Traceability and Primary Standards for Alpha Emitters used in TAT

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PHYSICAL MEASUREMENT LABORATORY

Disclosures

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Orano Med

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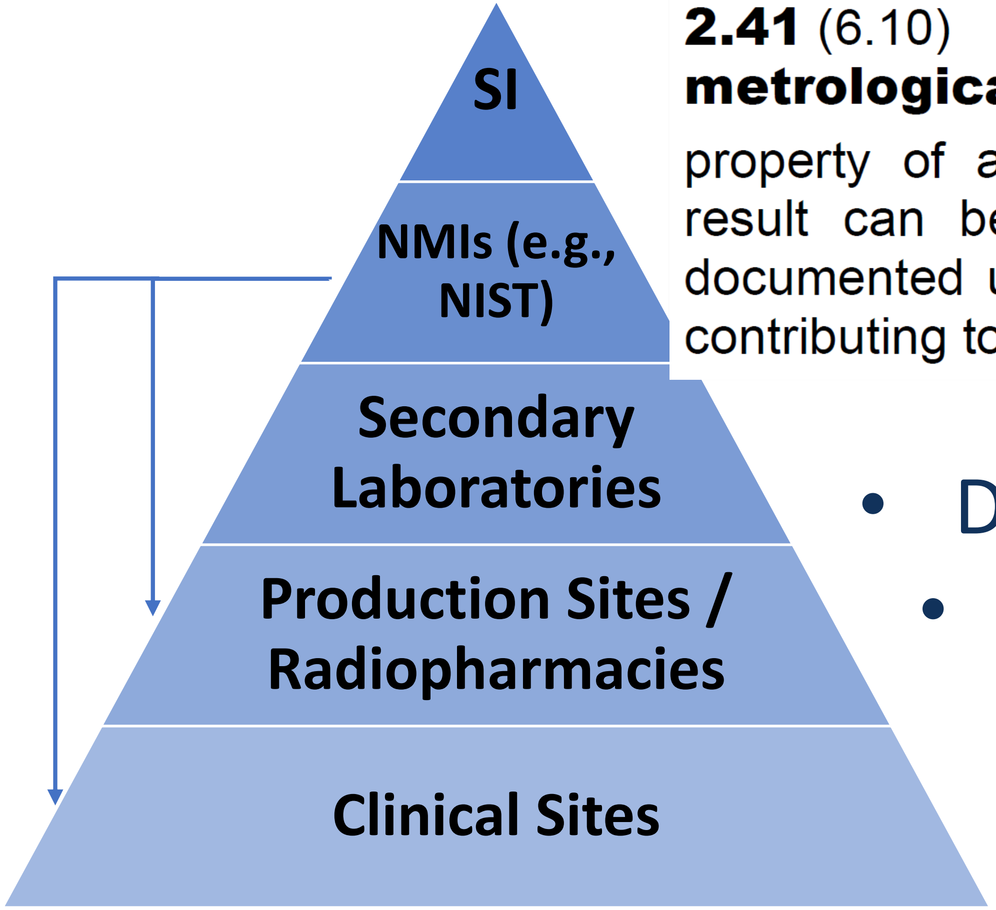
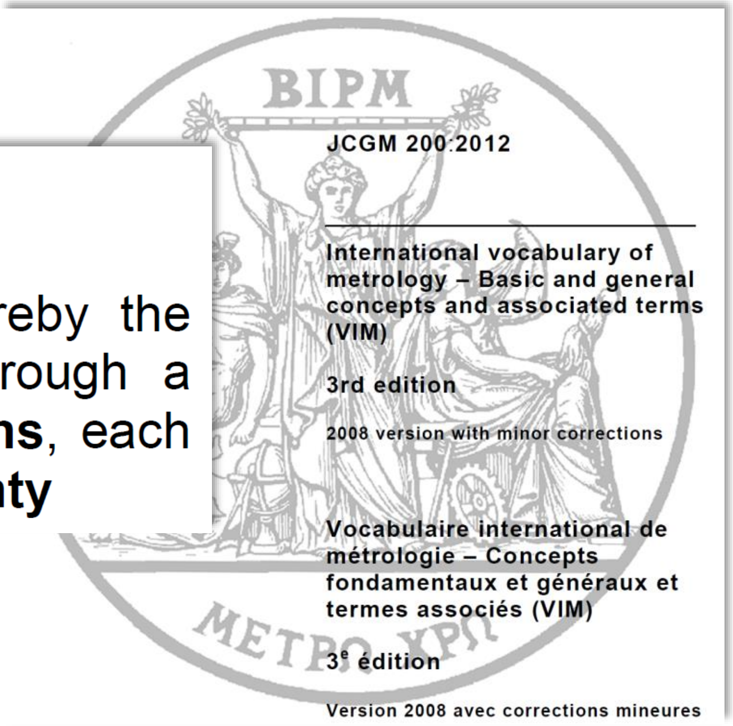
Traceability and Primary Standards for Alpha Emitters used in TAT

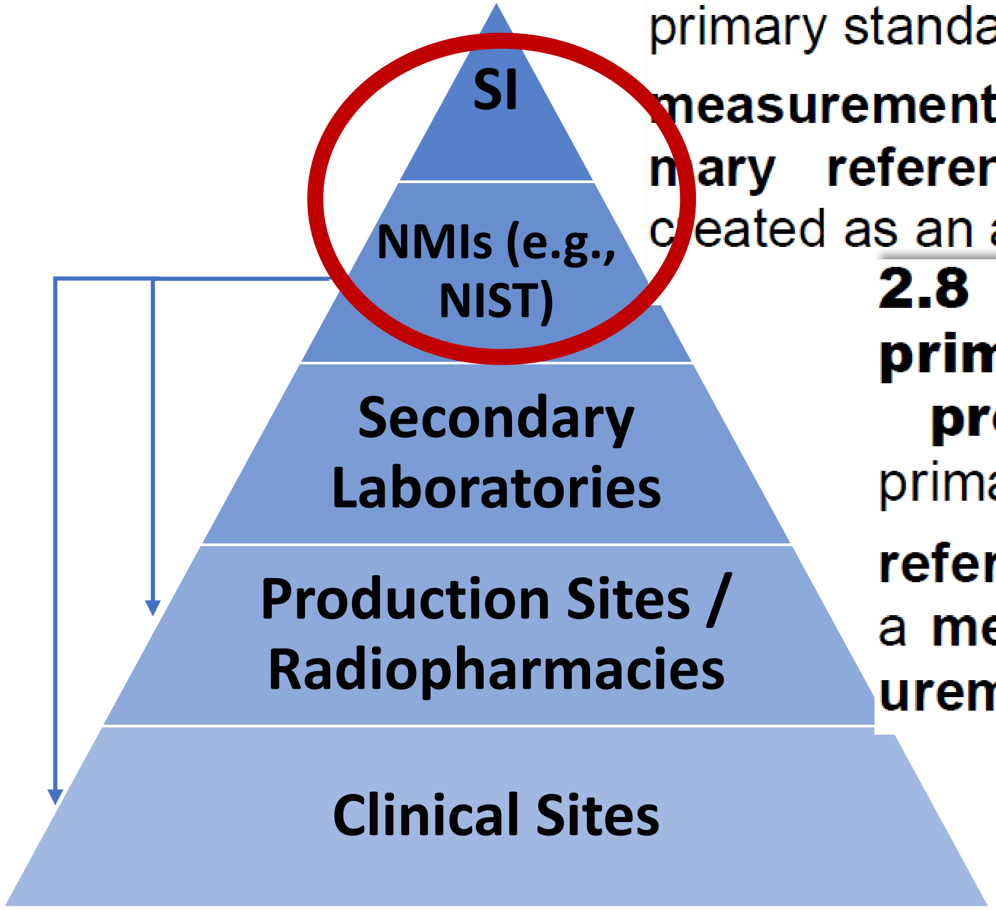


2.41 (6.10)
metrological traceability
property of a **measurement result** whereby the result can be related to a reference through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty**



- Direct calibration
  - Benchmark calibration factors/settings
    - Decay data

Traceability and Primary Standards for Alpha Emitters used in TAT

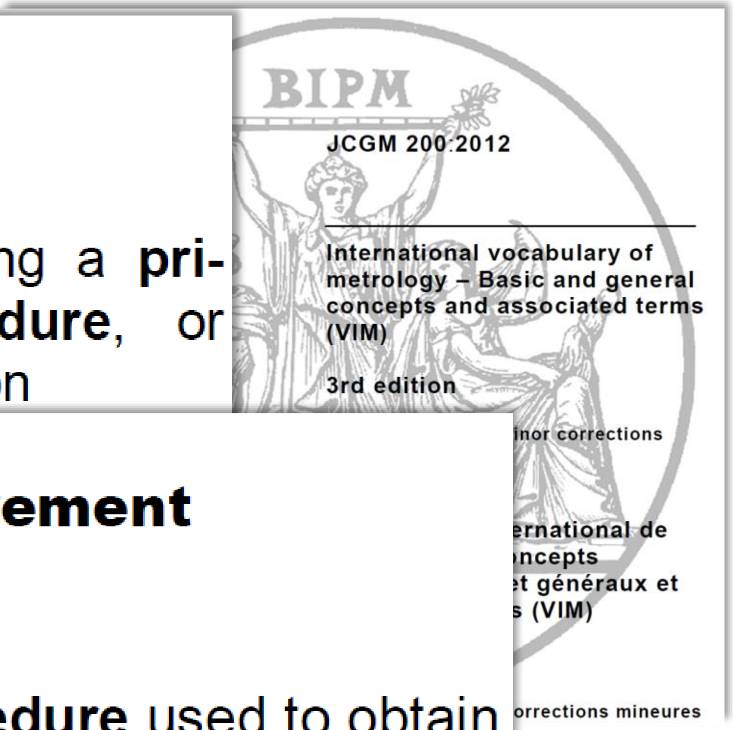


5.4 (6.4)
primary measurement standard
primary standard

measurement standard established using a **primary reference measurement procedure**, or created as an artifact, chosen by convention

2.8
primary reference measurement procedure
primary reference procedure

reference measurement procedure used to obtain a **measurement result** without relation to a **measurement standard** for a **quantity** of the same **kind**



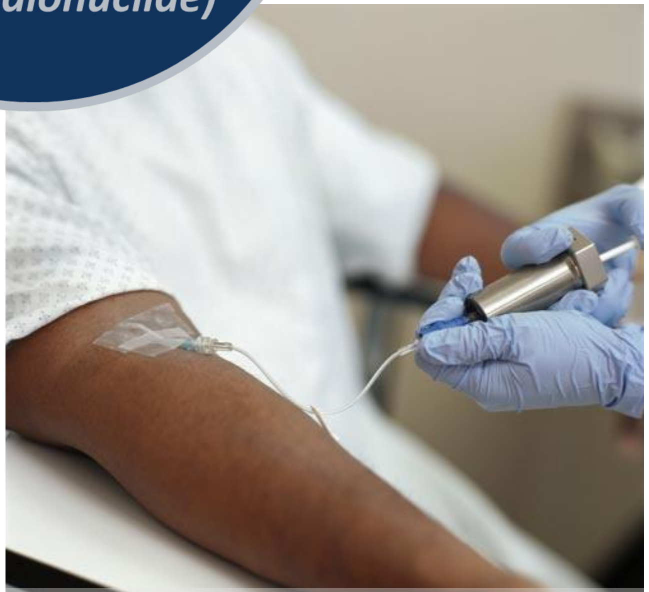
Measure the becquerel without calibrating to another becquerel.

Traceability and Primary Standards for Alpha Emitters used in TAT

NIST

Bq

Decays per second (of a radionuclide)



https://images.app.goo.gl/DEytSwNtUHjsYsov6

In TAT, we need to measure the <u>administered activity</u>

- Key input for dosimetry and quantitative molecular imaging
- For imaging or therapy, we want to administer enough activity to do the job, but not more

The SI derived unit for activity is the becquerel

Defining the becquerel

Bq

Decays per second (of a radionuclide)

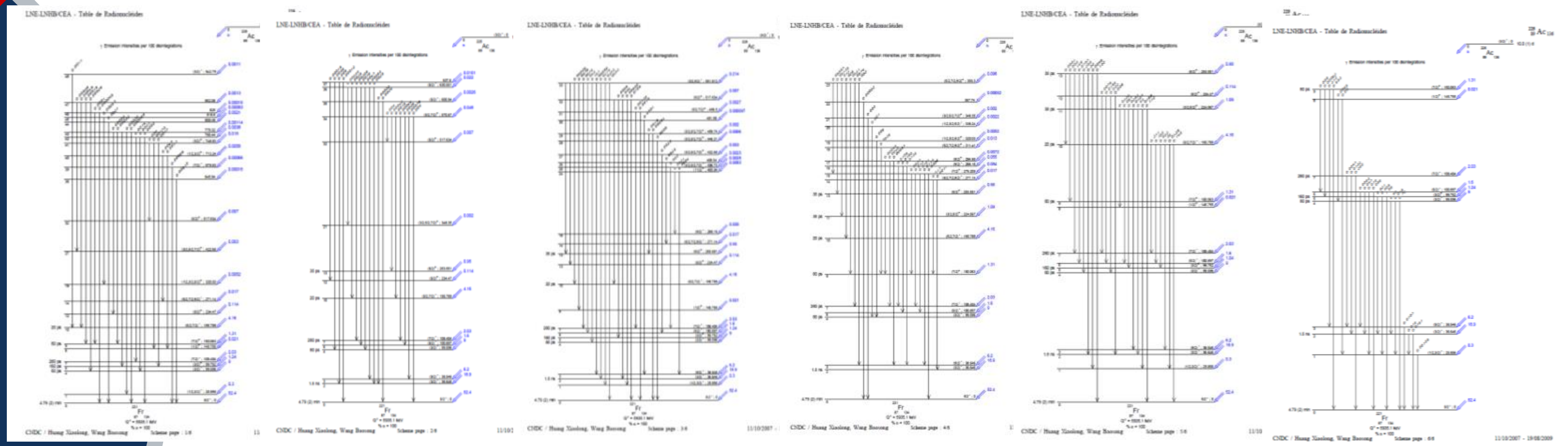
Defining the becquerel

NIST

Bq

Decays ***per second (of a radionuclide)***

Define "decays" for a nuclide



Ac-225 decays mostly (52 %) to the ground state of Fr-221. The other 48 % is split between 47 excited states in Fr-221, with attendant gamma-ray emissions.

From Decay Data Evaluation Project, accessed: http://www.lnhb.fr/nuclear-data/nuclear-data-table/

Defining the becquerel

NIST

Bq

Decays per second
(of a radionuclide)

The measurement… just counting the decays

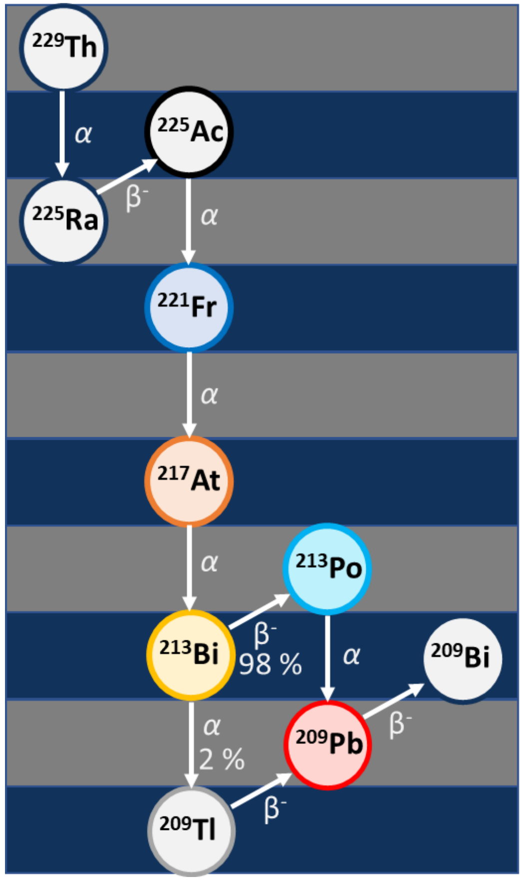
Counting methods must be appropriate to the decay types, with efficiency models to correct for missed counts

Defining the becquerel

The “a” here is really important

Account for radionuclidic impurities, including breakthrough of parents

Account for progeny



Primary standards for activity in TAT

Starting in about 2005, with work on ^{223}Ra, a wave of interest in therapeutic radiopharmaceuticals based on alpha-emitters has kept metrology institutes busy

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Review

Realization and dissemination of activity standards for medically important alpha-emitting radionuclides

