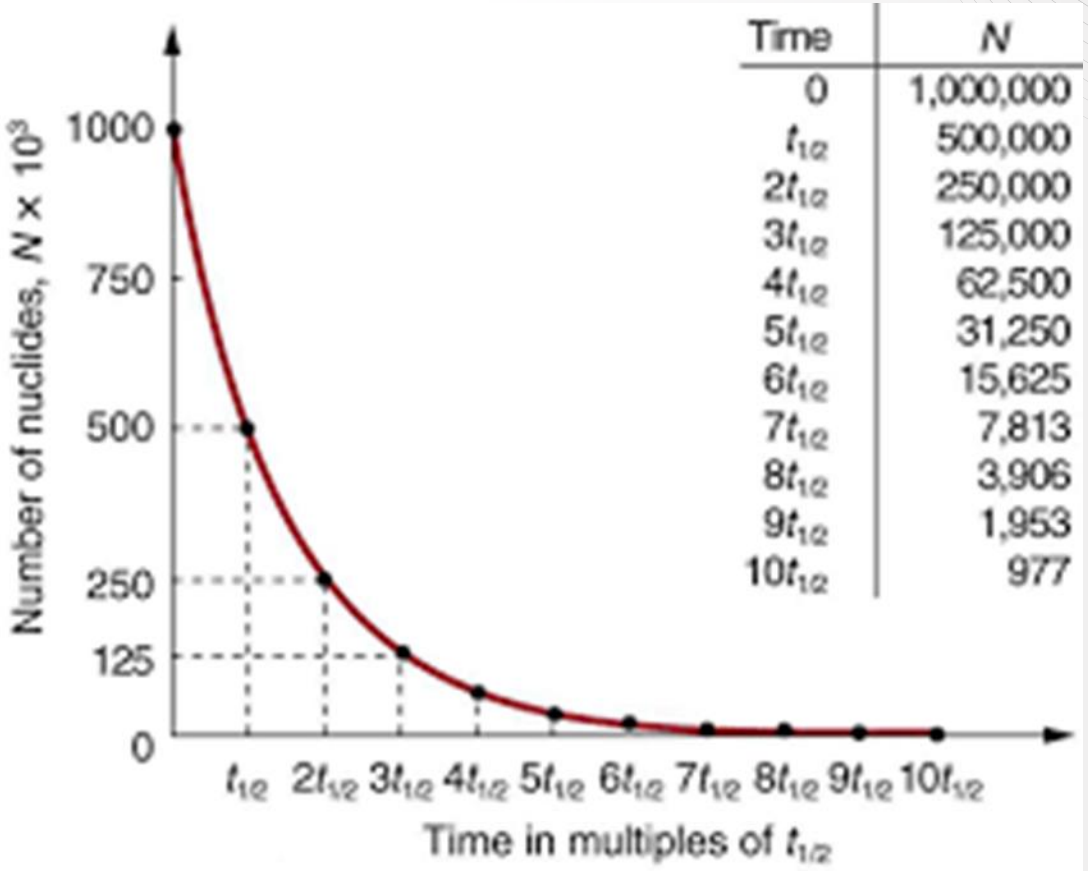
Nuclide	Max E (keV)	TVL (mm Pb)
Tc-99m	140.5	0.905
Cu-67	300.2	1.76
Lu-177	321.3	2.11
Pb-212	300.1	2.88
I-131	722.9	9.93
F-18	511	15.1
Cu-64	1345.8	16
Tl-208	2614.5	54.9

Th-228 & Progeny Energy

Th228		Ra224		Rn220		Po-216		Pb212		Bi212		Tl208	
keV	I%	keV	I%	keV	I%	keV	I%	keV	I%	keV	I%	keV	I%
12.3	8.4	11.7	0.371	549.7	0.114	804.9	0.0019	10.8	13.7	10.3	7	10.6	2.75
84.37	1.19	81.07	0.127					74.82	9.9	39.86	1.06	72.81	2.01
131.61	0.127	83.79	0.209					77.11	16.4	70.83	0.054	74.97	3.35
166.41	0.101	241	4.1					86.83	1.99	72.87	0.0905	84.45	0.404
215.98	0.247							87.35	3.81	82.12	0.0109	84.94	0.776
								89.78	1.4	82.57	0.0209	87.3	0.283
								115.18	0.596	84.87	0.00762	211.4	0.18
								176.68	0.052	288.2	0.337	233.36	0.31
								238.63	43.6	328.03	0.125	252.61	0.78
								300.09	3.3	433.7	0.017	277.37	6.6
								415.2	0.0131	452.98	0.363	485.95	0.049
										473.07	0.05	510.77	22.6
										493.37	0.0018	583.187	85
												763.13	1.79
												860.557	12.5
												2614.51	99.8