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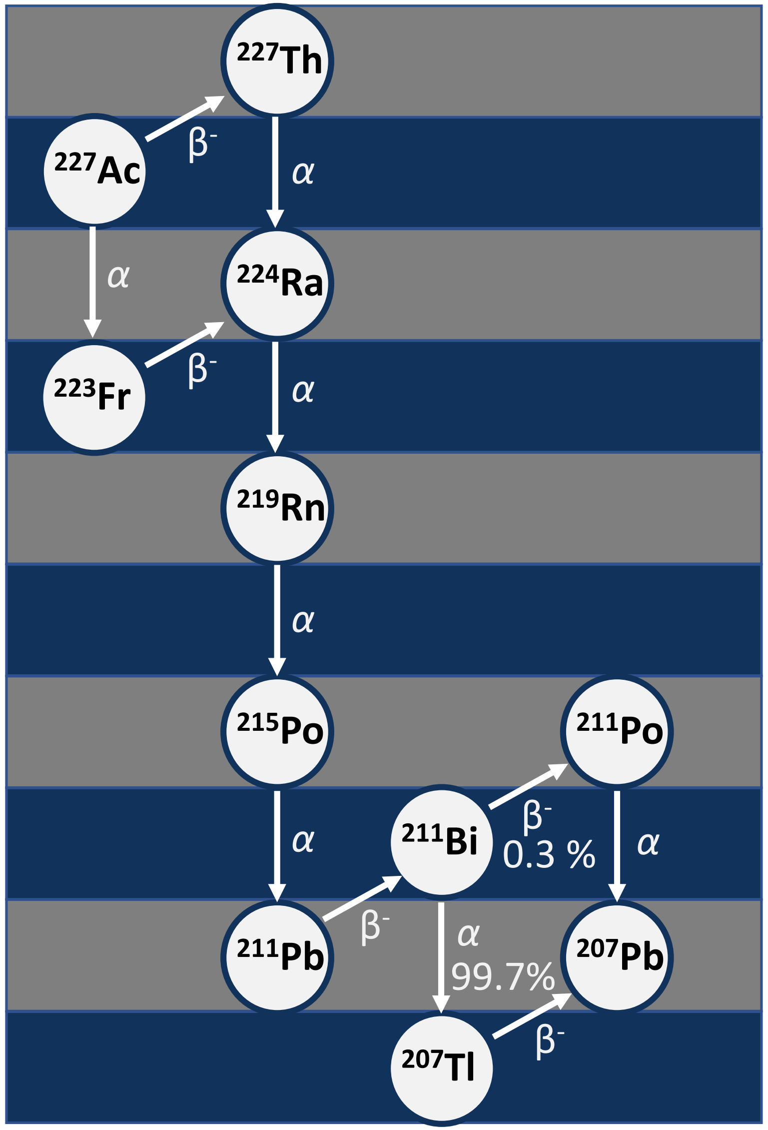
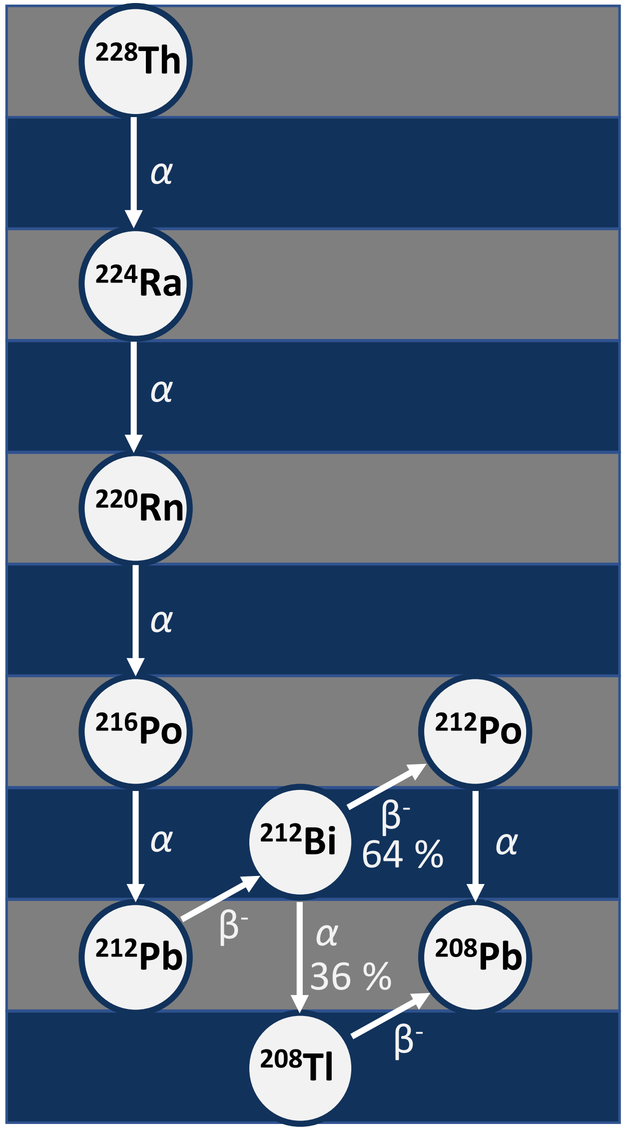
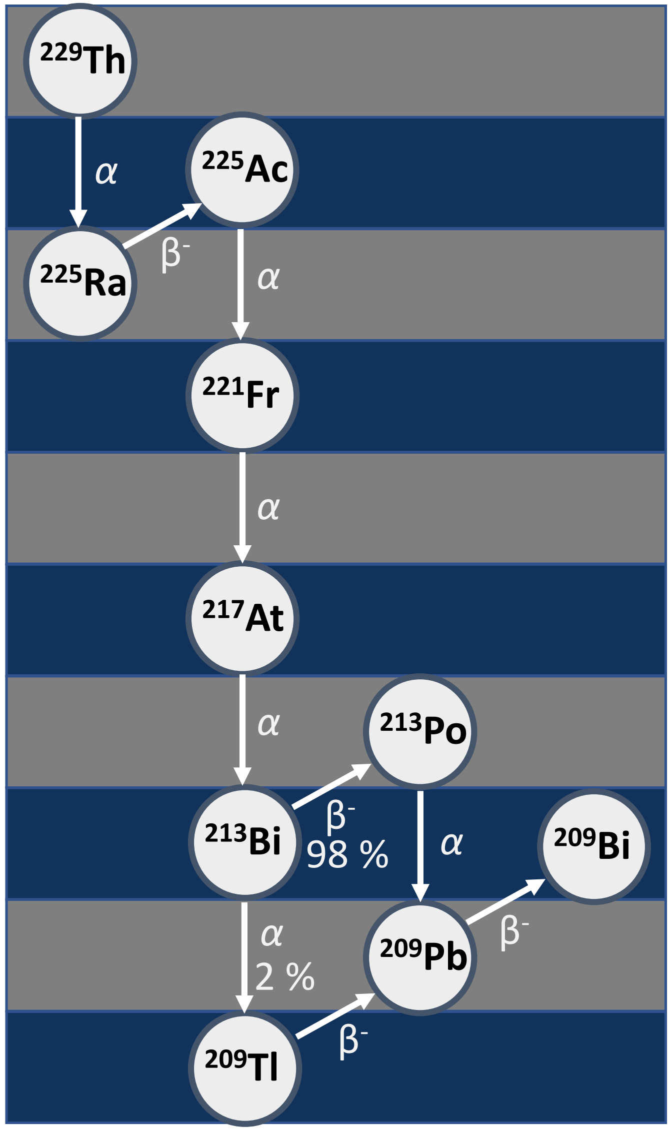
[c] National Physical Laboratory, Hampton Road, Teddington, Middlesex, TW11 0LW, UK

Medically important alpha emitters

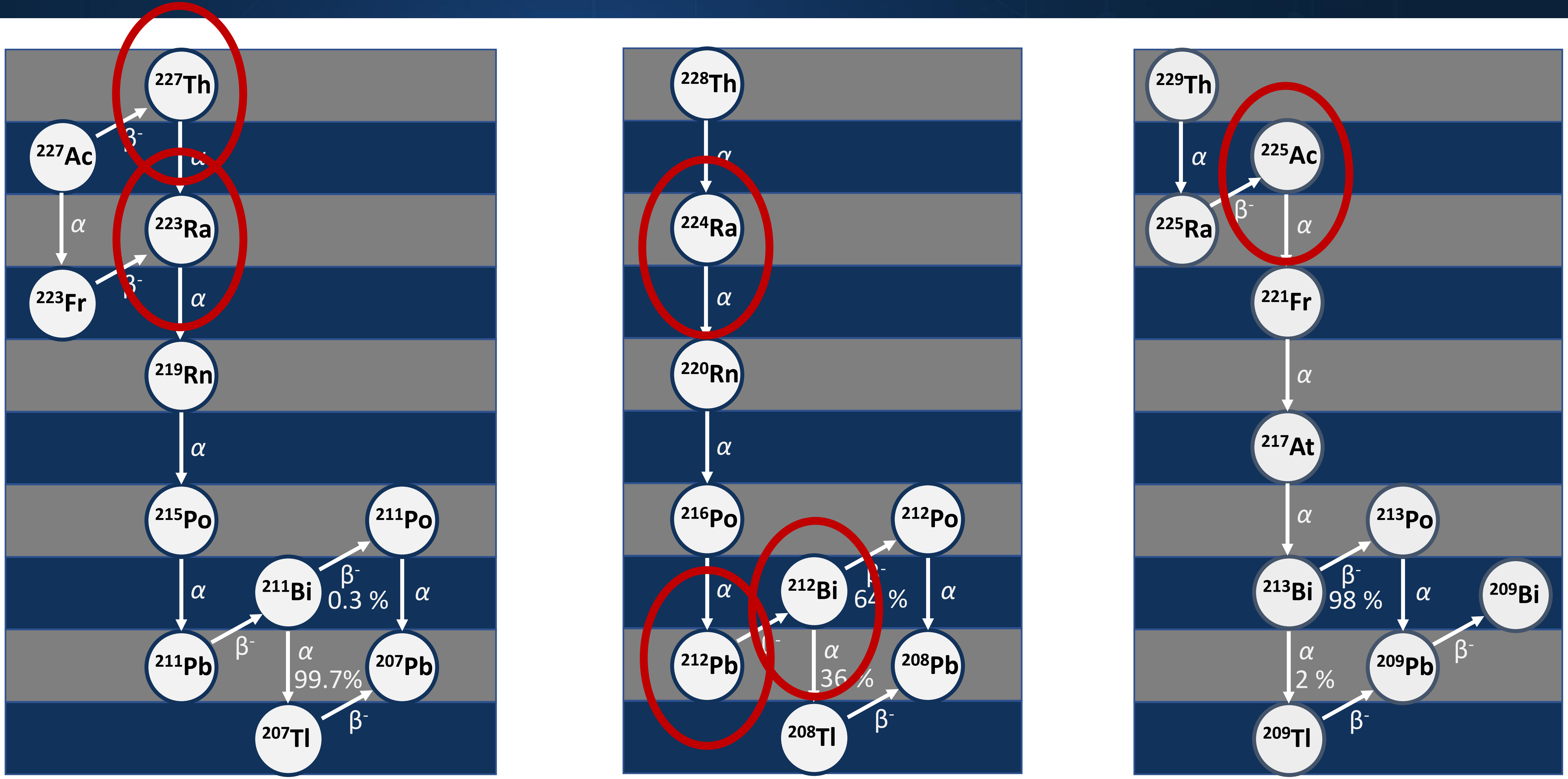




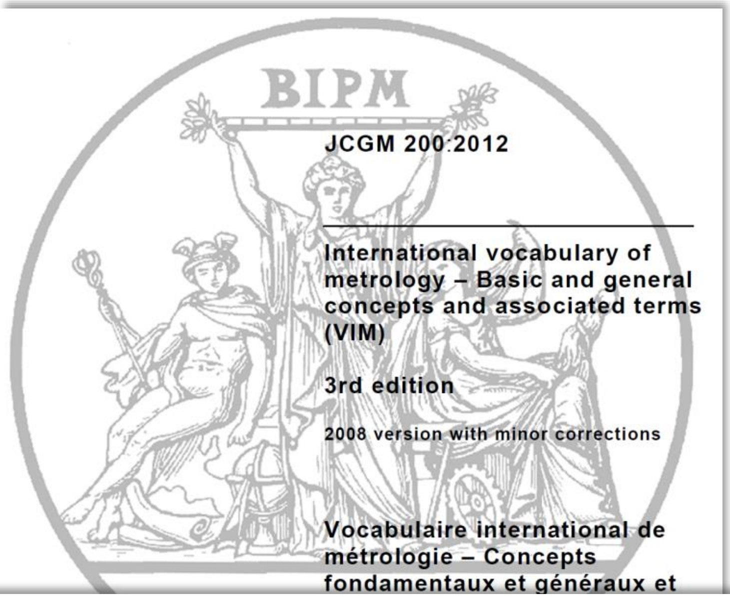


(Some) Medically important alpha emitters

NIST



Primary methods for TAT activity standards



2.8
primary reference measurement procedure
primary reference procedure

reference measurement procedure used to obtain a **measurement result** without relation to a **measurement standard** for a **quantity** of the same **kind**

isotropic source, which is combined with the decay data to calculate the source activity. While to date there are no examples of DSA being used to measure the activity of a medically important alpha emitting radionuclide, Marouli et al. (2019) discuss measurements of ^{227}Ac in equilibrium with its progeny, including ^{227}Th and ^{223}Ra. The contamination risks posed by diffusion of radon progeny and high energy recoils that Marouli et al. address will be common to the decay chains of interest for medical applications. For activity measurements "contamination" means lost counts, as do the common measures taken to avoid contamination, e.g., covering dried sources with thin protective films. Fortunately, liquid scintillation-based methods offer a 4π detection scheme with very high counting efficiencies and, in various forms, account for all primary activity standardizations of medically important alpha-emitting radionuclides to date.

2.1. Liquid scintillation

Liquid scintillation (LS) counting is a very powerful method for the

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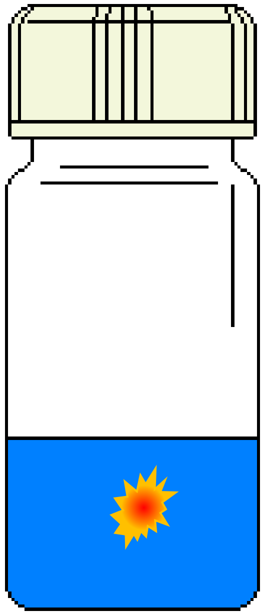
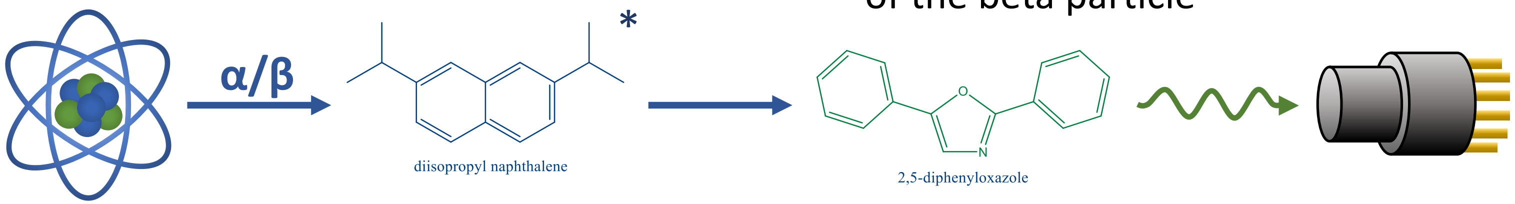
Liquid-scintillation based primary methods



Radionuclide decays, emitting alpha or beta particle

Energy is delivered to the solvent molecule and transferred to the fluor

Fluor molecules relax via photon emission, with the number of photons being proportional to the energy of the beta particle



Some quenching mechanisms prevent beta particle energy from exciting solvent molecules

Some quenching mechanisms inhibit energy transfer to fluor molecules

Color quenching and scattering inhibit PMT detection of optical photons

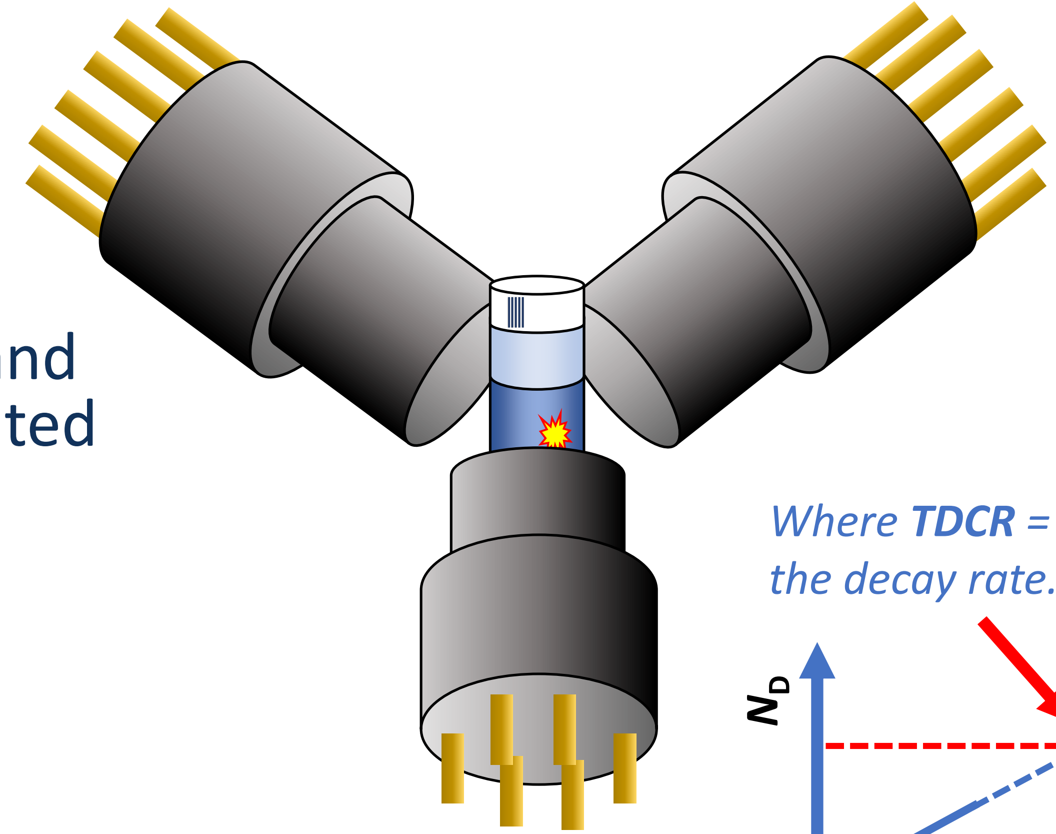
Challenges in LS measurements for TAT

- **Decay chains**
  - Progeny include beta-emitters ($\varepsilon < 1$)
  - Progeny include short-lived nuclides
  - Pre-equilibrium measurements (changing $\varepsilon(t)$)
- **Impurities**
  - Breakthrough
  - Co-produced isotopes

TDCR is well-suited for TAT nuclides

Triple-to-double Coincidence Ratio (TDCR) counting

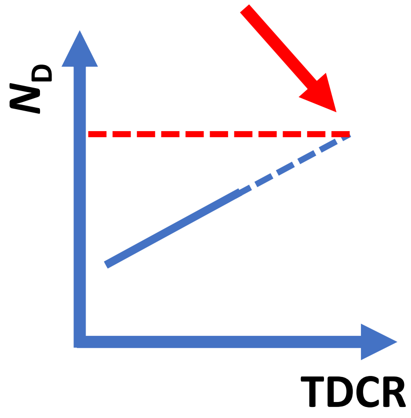
- Liquid scintillation counting
- 3-detector system where double and triple coincidence events are counted



$$TDCR = N_T/N_D = \varepsilon_T/\varepsilon_D$$

- Vary efficiency
- **As $\varepsilon_T/\varepsilon_D \rightarrow 1$, N_D (and N_T) $\rightarrow N$**
  - In practice, a bit more complicated, but we have good models!

*Where **TDCR** = 1, N_D is the decay rate.*

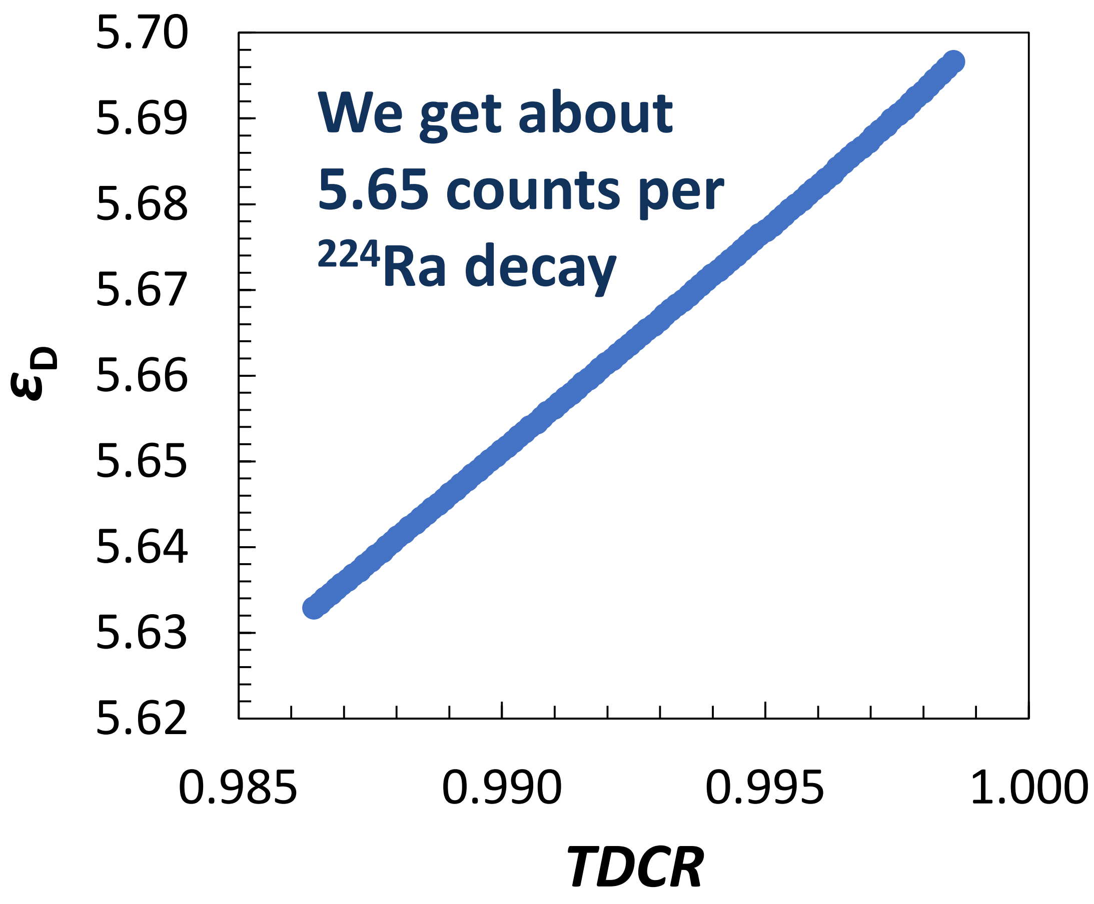


LS counting efficiencies are high

Triple-to-double Coincidence Ratio (TDCR) counting

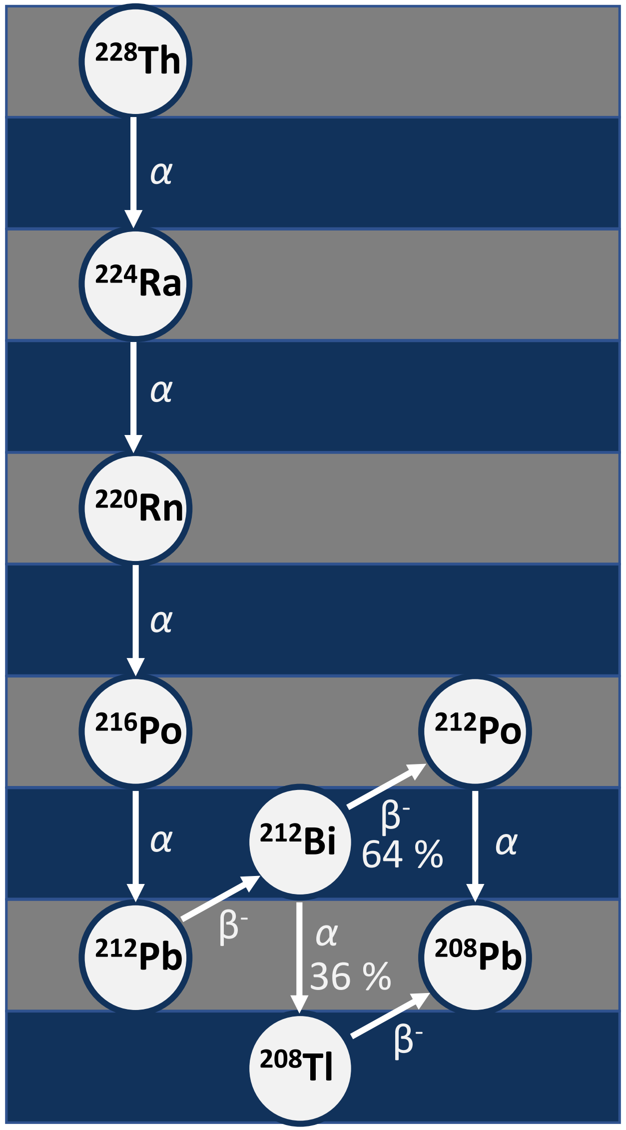
$$TDCR = N_T/N_D = \varepsilon_T/\varepsilon_D$$

The MICELLE2 model* uses a Monte Carlo approach to calculate ε_T and ε_D for β^- decay branches



*Kossert & Grau Carles, Appl. Radiat. Isotop. 68, 1482-1488 (2010).