Half-life

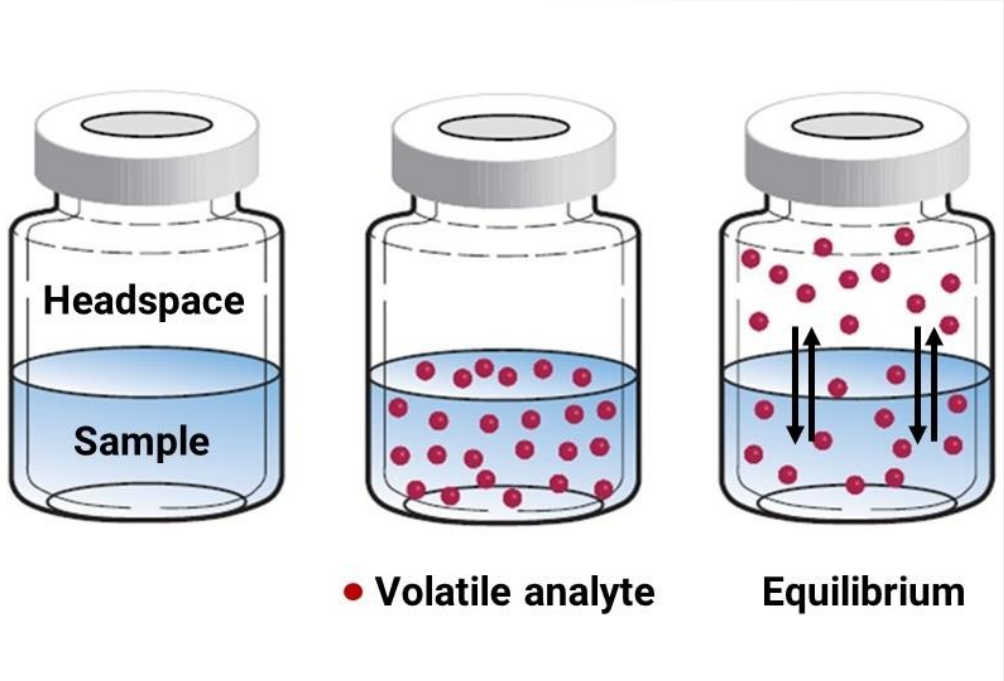
- Most important question – Is half-life >120 days?
  - If yes –
    - May require financial assurance/DFP
    - Cannot Decay in Storage (DIS)
  - If no –
    - No FA/DFP
    - Can DIS
- Other considerations
  - Even if <120 days, do you have room to store for 10 half-lives?
  - If it's 110 days, that's 3 years of DIS.
- Are there radioactive progeny? - again
  - Progeny may have longer half-lives
  - Will progeny buildup to significant activities?



Time	N
0	1,000,000
$t_{1/2}$	500,000
$2t_{1/2}$	250,000
$3t_{1/2}$	125,000
$4t_{1/2}$	62,500
$5t_{1/2}$	31,250
$6t_{1/2}$	15,625
$7t_{1/2}$	7,813
$8t_{1/2}$	3,906
$9t_{1/2}$	1,953
$10t_{1/2}$	977

Chemical/Physical Properties

- Most important question – Is it volatile?
  - Does your facility have proper containment?
    - Depends on activity
    - Fume hood, isolator/glove box, hot cell
  - Does your facility have adequate ventilation?
    - Differential pressure
    - Filtration – HEGA/charcoal?
- Other considerations
  - Is it “sticky”?
  - I.e., some compounds tend to adhere to surfaces (ductwork) and are difficult to decontaminate.



Nucleus
RadioPharma

Evaluating Program Requirements

Emergency Plan Consideration

- 10 CFR 30.72 Schedule C (MAR 4731.3150)
- Quantities of radioactive materials requiring consideration of the need for an emergency plan for responding to a release
    - Some example values
        - I-131 – 10 Ci
        - Cu-64 - 200,000 Ci
        - Most new therapeutic nuclides are not listed
        - Default values – Beta – 10,000 Ci
            - Alpha – 2 Ci
- Requirement based on sum of fractions
- Requires evaluation of need for EP
- EP required if release exceeds 1 rem WB or 5 rem thyroid