^{224}Ra decays by four α-emissions

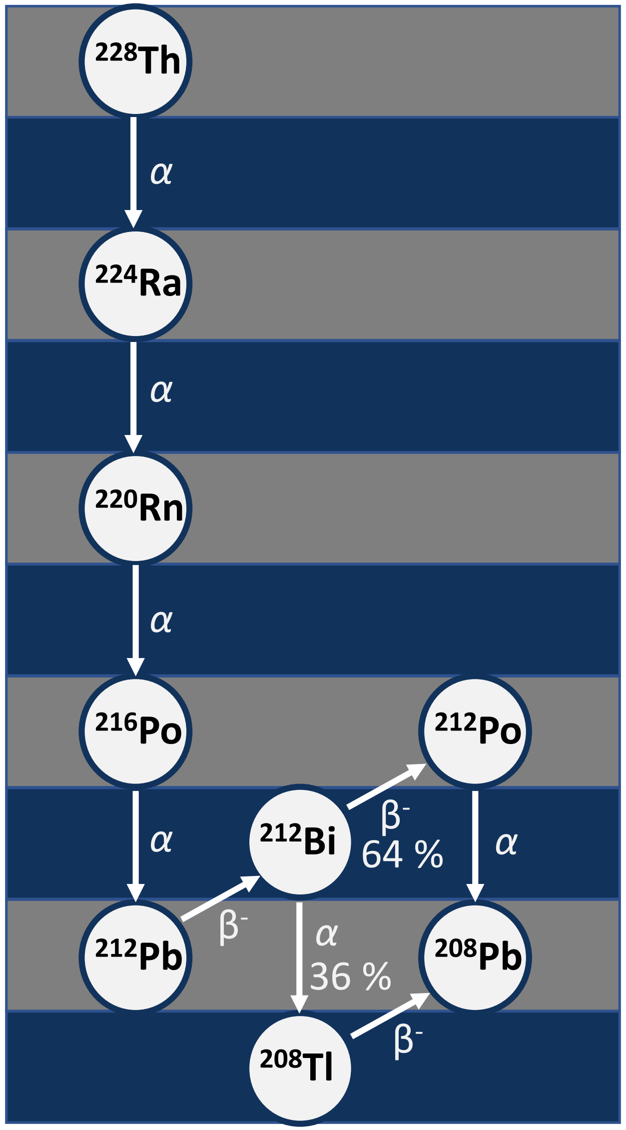


Following Bateman (1908), concentrations of isotopes in a decay chain are calculable from initial concentrations and decay constants (λ)

$$\frac{\mathrm{d}N_1}{dt} = -\lambda_1 N_1$$

$$\frac{\mathrm{d}N_i}{dt} = \lambda_{i-1} N_{i-1} - \lambda_i N_i \;\; (i = 2, n)$$

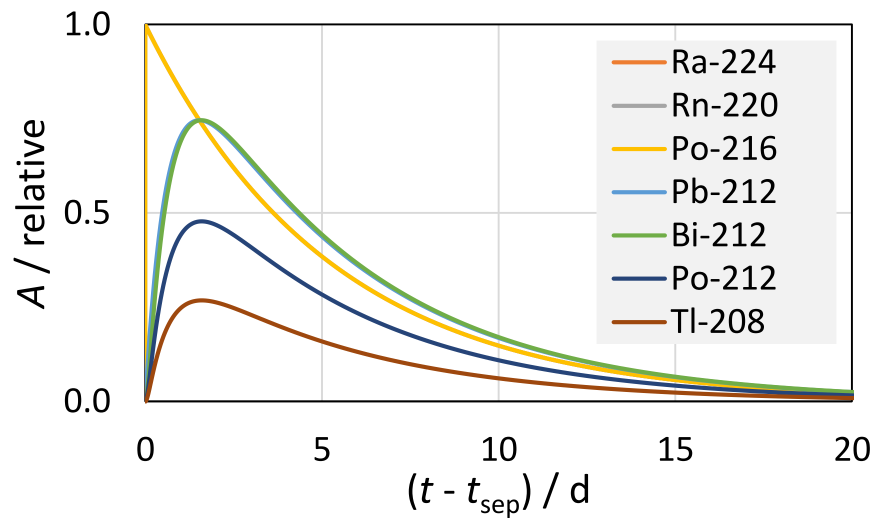
^{224}Ra reaches equilibrium 6 d after t_{sep}

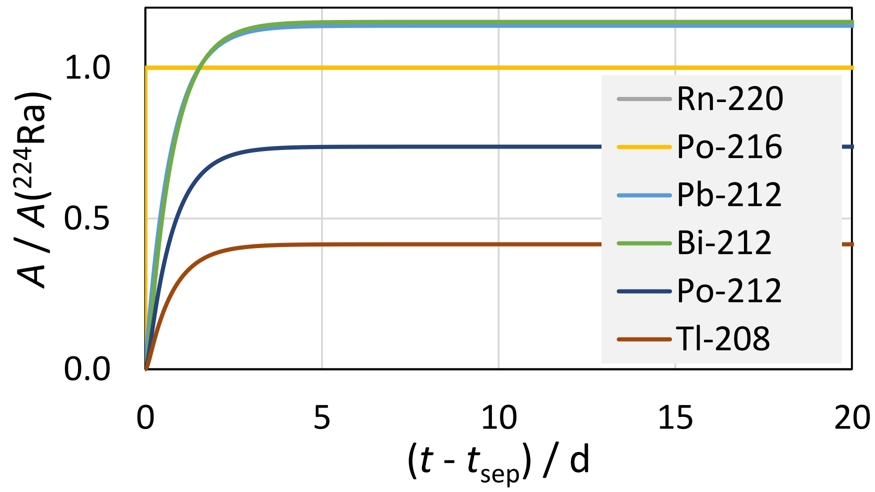


	$T_{1/2}$	$A/A_{Ra\text{-}224}$
^{224}Ra	3.631(2) d	1
^{220}Rn	55.8(3) s	1.000178(1)
^{216}Po	0.148(4) s	1.000178(1)
^{212}Pb	10.64(1) h	1.13928(15)
^{212}Bi	60.54(6) min	1.15263(15)
^{212}Po	300(2) ns	0.7385(11)
^{208}Tl	3.058(6) min	0.4144(20)

Beta-decaying nuclides:

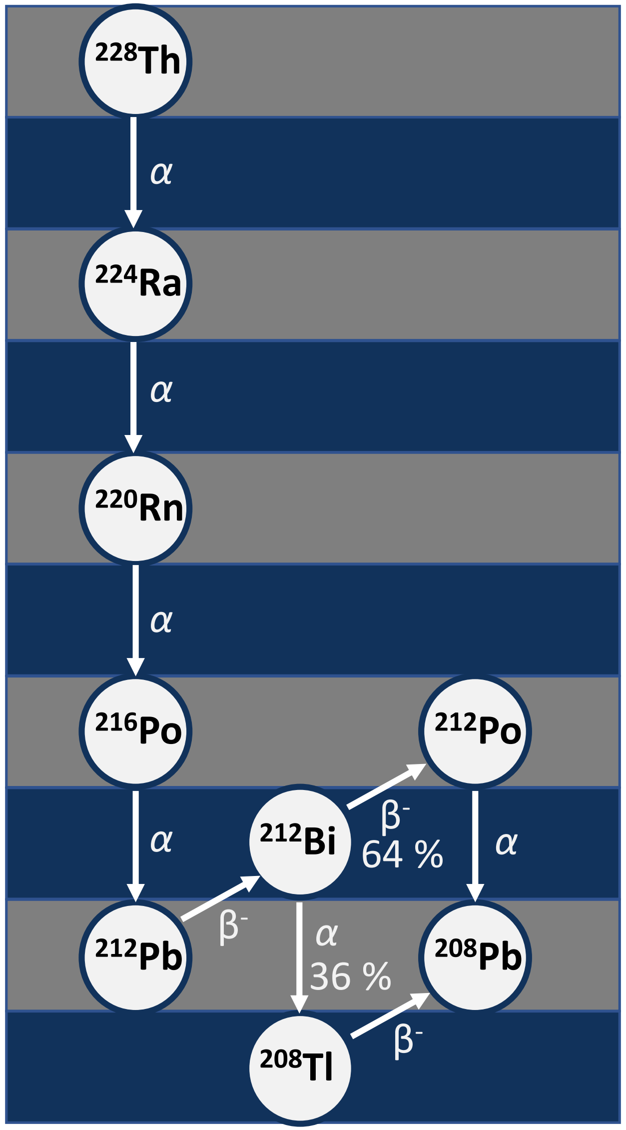
^{212}Pb, ^{212}Pb, ^{208}Tl





***Pre-equilibrium activity assays are tricky**

More than summing the activities



	$T_{1/2}$	$A/A_{\text{Ra-224}}$
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^{212}Po	300(2) ns	0.7385(11)
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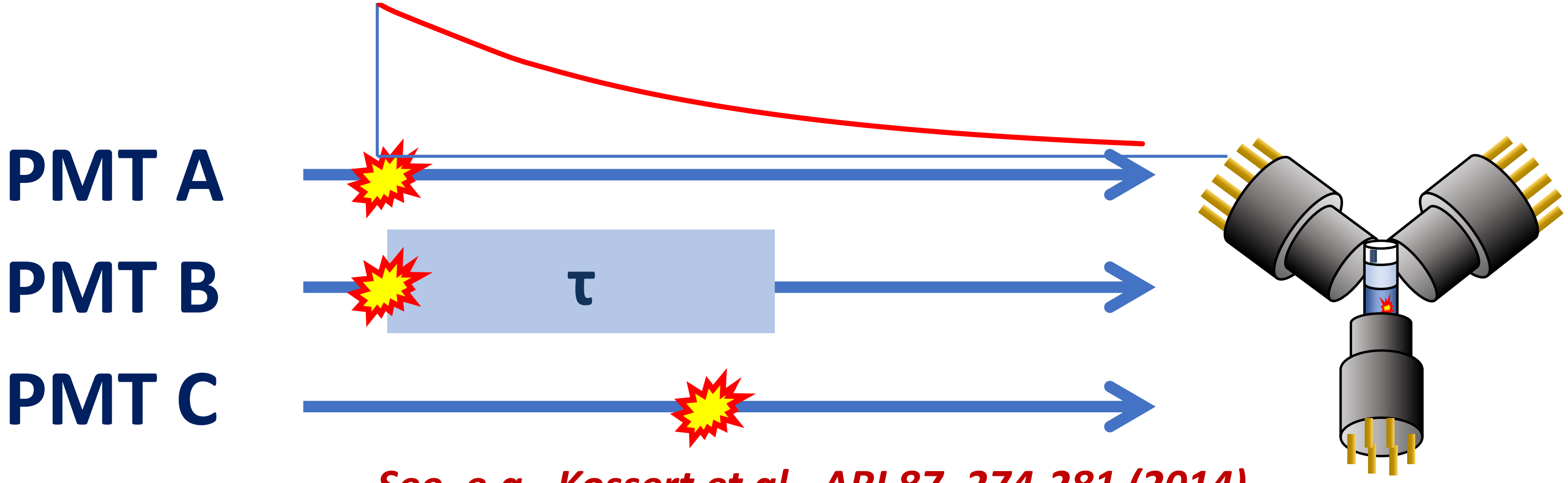
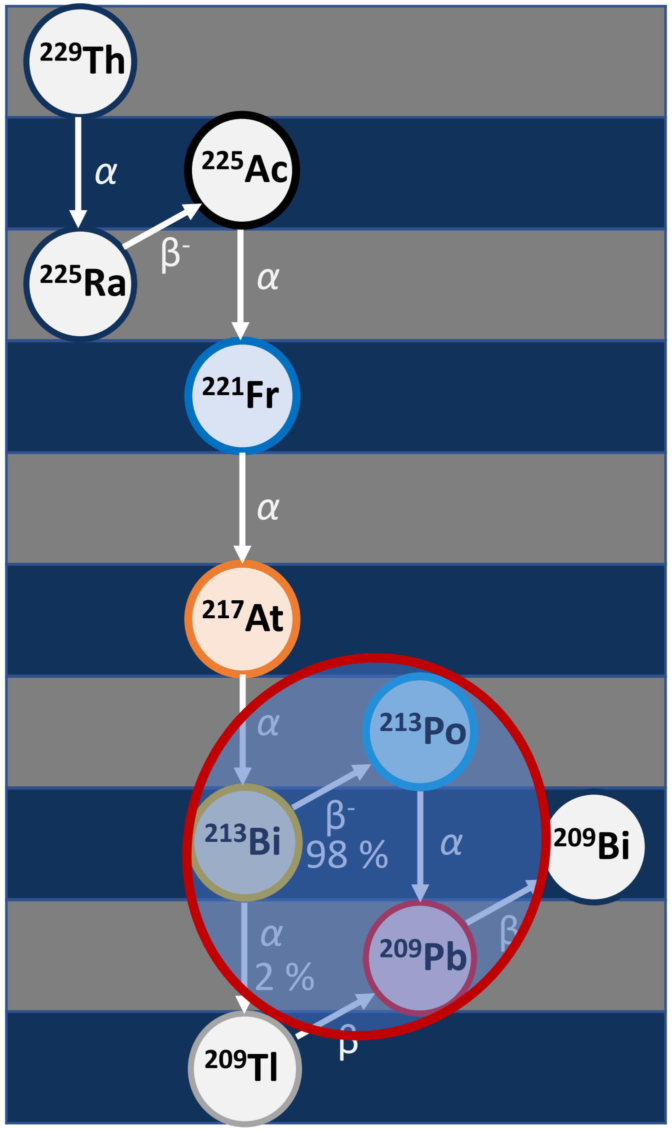
(^{212}Bi + ^{212}Po) LS efficiency demands special attention



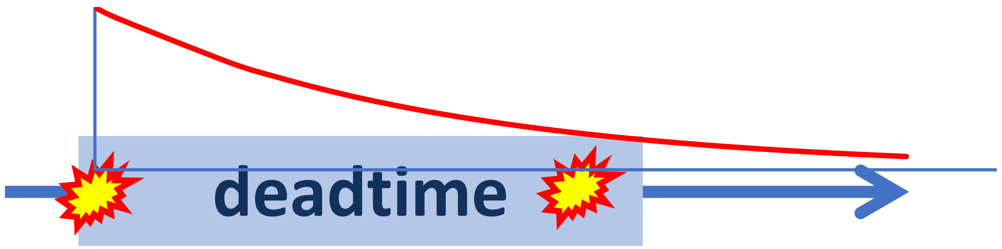
See, e.g., Kossert et al., ARI 87, 274-281 (2014)

Importance of survival corrections

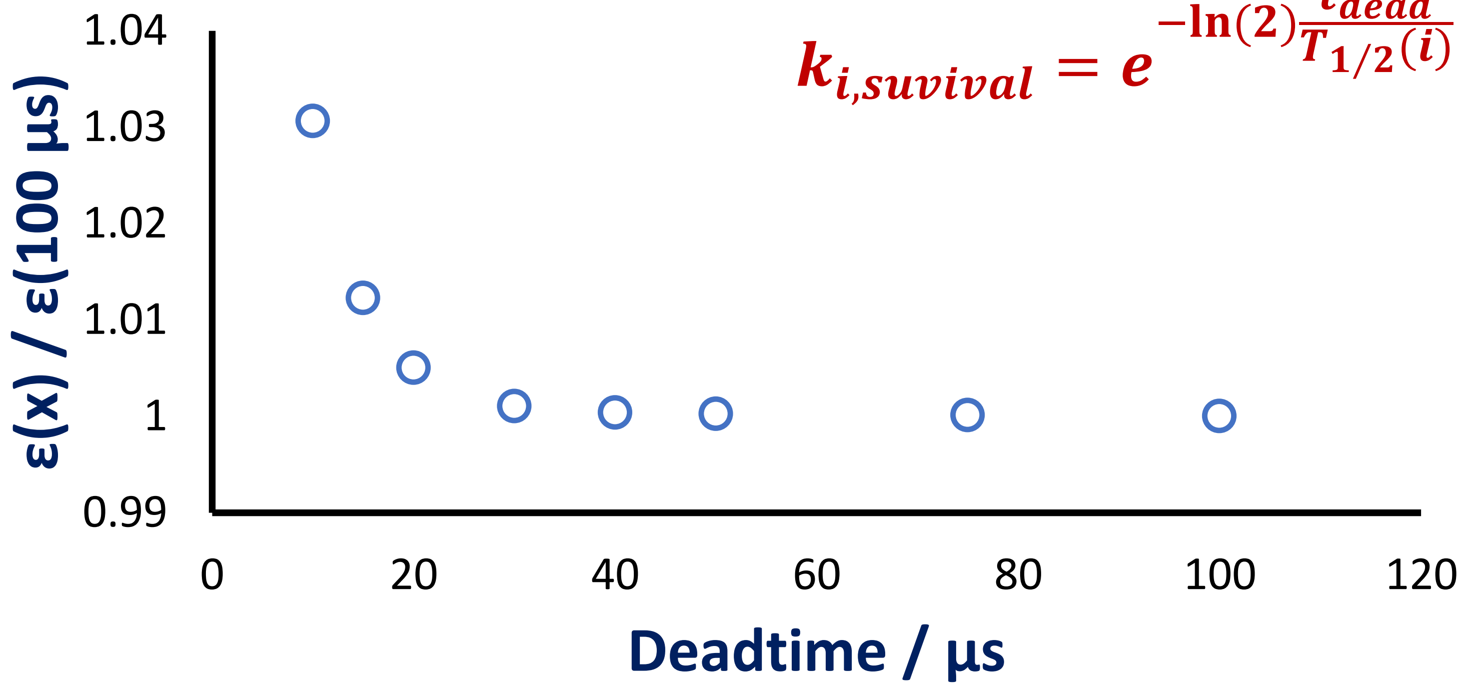


$T_{1/2}$ (At-217) = 32.3 ms

$T_{1/2}$ (Po-213) = 3.7 µs



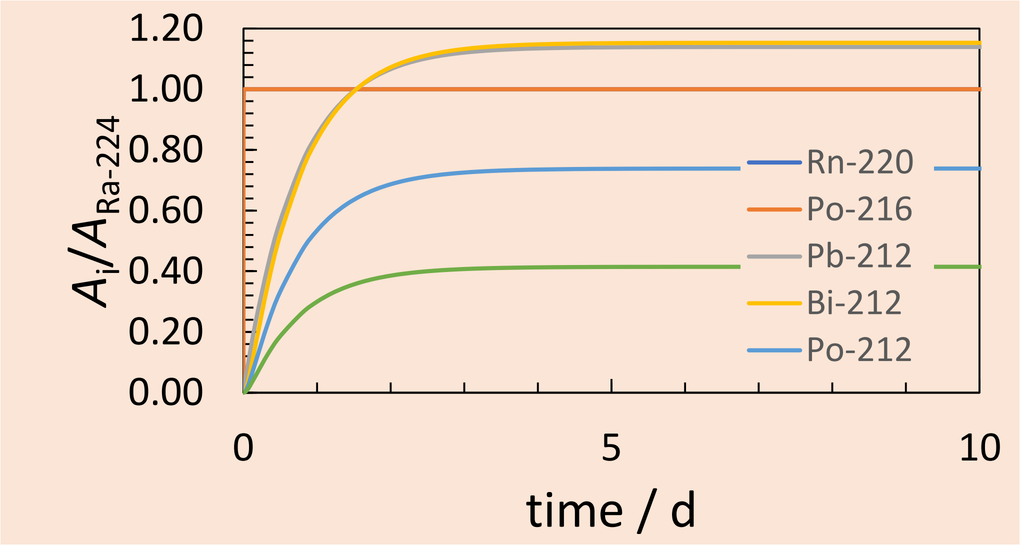
$$k_{i,suvival} = e^{-\ln(2)\frac{t_{dead}}{T_{1/2}(i)}}$$

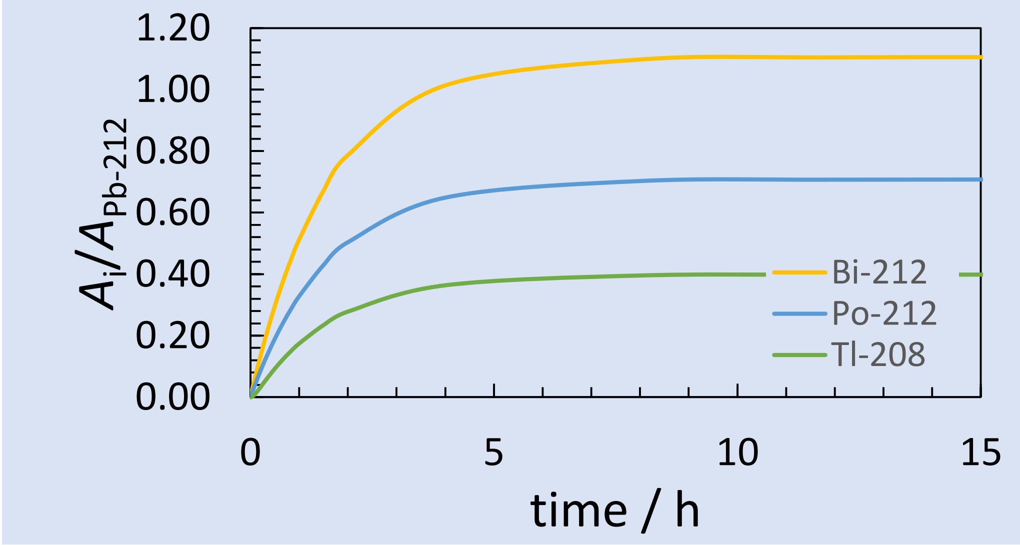


Challenges in LS measurements for TAT

- **Decay chains**
  - ✓ Progeny include beta-emitters ($\varepsilon < 1$)
  - ✓ Progeny include short-lived nuclides
  - Pre-equilibrium measurements (changing $\varepsilon(t)$)
- **Impurities**
  - Breakthrough
  - Co-produced isotopes

Equilibration considerations





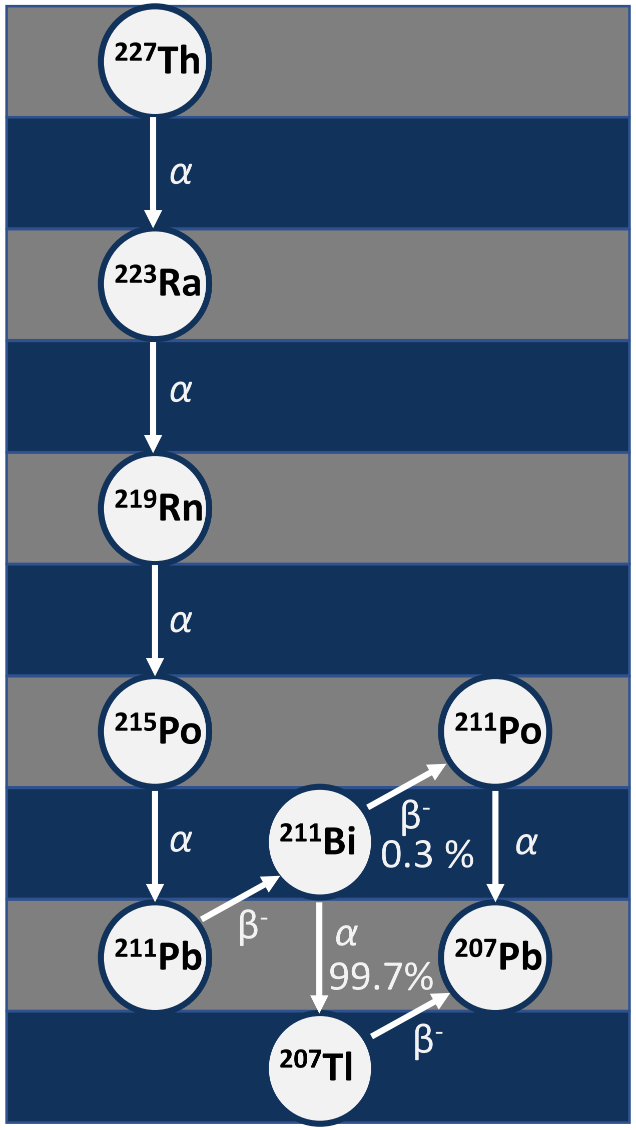
^{224}Ra (longest-lived progeny is ^{212}Pb, $T_{1/2}$ = 10.6 h) takes > 6 d to reach equilibrium

Separated from its parent, ^{212}Pb (longest-lived progeny is ^{212}Bi, $T_{1/2}$ = 60.55 min) reaches equilibrium in ~ 12 h.

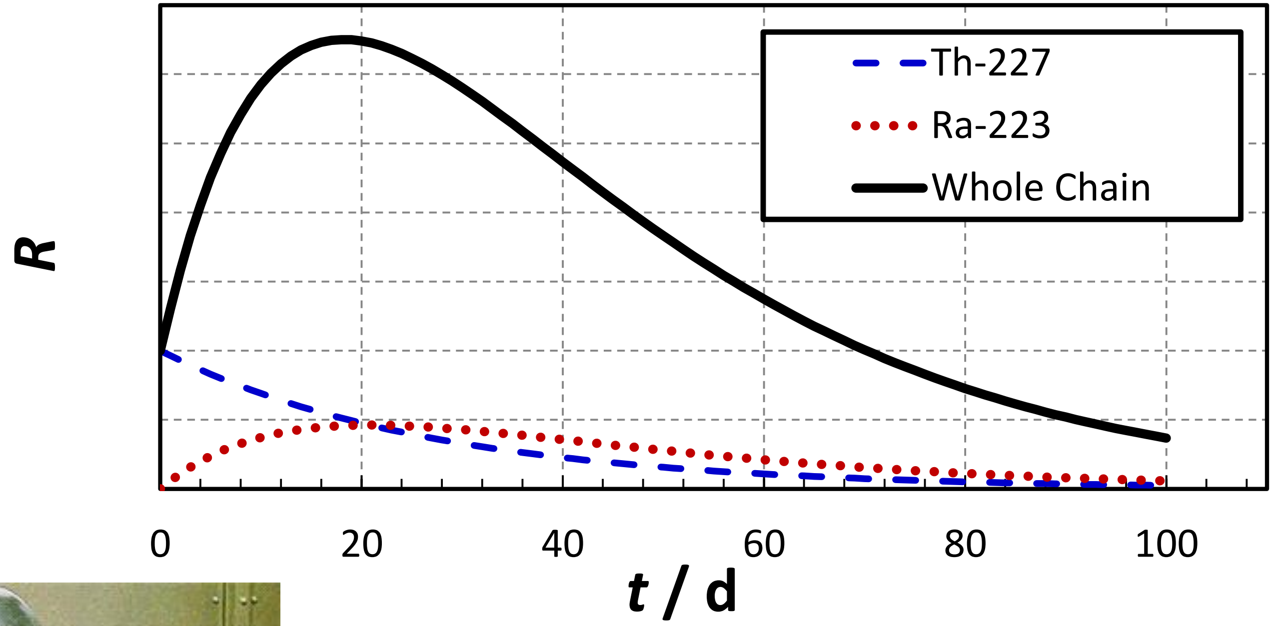
Breakthrough of the parent leads to "supported" ^{212}Pb

Measuring during ingrowth

NIST

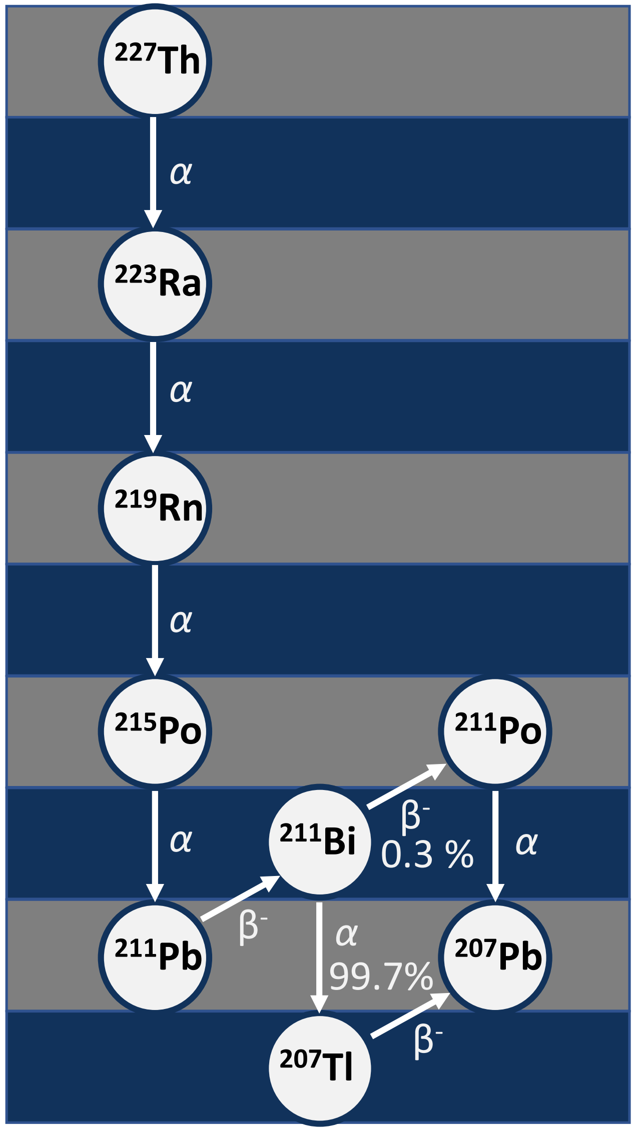


Th-227 differs from previously considered decay chain nuclides because we cannot wait for equilibrium.



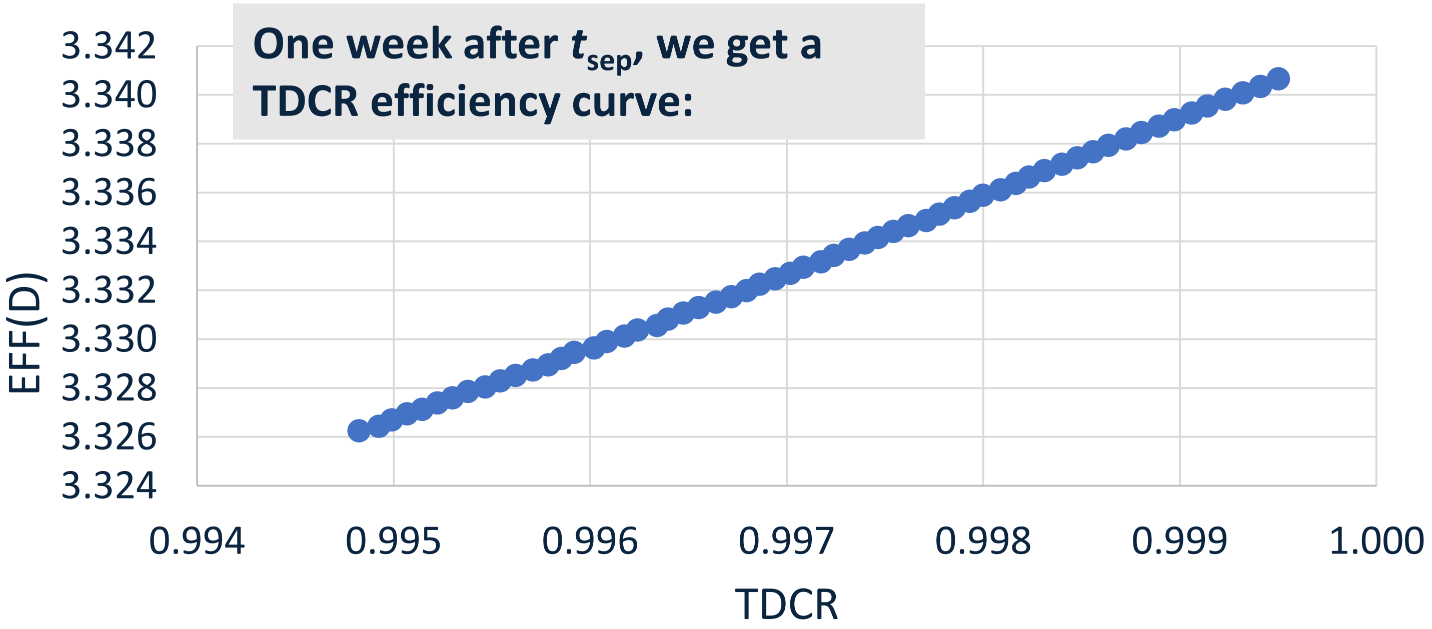
"If there's one thing I despise, it is a fair fight. But if I must, then I must…"
--Dark Helmet

Preliminary LS efficiency calculations



Estimate 100 % LS counting efficiency for alpha emissions

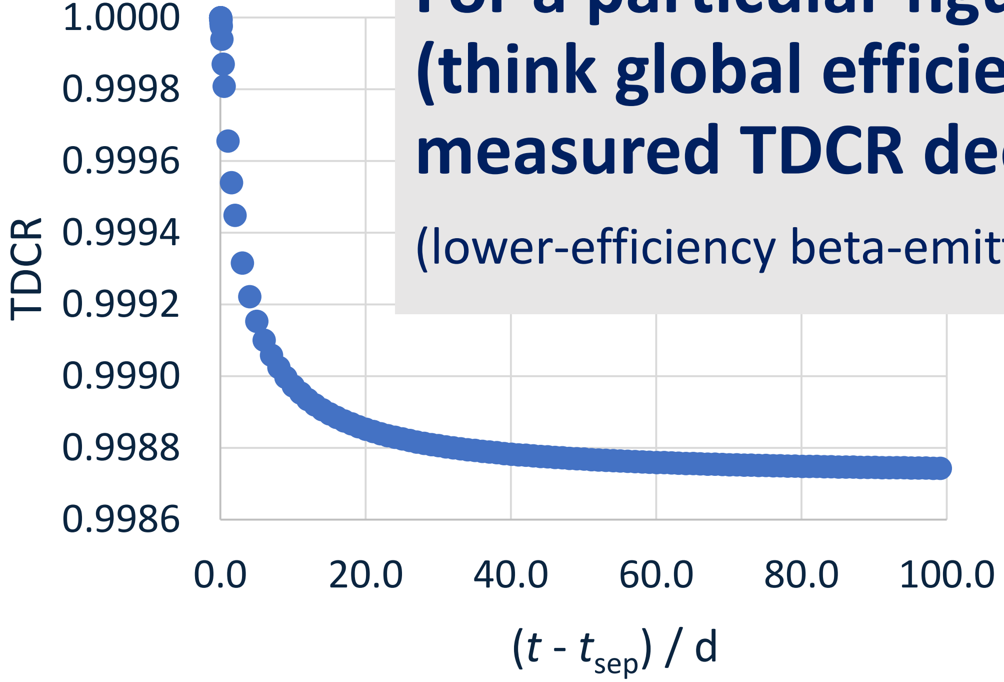
Calculate efficiencies for beta emissions with MICELLE2



Time evolution of LS efficiencies

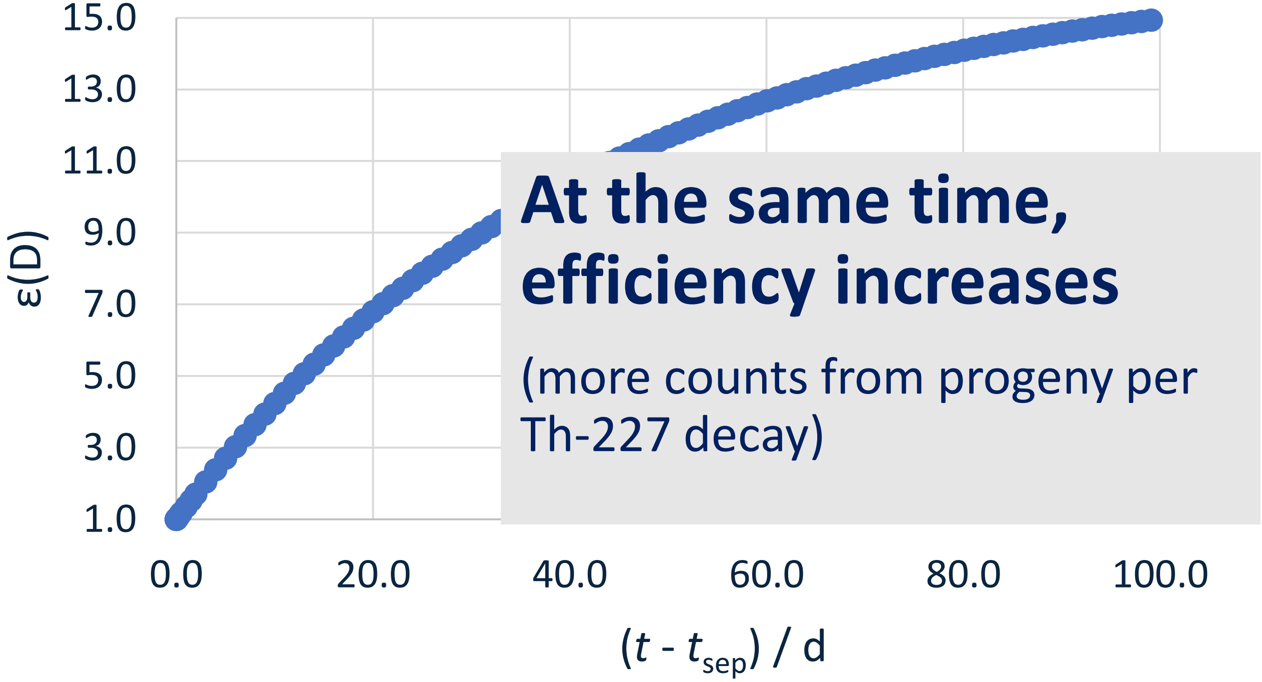
For a particular figure-of-merit (think global efficiency), the measured TDCR decreases with time