Financial Assurance Requirements

- 10 CFR 30 App. B (MAR 4731.3160)
- Half-life >120 days
- Quantities of radioactive materials exceeding 10^3 times table quantity require FA (unsealed)
  - 10^3 – 10^4 - $225,000
  - 10^4 – 10^5 - $1,125,000
  - >10^5 – Decommissioning Funding Plan
- Requirement based on sum of fractions
- Radiopharmaceutical half-lives are hours to a few days
- Could be required for parent nuclide in generator (i.e. Th-228) or long lived impurities (Ac-227)

Nucleus RadioPharma

Instrument Evaluation

- Are your current instruments adequate for detection of the new nuclide
  - Based on emission type and energy
- Portal monitor – for example GEM-5 only detects gamma
- Air monitor (stack and room)
  - Alpha/beta/gamma?
  - Particulate/vapor (iodine)/gas (radon)
  - If radon is part of product chain will natural radon interfere?
- Portable contamination monitors
  - Pancake probes have low alpha efficiency and don't discriminate
- Portable radiation monitors – sensitive to energy of new nuclide?
- Wipe counters – α/β counters have low gamma efficiency
  - γ counters will not detect α/β
- Following are examples of what I chose/am familiar with

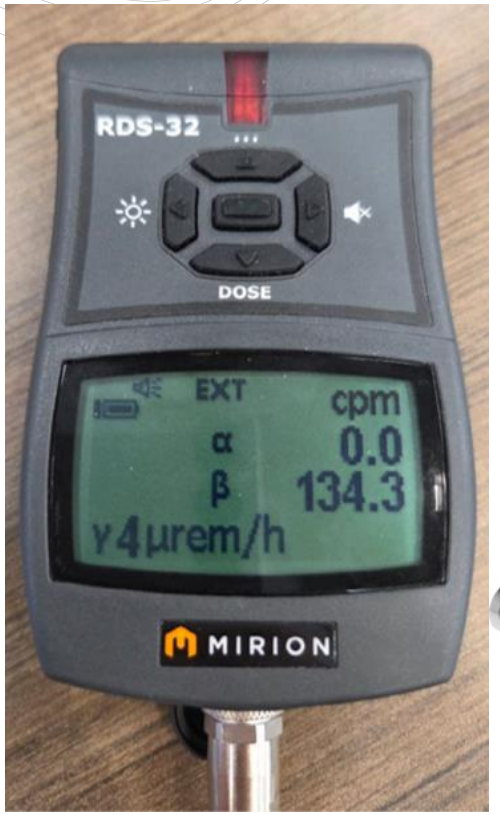
Portal Monitors

- GEM-5
  - Plastic scintillator - gamma only
  - Evaluate if your nuclide has sufficient gamma emissions
  - Not suitable for pure alpha or pure beta (Y-90)
  - Will have low efficiency for low energy gamma (I-125)

- Argos
  - Gas flow or gasless scintillator options
  - Alpha and beta (gamma optional)
  - Efficiency dependent on energy, especially for beta

Potable Contamination Meters

- G-M (pancake)
  - Generally high beta efficiency (energy dependent)
  - Low gamma efficiency
  - Generally moderate alpha efficiency
- Alpha scintillation detector (SAB-100)
  - Approximately 3x alpha efficiency
  - Discriminates alpha v beta
- X-ray Probe (SX-2R)
  - Low energy photons (I-125)
  - 5 keV – 200 keV