(lower-efficiency beta-emitting progeny grow in)

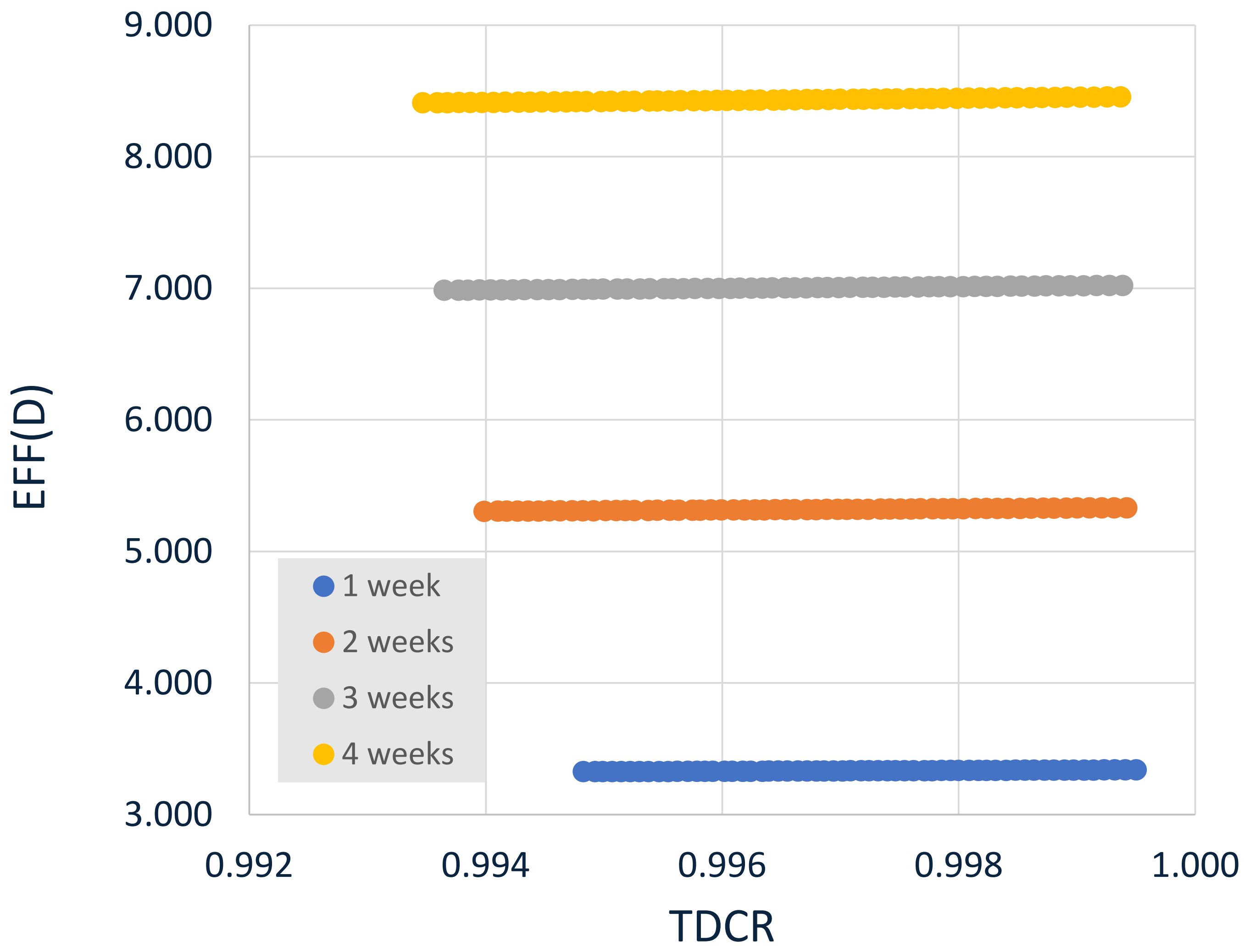


At the same time, efficiency increases

(more counts from progeny per Th-227 decay)

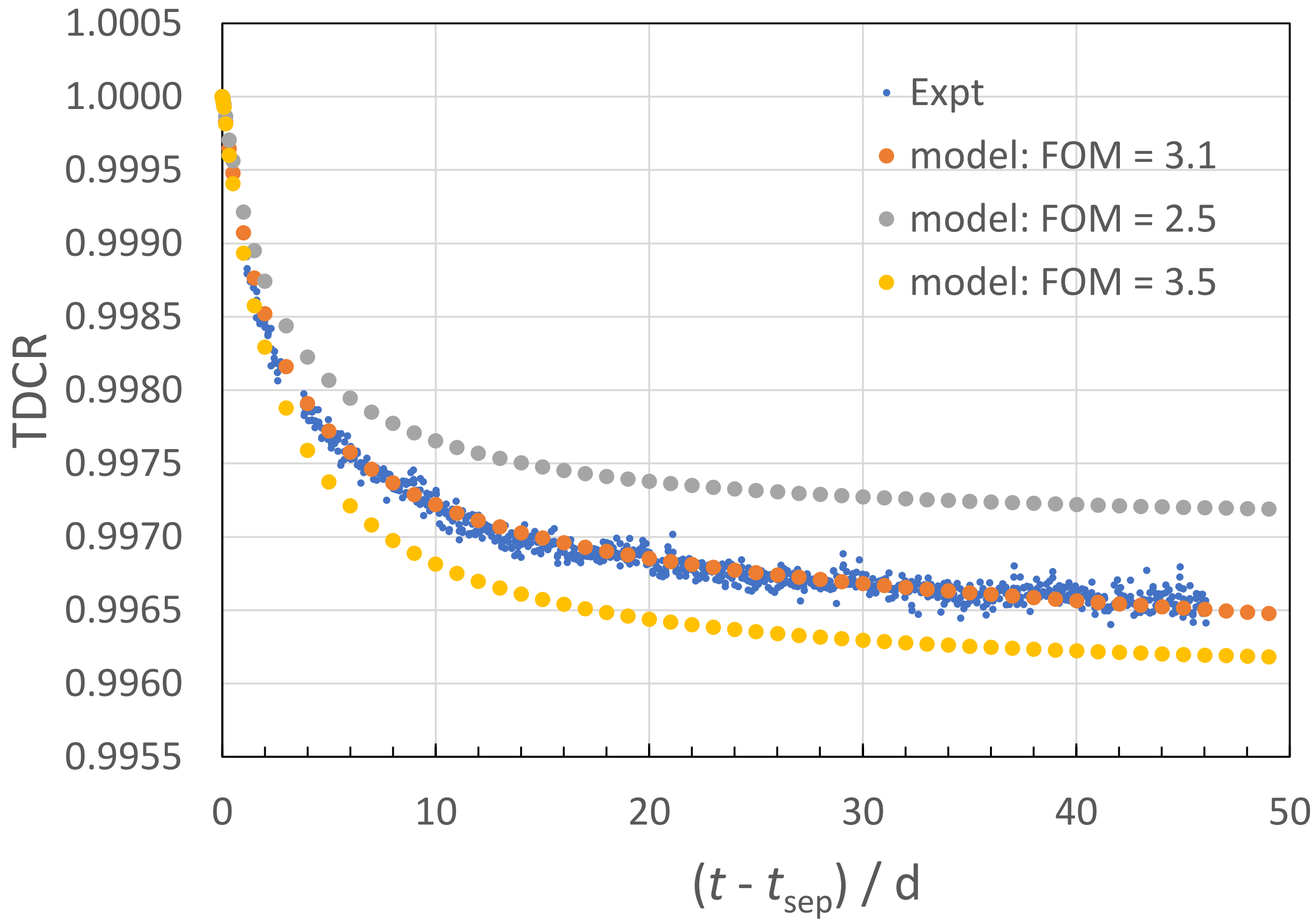


Time-dependent efficiency curves



So, for a given LS source, we predict the decrease in experimental TDCR and an increase in efficiency over time.

The single Figure-of-Merit model

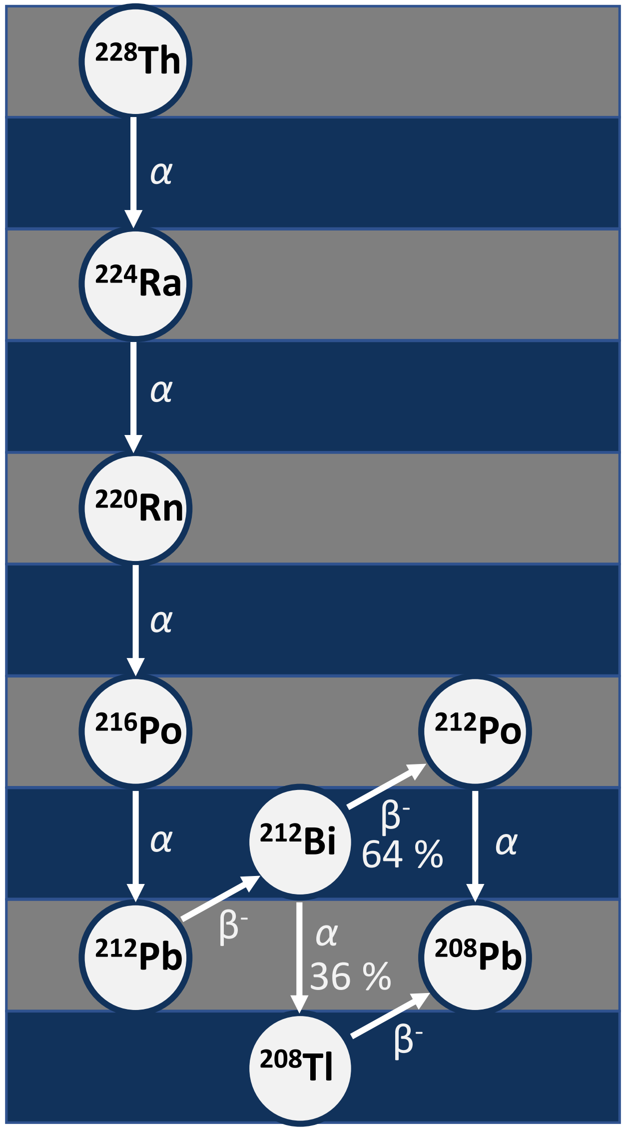


- **If we assume the LS source is stable, then the observed triple-to-double coincidence ratio is expected to change as the beta-emitting progeny grow in**
- **Our efficiency model tracks the ingrowth**
- **The slope of the curve is predicted by the counting efficiencies for the beta-emitters, so the free parameter (figure-of-merit) can be adjusted to fit the experimental data to the model**
- **Modeled efficiencies are then used to calculate activity**

Challenges in LS measurements for TAT

- **Decay chains**
  - ✓ Progeny include beta-emitters ($\varepsilon < 1$)
  - ✓ Progeny include short-lived nuclides
  - ✓ Pre-equilibrium measurements (changing $\varepsilon(t)$)
- **Impurities**
  - Breakthrough
  - Co-produced isotopes

The problem of breakthrough



In our ^{224}Ra standardization campaigns, ^{228}Th breakthrough was mostly insignificant. Except for the one time it wasn't.

t_{sep}	$f_{Th\text{-}228}$ at t_{sep}
9/14/2018	$(3.3 \pm 0.4) \times 10^{-6}$
11/2/2018	$(5.0 \pm 1.6) \times 10^{-6}$
2/8/2019	$(4.2 \pm 0.6) \times 10^{-6}$
4/22/2019	$(9.7 \pm 0.1) \times 10^{-4}$

See: https://doi.org/10.1021/scimeetings.0c01048
Bergeron et al., ARI 155, 108933 (2020).

'Negligible' breakthrough in the literature

NIST

Appl. Radiat. Isot. Vol. 39, No. 4, pp. 283–286, 1988
Int. J. Radiat. Appl. Instrum. Part A
Printed in Great Britain

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An Improved Generator for the Production of ^{212}Pb and ^{212}Bi from ^{224}Ra

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(Received 7 October 1987)

We have developed an improved generator for the production of the alpha emitting radionuclide ^{212}Bi and its parent, ^{212}Pb. These radionuclides are well suited to use as radiotherapeutic agents due to their relatively

the activity remains on the anion exchange resin. Breakthrough of the thorium in the radium solution is negligible, less than 1 ppm. Generators which have been returned to ANL decay with the half life of ^{224}Ra.

The yield of the generator as a function of HI

Received: 8 November 2017 | Revised: 16 December 2017 | Accepted: 17 January 2018
DOI: 10.1002/jlcr.3610

RESEARCH ARTICLE

WILEY Journal of Labelled Compounds and Radiopharmaceuticals

Ra-224 labeling of calcium carbonate microparticles for internal α-therapy: Preparation, stability, and biodistribution in mice

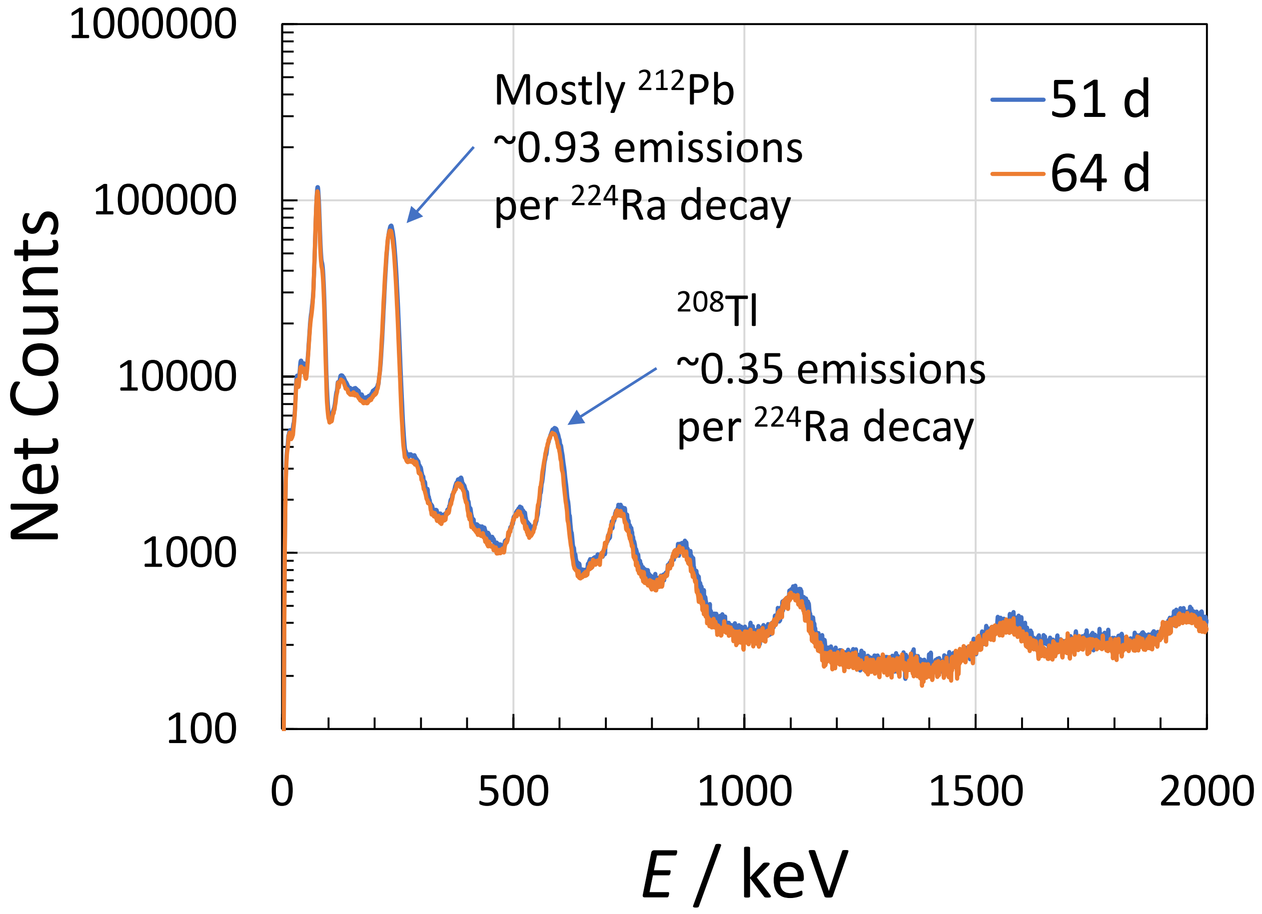
Sara Westrøm[1,2,3] | Marion Malenge[1] | Ida Sofie Jorstad[1] | Elisa Napoli[1,3,4] | Øyvind S. Bruland[1,3,5] | Tina B. Bønsdorff[1] | Roy H. Larsen[1]

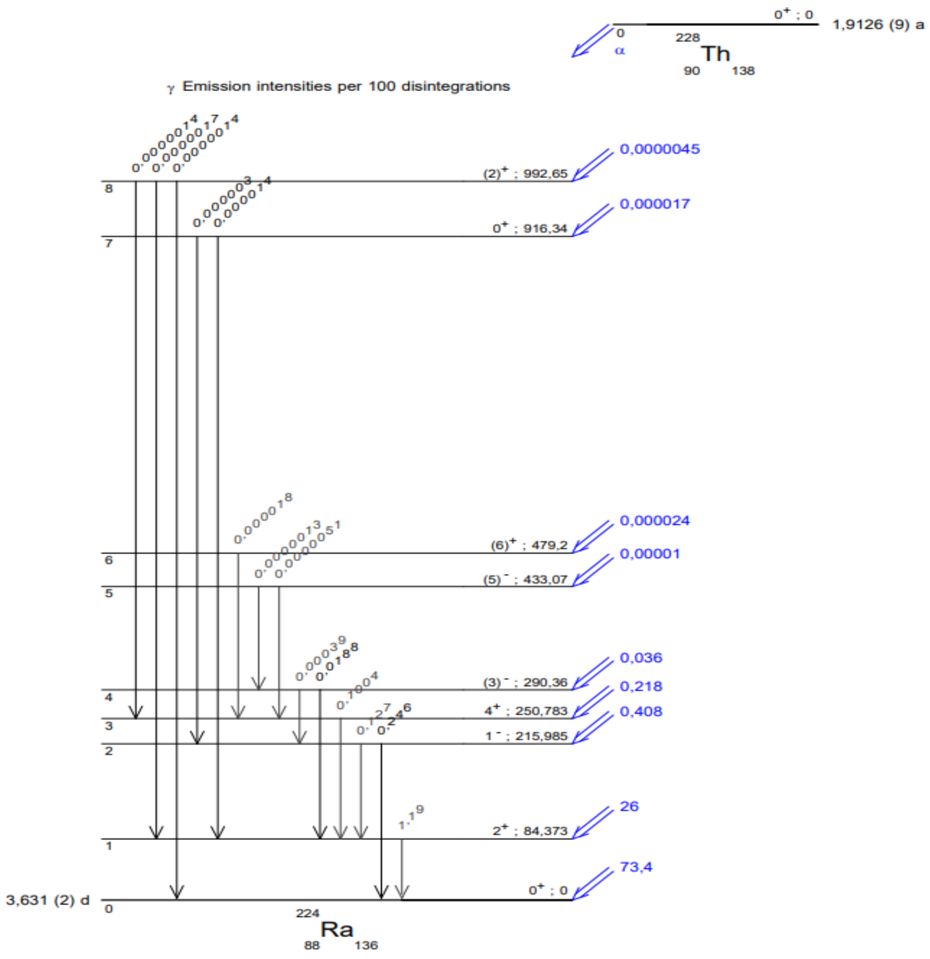
3.2 | Ra-224 generator performance

Breakthrough of the ^{228}Th parent was determined with α-spectroscopy to be less than or equal to 1.5×10^{-3} Bq/mL. This amount corresponds to less than 3×10^{-7} of the original ^{224}Ra activity. No ingrowth of ^{224}Ra from ^{228}Th was detected when half-life measurements with liquid scintillation were performed. Altogether, the results from these 2 analyses suggest that the quality of the prepared ^{224}Ra solution was satisfactory.

NaI(Tl) won't see ^{228}Th in spectrum

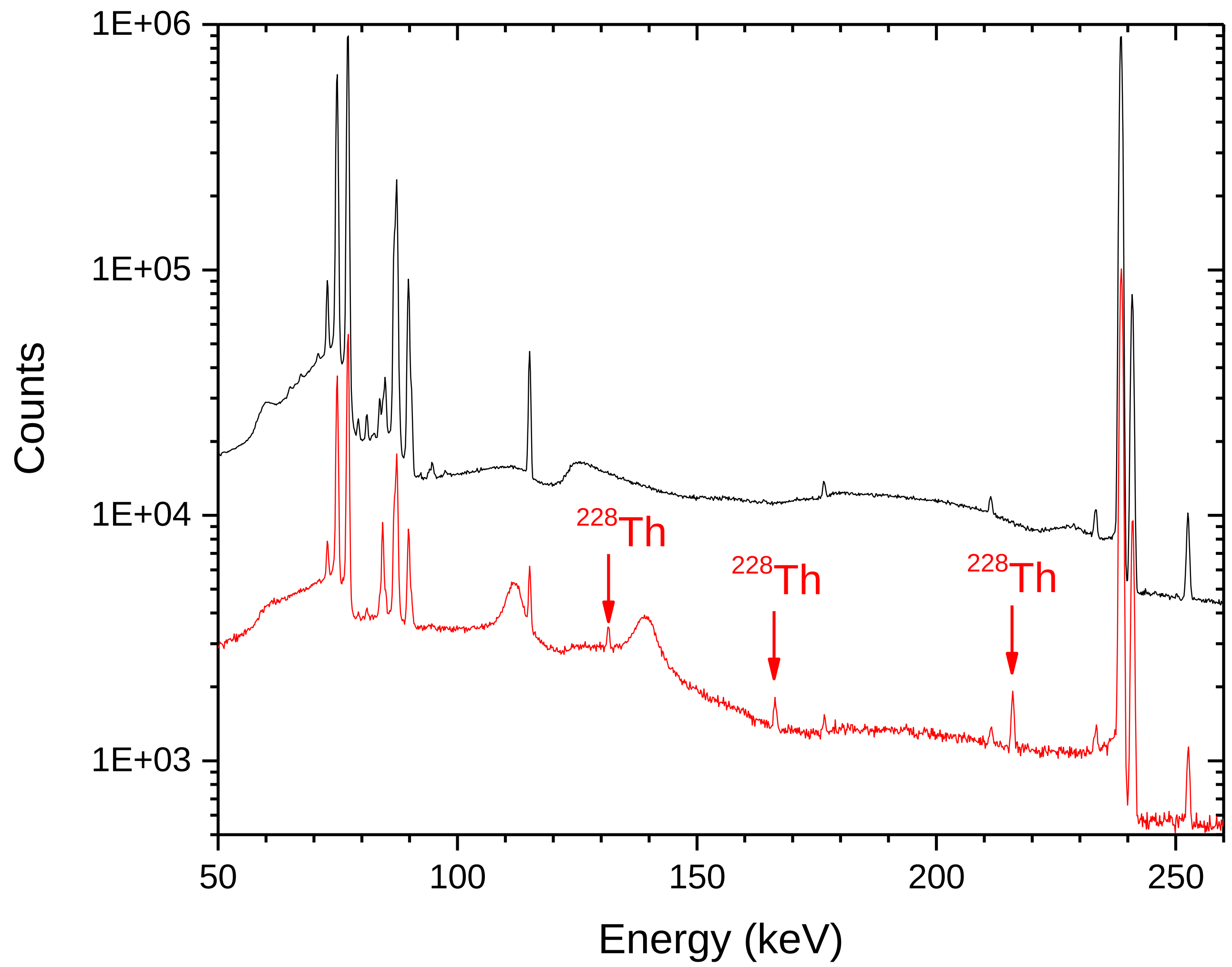
^{228}Th decays mostly to the ground state of ^{224}Ra





http://www.lnhb.fr/nuclides/Th-228_tables.pdf

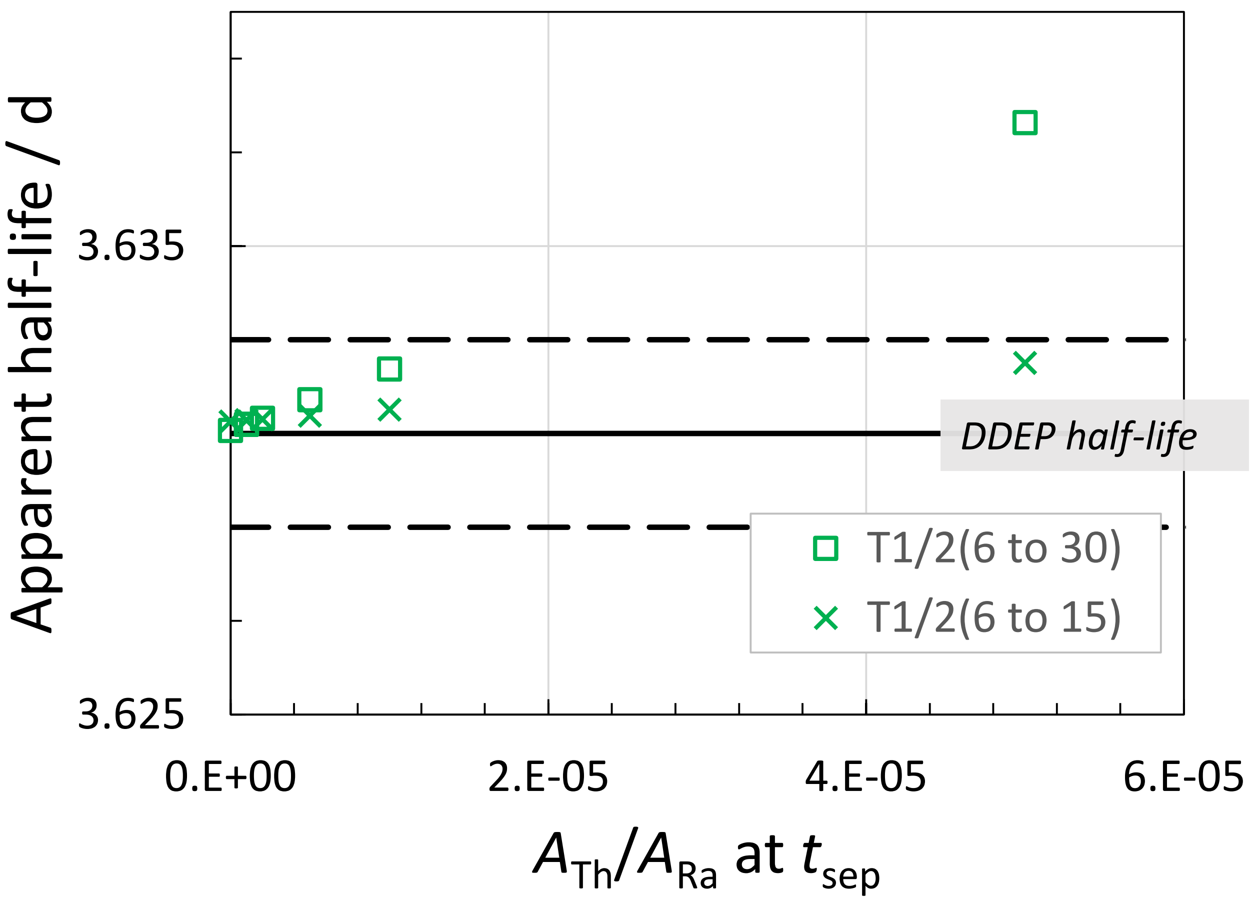
HPGe detection of ^{228}Th faces challenges



The resolution of HPGe allows identification of the weak γ-ray peaks from ^{228}Th decay

Minimum detectable activities at early times are high, due to the Compton background from ^{224}Ra and its progeny

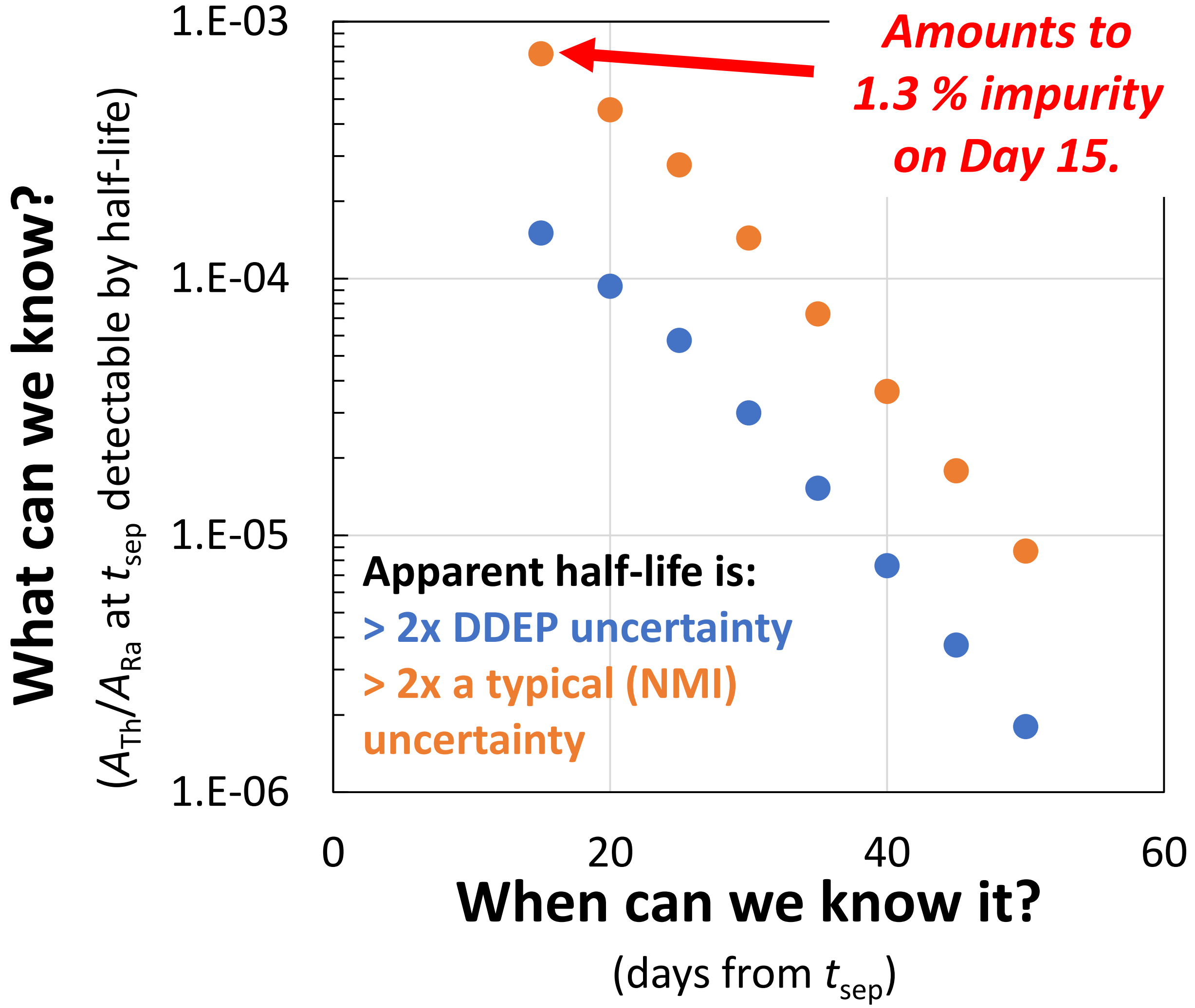
Can half-life detect < 1 ppm ^{228}Th?



Half-lives determined with pre-equilibration data require more complicated fitting

Half-lives determined with post-equilibration (> 6 d past t_{sep}) data are fairly robust against ^{228}Th breakthrough

Plotting what v. when

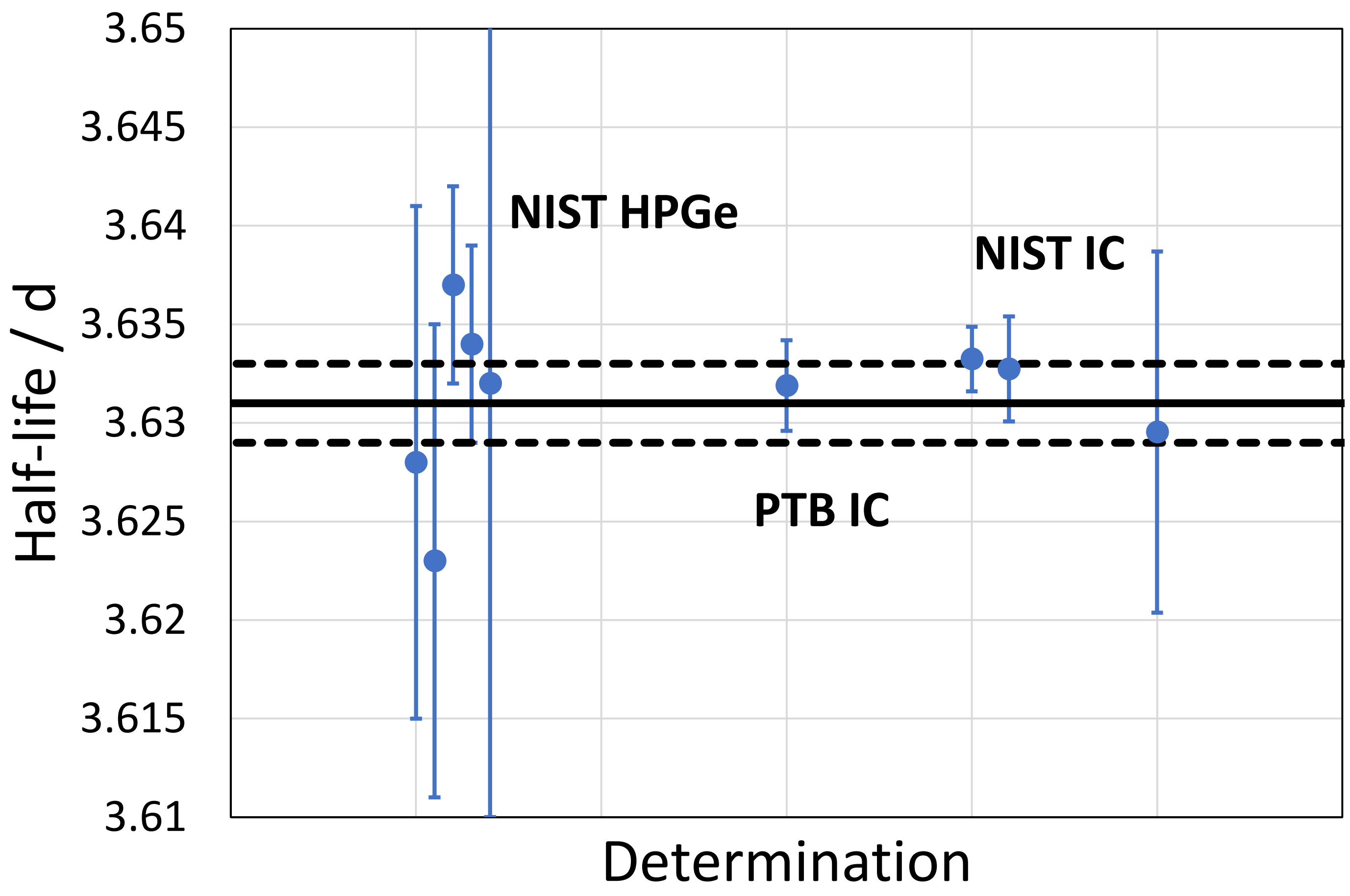


Monitoring half-life can provide sensitivity to ppm-level ^{228}Th breakthrough…

….if you can distinguish a deviation of 2σ from the evaluated half-life (i.e., you're the ***best in the world*** *at measuring half-lives)*

…and you measure until 50 days post-separation

Nobody's that good!

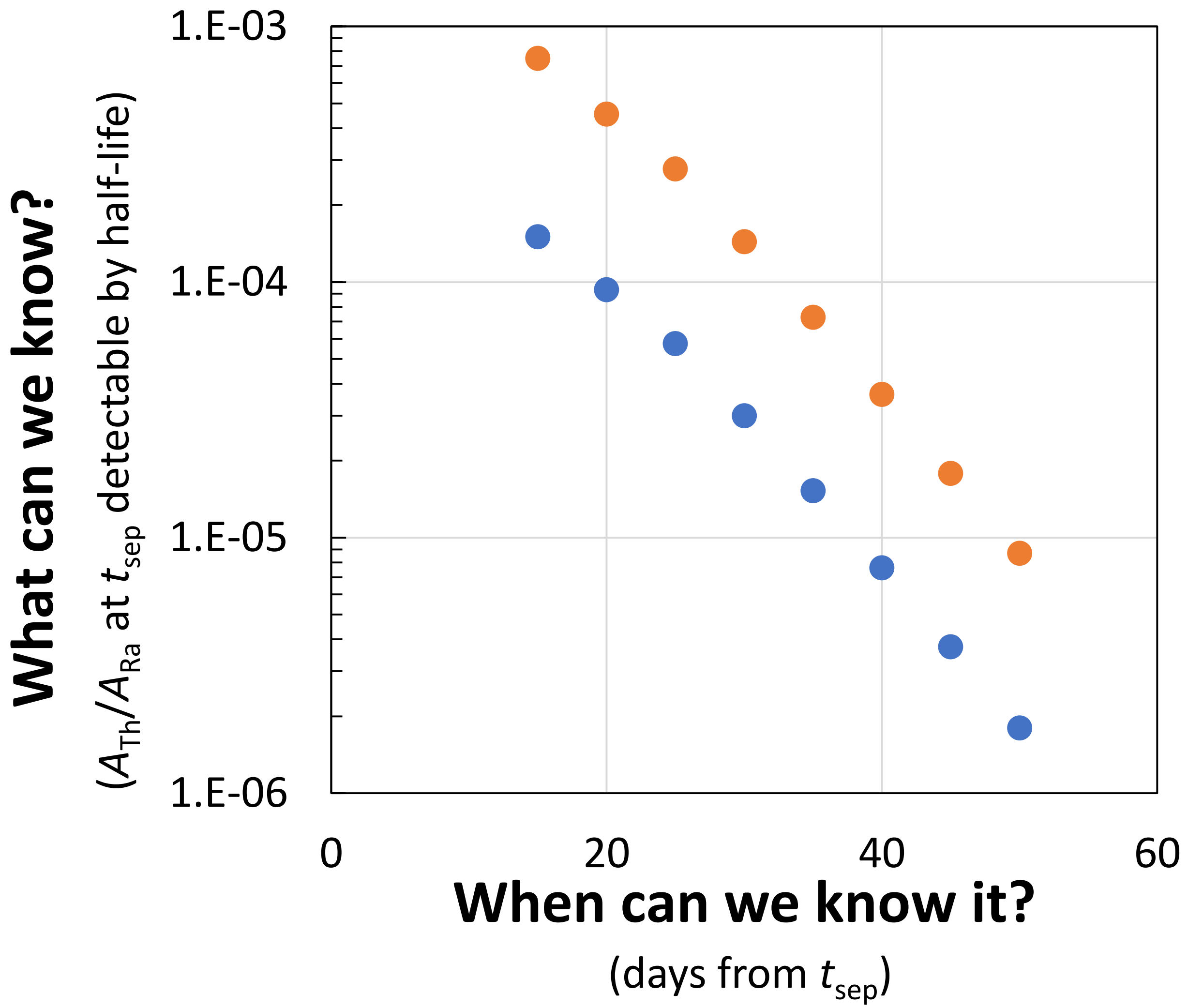


Data are being considered for a new half-life evaluation (DDEP*)

There is spread in the dataset, and estimated uncertainties vary

*http://www.lnhb.fr/nuclear-data/nuclear-data-table/
Bergeron et al., ARI 170, 109572 (2021).