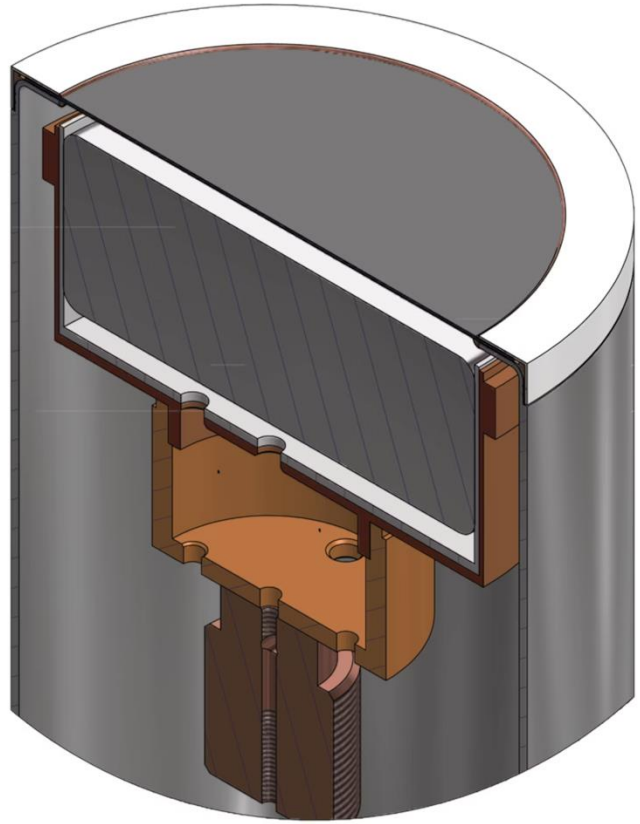


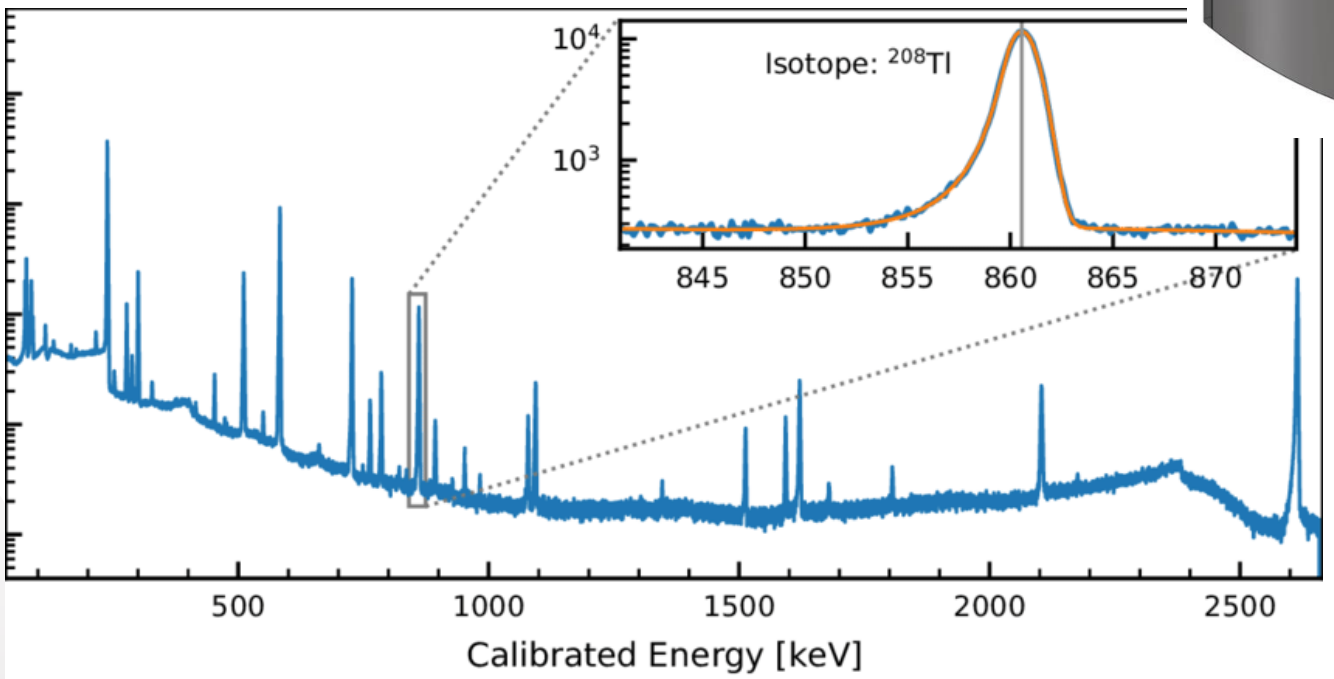
Portable Radiation Survey Meters

- G-M
  - Gamma dose rate
  - Energy range ~50 keV – 2 MeV
  - Adequate for most nuclides
- Ion Chamber
  - Wider gamma energy range –
  - ~20 keV – 3 MeV
  - Useful for beta dose rate with window
- High Range Meter (telescoping)
  - Several options available
  - Several ranges (100 R/hr - >20k R/hr)
  - Useful for hot cell entry, etc.

Other Instruments

- Gamma Spec (HPGe)
  - Typical energy range (SEGe)
    - 40 keV – 2 MeV
  - BEGe energy range
    - 3 keV – 3 MeV
  - I-125 – 35 keV
  - Tl-208(Pb-212) – 2.6 MeV
- Wipe/Filter Counter
  - α/β
    - Proportional
    - PIPS
    - LSC
  - Gamma
    - NaI





Evaluate Need for Bioassay

- Radioiodine use requires thyroid monitoring (Reg. Guide 8.20)
  - Example – Captus 4000
  - NaI with MCA
- Determine bioassay requirements for other nuclides
  - (Reg. Guide 8.9)
- Determine appropriate bioassay method
  - Urinalysis
  - Fecal analysis – many alpha emitters
  - In-vivo

Nucleus RadioPharma

THANK YOU!