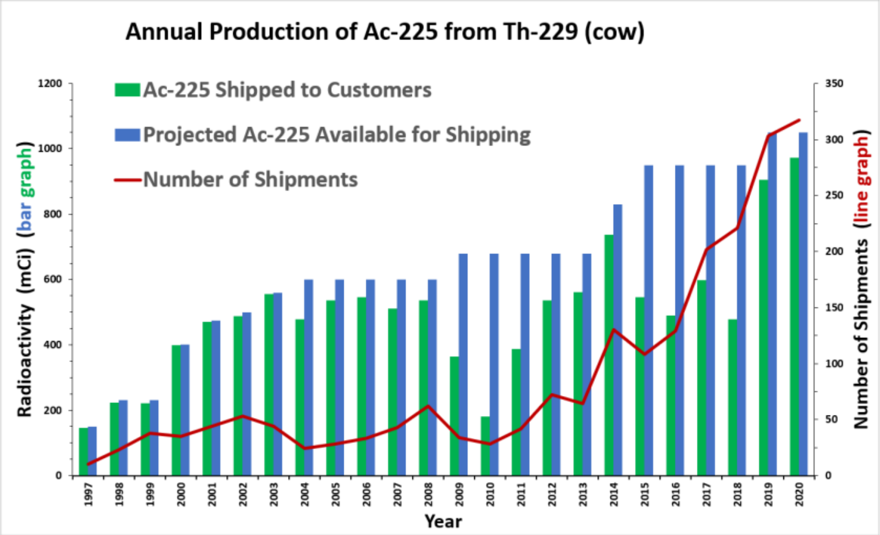
So, catching breakthrough is a challenge



Gamma-ray spectrometry and half-life cannot provide an early measure of ^{228}Th breakthrough in ^{224}Ra

This is a problem for any column-produced TAT nuclide (e.g., ^{212}Pb from ^{224}Ra, ^{225}Ac from ^{229}Th)

Other impurities are tricky, too



https://www.fda.gov/media/152472/download

From the 2021 FDA-NRC Workshop on Ac-225.

Along with breakthrough for column-produced materials, there is serious concern right now about co-produced isotopes that cannot be easily separated

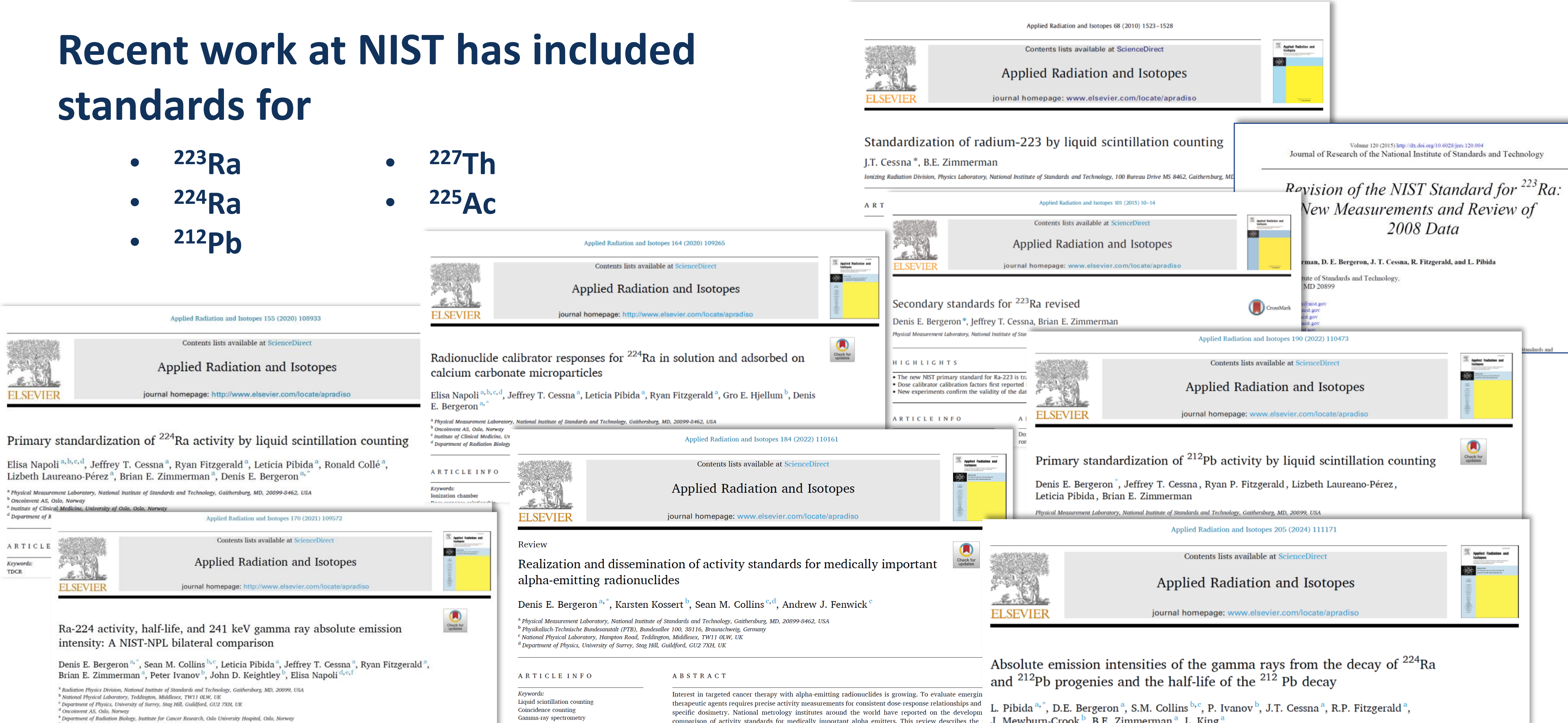
The ^{227}Ac impurity in accelerator-produced ^{225}Ac has regulators concerned with licensing

It's not the dose to patients that's the concern; it's the occupational exposure to workers and the disposal questions. (Similar issues have come up with ^{177m}Lu impurities in ^{177}Lu radiopharmaceuticals.)

Recently standardized alpha-emitters (NIST) NIST

Recent work at NIST has included standards for

- ^{223}Ra
- ^{224}Ra
- ^{212}Pb
- ^{227}Th
- ^{225}Ac



Recently standardized alpha-emitters (NIST) NIST

Recent work at NIST has included

Applied Radiation and Isotopes 68 (2010) 1523–1528
Contents lists available at ScienceDirect

Table 2
TDCR ^{212}Pb massic activity uncertainty budget.

Uncertainty Component	u/% E1	u/% E2
Counting statistics (within and between insertions)	0.11	0.11
Model uncertainty (efficiency variation); estimated as the typical standard deviation on measurements of a source with (N = 3) different gray filters	0.05	0.08
Between sources; estimated as the standard deviation on the activity concentration obtained with (N = 3) LS sources	0.09	0.03
Background	2E-05	4E-05
Pb-212 half-life; propagation of the standard uncertainty on the half-life for ^{212}Pb (DDEP: 10.64(1) h)	0.002	0.005
Nuclear decay data: estimated uncertainty due to the half-lives and branching ratios of ^{212}Pb and its progeny at equilibrium predicted by the Bateman Equation (dominated by the uncertainty on the ^{212}Bi decay branching ratio); uncertainty due to beta shape and endpoint uncertainties; uncertainty due to missed coincidences in the ^{212}Bi+^{212}Po decay	0.12	0.11
Efficiency Model (quenching model); propagation of an estimated uncertainty on the Birks parameter (kB = 0.0075(15) MeV/cm)	0.03	0.03
Mass determinations	0.05	0.05
Combined standard uncertainty	**0.20**	**0.18**

ARTICLE
Keywords:
TDCR

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journal homepage: http://www.elsevier.com/locate/apradiso

Ra-224 activity, half-life, and 241 keV gamma ray absolute emission intensity: A NIST-NPL bilateral comparison

Denis E. Bergeron[a,*], Sean M. Collins[b,c], Leticia Pibida[a], Jeffrey T. Cessna[a], Ryan Fitzgerald[a], Brian E. Zimmerman[a], Peter Ivanov[b], John D. Keightley[b], Elisa Napoli[d,e,f]
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Review

Realization and dissemination of activity standards for medically important alpha-emitting radionuclides

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ARTICLE INFO
Keywords:
Liquid scintillation counting
Coincidence counting
Gamma-ray spectrometry

ABSTRACT
Interest in targeted cancer therapy with alpha-emitting radionuclides is growing. To evaluate emergin
therapeutic agents requires precise activity measurements for consistent dose-response relationships and
specific dosimetry. National metrology institutes around the world have reported on the developm
comparison of activity standards for medically important alpha emitters. This review describes the

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Absolute emission intensities of the gamma rays from the decay of ^{224}Ra and ^{212}Pb progenies and the half-life of the ^{212}Pb decay

L. Pibida[a,*], D.E. Bergeron[a], S.M. Collins[b,c], P. Ivanov[b], J.T. Cessna[a], R.P. Fitzgerald[a], J. Mewburn-Crook[b], B.E. Zimmerman[a], L. King[a]

Recently standardized alpha-emitters (NIST)

	u_c / %
^{223}Ra	0.21
^{224}Ra	0.31
^{212}Pb	0.23
^{227}Th	0.30 to 0.45
^{225}Ac	0.27

- **Preliminary (unpublished) results in red**
- **Uncertainties on ^{227}Th activity calibrations vary with time**

Disseminating the becquerel

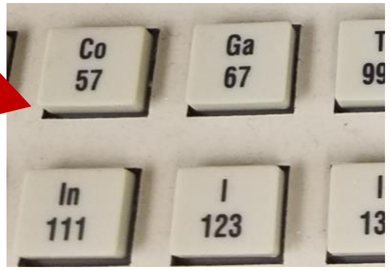
Bq

Decays per second (of a radionuclide)

Using liquid-scintillation-based primary methods, NMIs have developed standards for a (growing) list of alpha emitters for TAT

Dissemination of these standards proceeds by different paths

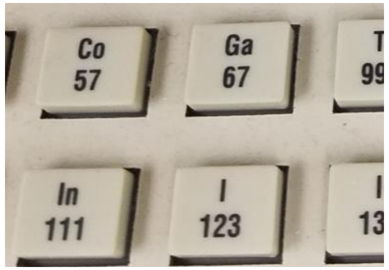
I_γ



End-user measurements

In most cases, producers and end-users measure activity via

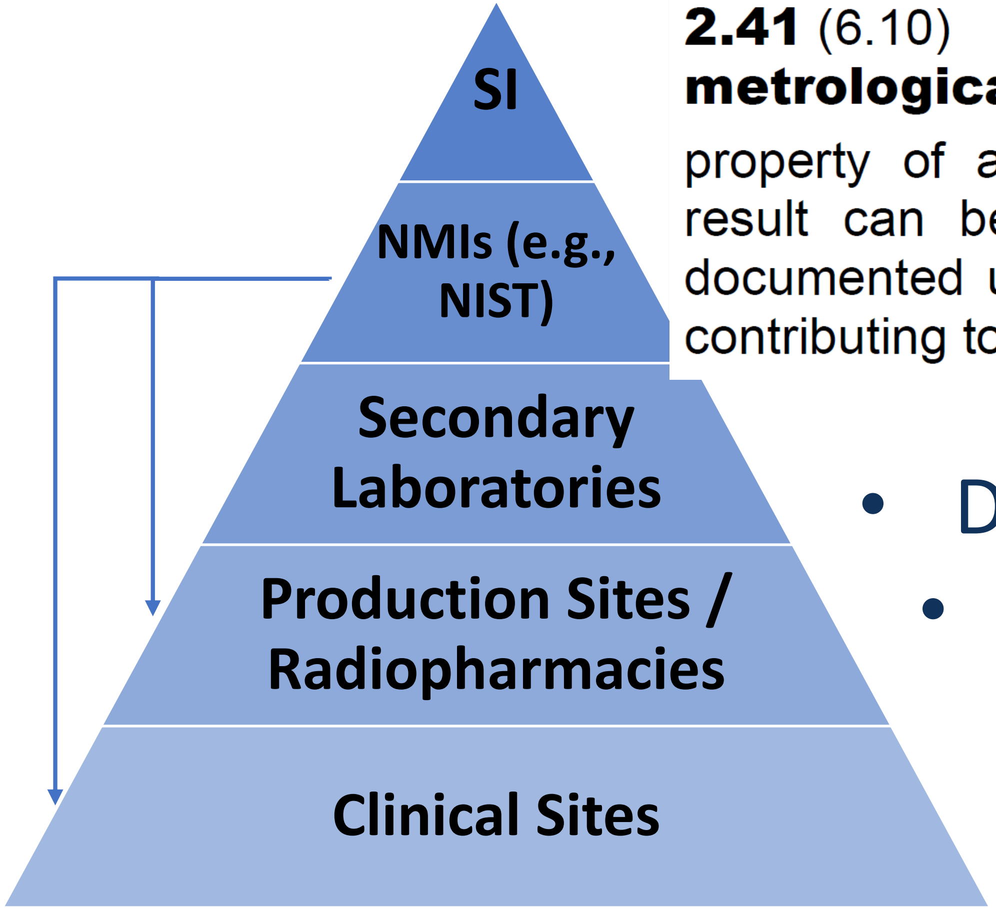
- Radionuclide calibrator (reentrant well-type ionization chamber)



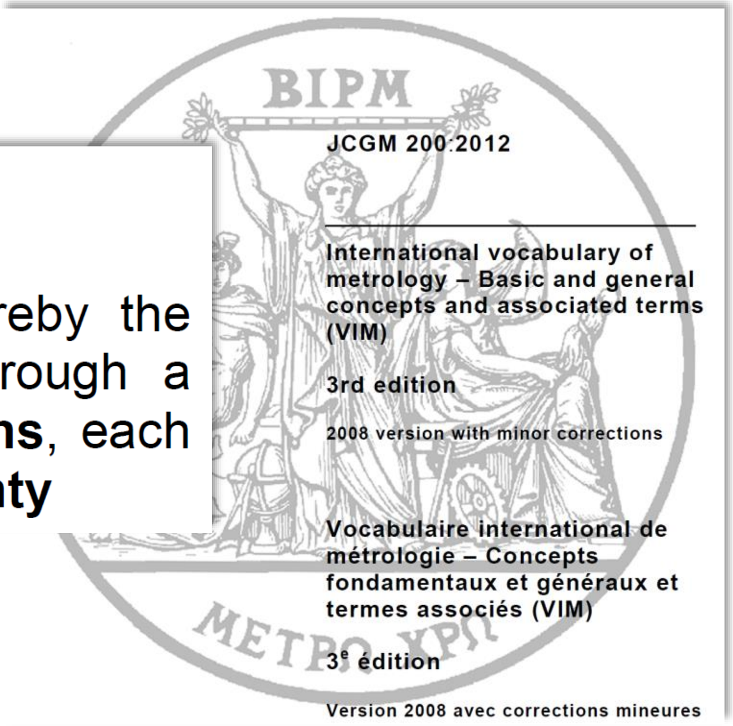
- Gamma-ray spectrometry

I_γ

Traceability and Primary Standards for Alpha Emitters used in TAT



2.41 (6.10)
metrological traceability
property of a **measurement result** whereby the result can be related to a reference through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty**

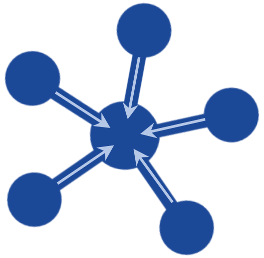


- Direct calibration
  - Benchmark calibration factors/settings
    - Decay data

Direct calibration

NIST

- **Submit source to calibration lab**
  - Certification of massic activity
  - Local calibrations can be adjusted based on results

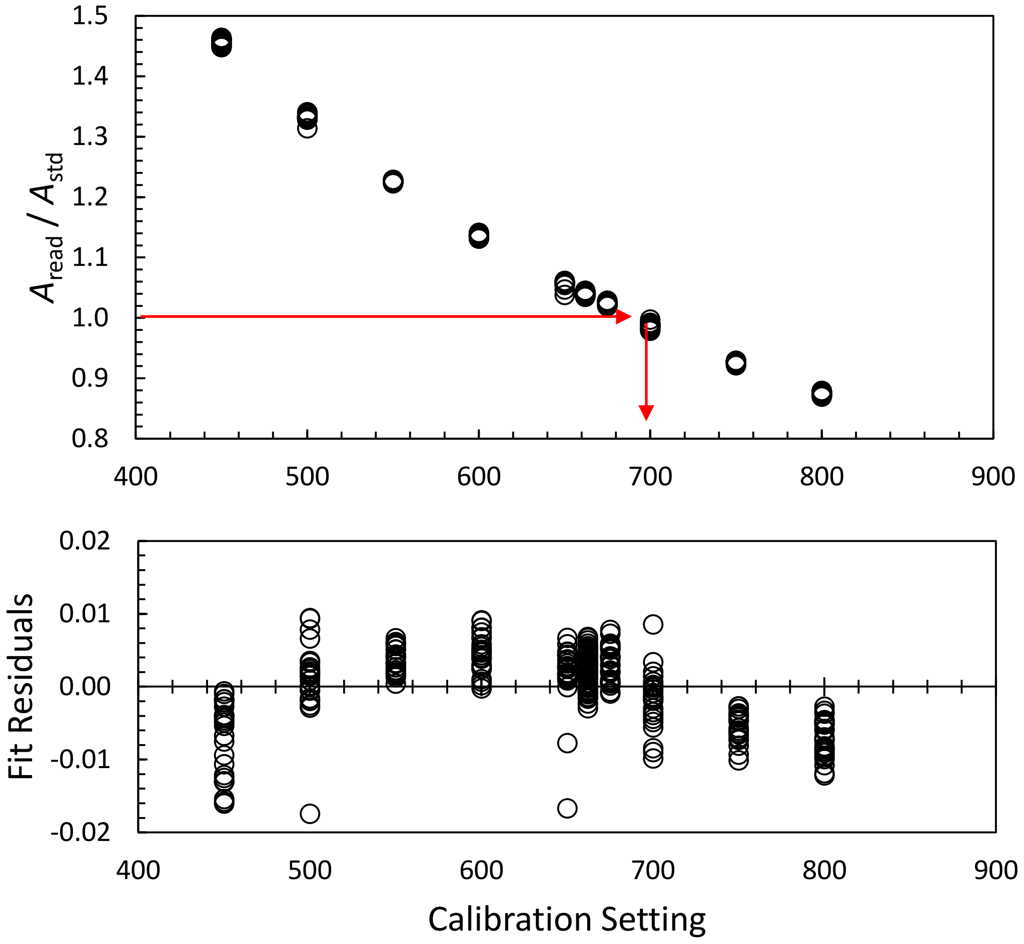


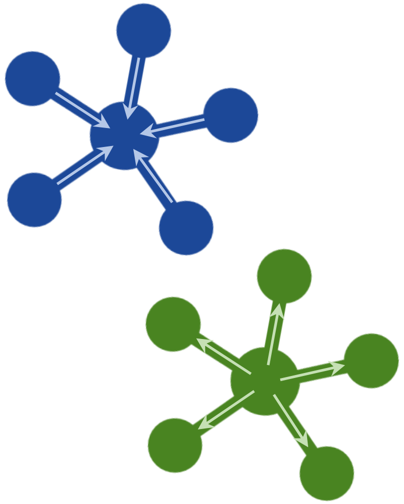
- **Receive calibrated source**
  - Certified for massic activity and total activity
  - Local calibrations can be performed with received source

https://www.nist.gov/calibrations

Contact: jeffrey.cessna@nist.gov

The calibration curve

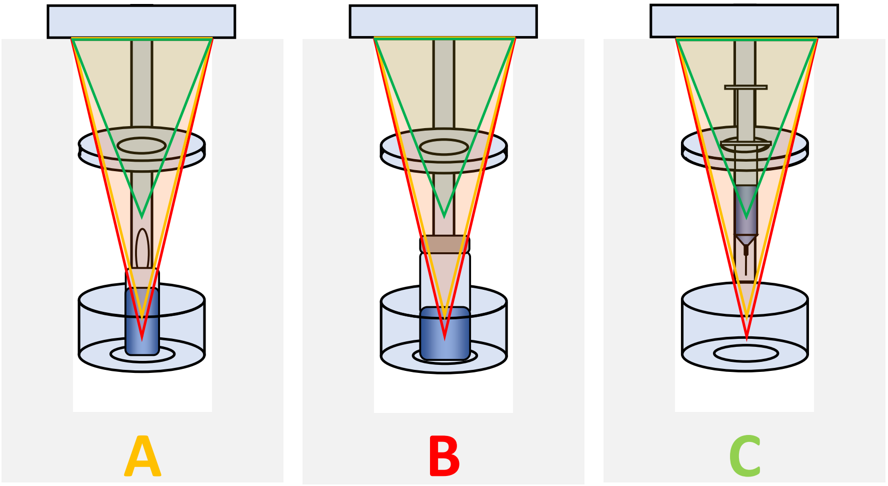




- **The calibration curve approach can be used whether the standard activity (A_{std}) of the calibration source is known at the time of measurement or not**
- **The uncertainty on A_{std} is combined with the uncertainty on A_{read} (including fit, decay correction, etc.) to determine the uncertainty on any activity measured with the determined calibration setting**
- **"Dialing in" is also possible if A_{std} is known**

Practical considerations for calibrations

- **Geometry matters: the calibration geometry should match the measurement geometry**
- **Benchmark settings: may come from instrument manufacturer or literature – should be verified for specific instrument**



- **Traceable calibration means a "*documented unbroken chain of calibrations*"**
  - Using a calibration setting from a NIST (or NPL…) publication does not make a measurement "NIST-traceable"

Pictures from biodex.com, capintec.com

Pb-212 radionuclide calibrator settings

NIST

^{207}Bi	Bismuth	846		1.7	38 Y	NBS73	Ref. for 1064, 569.7, 76.7, 1772 keV
^{208}Tl	Thallium	571÷2			3.07 M	NM75	
^{212}Pb	Lead	101			10.6 H	NM75	Decays to ^{212}Bi; eqb. after 1 hr. See App. II.
^{212}Bi	Bismuth	489×10			60.5 M	NM75	
^{212}Pb (Eqb. ^{212}Bi)	Lead	158					Eqb. after 8 hrs. Reading gives Act. of Pb in eqb. sample.
^{212}Bi (Eqb. ^{212}Pb)	Bismuth	135					Reading gives Act. of Bi in eqb. sample.
^{212}Pb / ^{212}Bi Eqb.	Lead, / Bismuth	030 or 146×2					Reading gives Total Act. of Pb & Bi in eqb. sample.
^{224}Ra	Radium	646×100			3.64 D	NM75	
^{226}Ra	Radium	778		0.5	1622 Y	NBS73	Reading in grams. Com-

Capintec Inc, 1986. Radionuclide Calibrator Owner's Manual, Revision E. Ramsey. Capintec Inc, NJ.

Pb-212 radionuclide calibrator settings

^{207}Bi	Bismuth	846		1.7	38 Y	NBS73	Ref. for 1064, 569.7, 76.7,
^{208}Tl	Thallium	571÷2					
^{212}Pb	Lead	101					
^{212}Bi	Bismuth	489×10					
^{212}Pb	Lead (Eqb. ^{212}Bi)	158					
^{212}Bi	Bismuth (Eqb. ^{212}Pb)	135					eqb. sample.
^{212}Pb / ^{212}Bi Eqb.	Lead, / Bismuth	030 or 146×2					Reading gives Total Act. of Pb & Bi in eqb. sample.
^{224}Ra	Radium	646×100			3.64 D	NM75	
^{226}Ra	Radium	778		0.5	1622 Y	NBS73	Reading in grams. Com-

nuclide in isolation and as m2 when in equilibri…

IC model	^{212}Pb			
	DS	u_c/%	u_A/%	m…
CRC-55tR	662	5.7	3.4	10…
CRC-25R	662	5.7	3.4	

Napoli et al., ARI 166, 109362 (2020).

Capintec Inc, 1986. Radionuclide Calibrator Owner's Manual, Revision E. Ramsey. Capintec Inc, NJ.

Pb-212 radionuclide calibrator settings

Seems Capintec settings neglect progeny beyond ^{212}Bi

The 2.6 MeV γ-ray from ^{208}Tl accounts for much of the overall ionization chamber response to ^{212}Pb and its progeny

For decay chain nuclides especially, users should take care when referencing theoretically-determined radionuclide calibrator settings

DS	A_{read} / A_{TDCR}	Note
101	4.20	DS given in manual for ^{212}Pb in isolation.
158	3.23	DS given in manual for ^{212}Pb in equilibrium with ^{212}Bi.
30	6.83	DS given in manual for sum of ^{212}Pb and ^{212}Bi activity
146	3.40	DS given in manual for sum of ^{212}Pb and ^{212}Bi activity (to be multiplied by 2)
571	1.18	DS given in manual for ^{208}Tl (to be divided by 2)
662	1.04	DS reported by Napoli et al. for ^{212}Pb

Settings can result in 3.2x to 6.8x errors.

Capintec Inc, 1986. Radionuclide Calibrator Owner's Manual, Revision E. Ramsey. Capintec Inc, NJ.

Pb-212 radionuclide calibrator settings

Table 8

Dial settings (*DS*) determined by the calibration curve method to give the correct ^{212}Pb activity for 5 mL of a 1 mol/L HCl solution of ^{212}Pb in equilibrium with its progeny in a NIST standard 5 mL flame sealed ampoule. Uncertainties on the dial settings, in dial setting units, are given in parentheses and are expanded ($k = 2$) uncertainties. The resulting relative expanded uncertainty on the measured activity (U_A) is given in the last row.

	CRC-15R	CRC-35R	CRC-55tR	CRC-25PET	CRC-55tPET
DS_{TDCR}	690(4)	693(3)	688(4)	696(3)	685(3)
U_A/%	0.45	0.41	0.49	0.38	0.37

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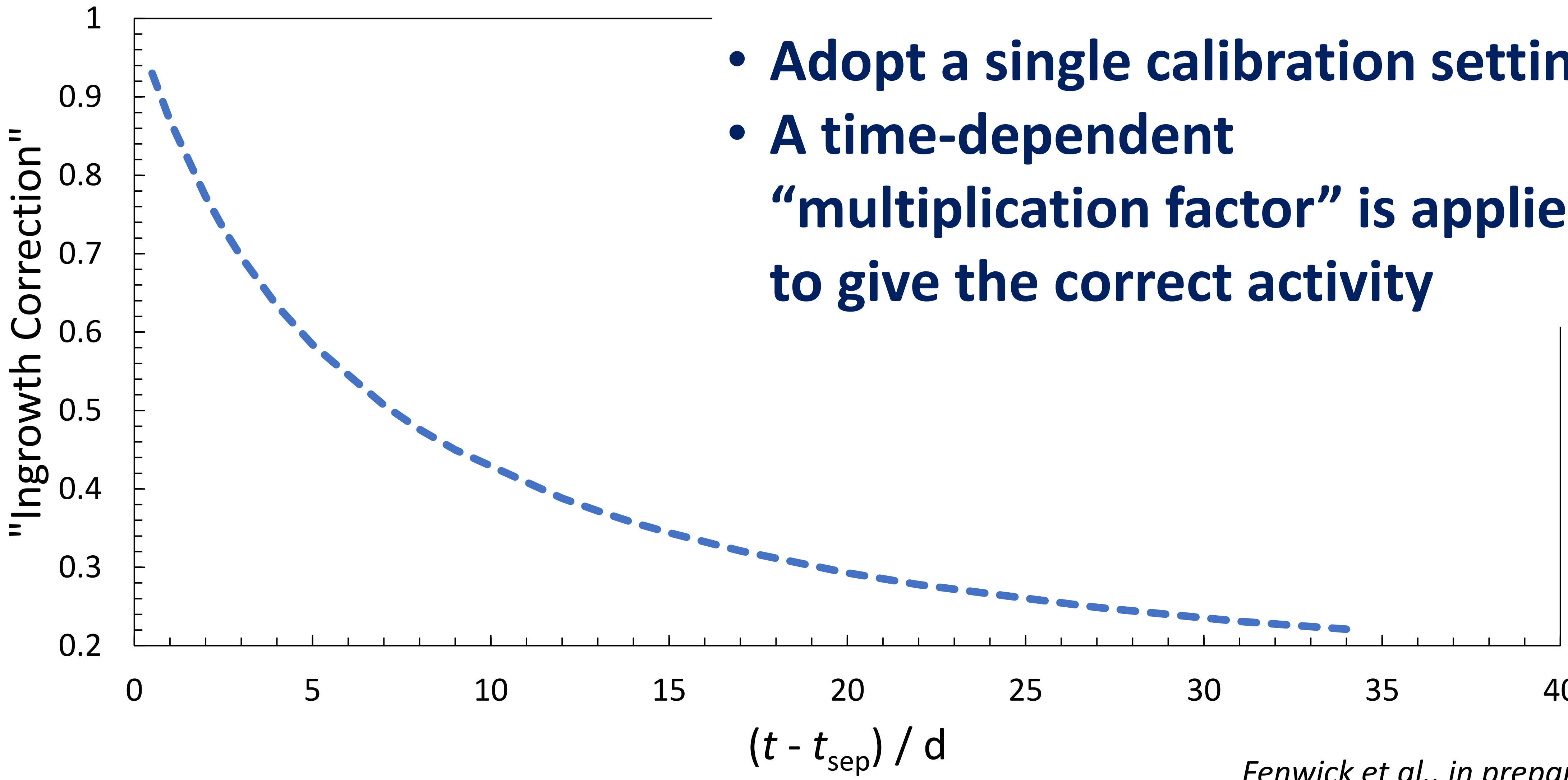
^{224}Ra	Radium	646×100	
^{226}Ra	Radium	778	0.5

3.2x to 6.8x errors.

Capintec Inc, 1986. Radionuclide Calibrator Owner's Manual, Revision E. Ramsey. Capintec Inc, NJ.

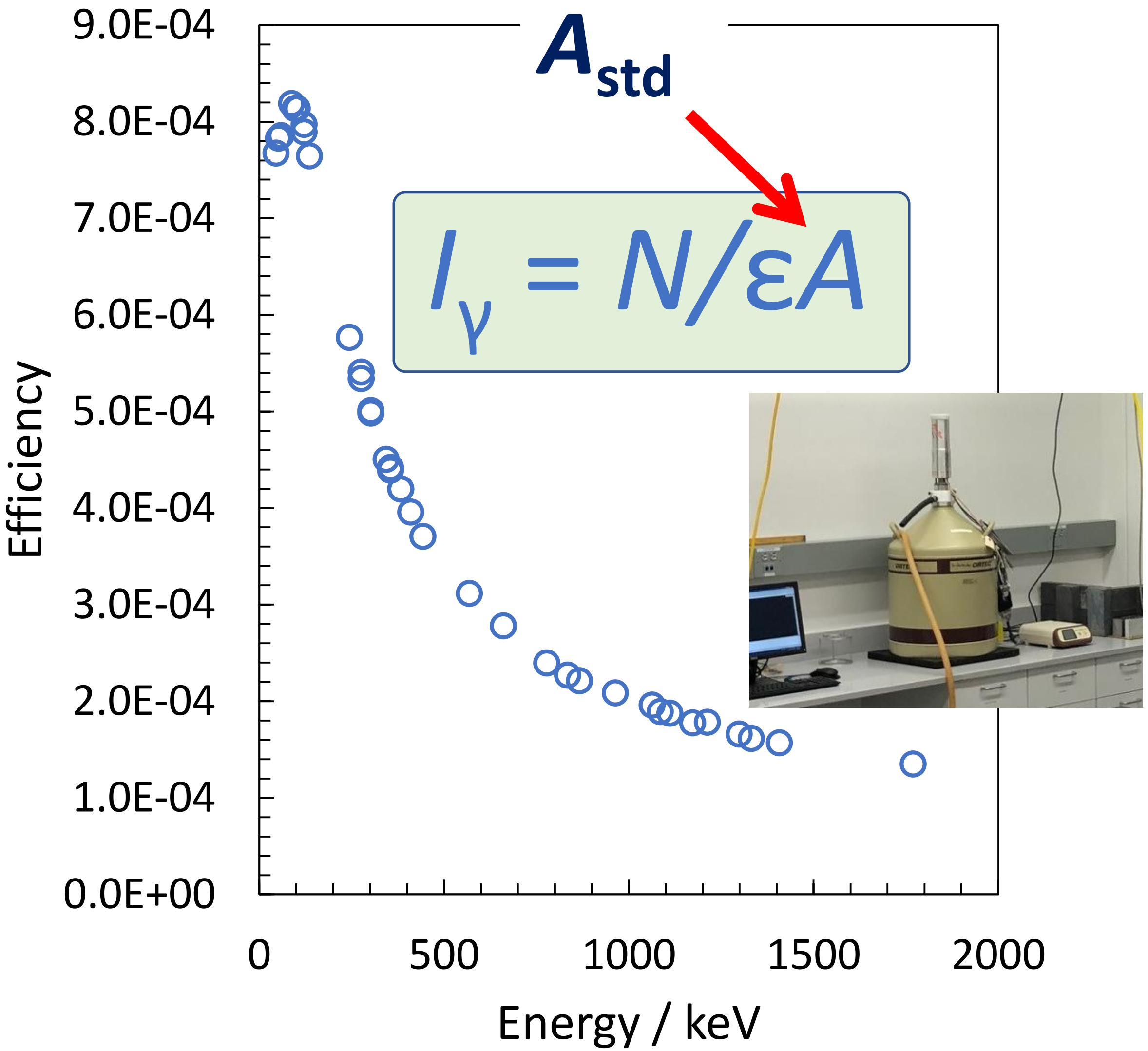
Pre-equilibrium calibrations (e.g., ^{227}Th)



- **Adopt a single calibration setting**
- **A time-dependent "multiplication factor" is applied to give the correct activity**

Fenwick et al., in preparation.

Standards dissemination via decay data



- **Determination of absolute gamma-ray emission intensities (I_γ) supports calibrations via gamma-ray spectrometry**
  - Opportunities to improve evaluated decay data
  - Benchmarks to compare calibrations/standards
- **Here again, traceable calibration means a *"documented unbroken chain of calibrations"***

Re-evaluated data impact calibrations

NIST

Table 2

Relative deviation of the absolute gamma-ray emission intensities determined by Pibida et al. (2015), Collins et al. (2015a), Kossert et al. (2015b), Marouli et al. (2019) and Simões et al. (2021) to the evaluated intensities by the DDEP for the main gamma rays of ^{223}Ra and progeny. The reduced χ^2 for these new determinations is also shown.

Energy /keV	Radionuclide	DDEP (Bé et al., 2011) $/I_\gamma$	Pibida et al. (2015) $(I_{ref}/I_{DDEP})/\%$	Collins et al. (2015a)	Kossert et al. (2015b)	Marouli et al. (2019)	Simões et al. (2021)	$\chi^2/(\nu\text{-}1)$
122.3	^{223}Ra	1.238(19)	5.0	6.0	5.3	12.3	−1.0	2.1
144.3	^{223}Ra	3.36(8)	4.5	3.6	3.2	10.4	−1.2	2.7
154.2	^{223}Ra	5.84(13)	4.1	3.1	3.3	10.1	−0.2	2.5
269.5	^{223}Ra	14.23(32)	−7.0	−6.0	−7.5	−0.9	−1.5	5.9
271.2	^{219}Rn	11.07(22)	−3.4	−2.9	−1.8	2.1	−4.0	1.1
323.9	^{223}Ra	4.06(8)	−10.6	−10.0	−9.8	−5.2	−6.2	2.4
338.3	^{223}Ra	2.85(6)	−9.1	−8.6	−8.3	−3.2	0.0	6.6
351.0	^{211}Bi	13.00(19)	0.9	1.3	1.9	6.9	3.62	1.2
401.8	^{219}Rn	6.75(22)	−2.8	−2.7	−1.9	3.4	−2.1	0.9
404.8	^{211}Pb	3.83(6)	4.7	4.7	5.7	9.7	10.2	0.9
427.2	^{211}Pb	1.81(4)	4.4	4.4	5.6	8.3	0.0	1.8
445.0	^{223}Ra	1.28(4)	−4.9	−4.8	−4.5	0.0	0.8	0.6
832.0	^{211}Pb	3.5(5)	−0.6	−1.5	−2.0	6.3	0.6	1.8

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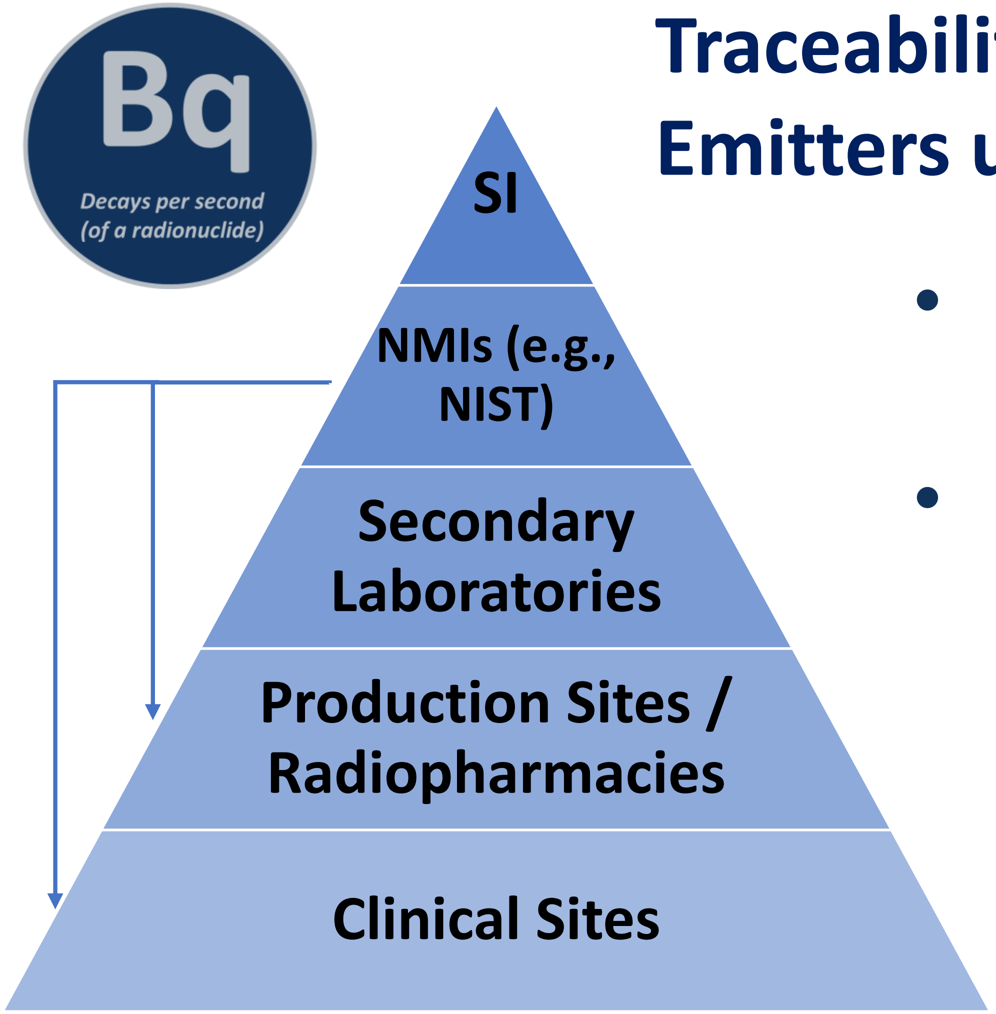
Summary and conclusions



Traceability and Primary Standards for Alpha Emitters used in TAT

- Primary standards from NMIs – 'realizing the becquerel'
- Traceability can be achieved through direct calibration or through a chain
  - Each link in the chain introduces uncertainty

Thanks to

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Collaborators: Elisa Napoli, Gro Hjellum (Oncoinvent, AS); Seán Collins, Andy Fenwick, Peter Ivanov, John Keightley (NPL); Karsten Kossert (PTB); Sean Jollota, Larry DeWerd (U. Wisconsin)

Ask me about opportunities to join our team at NIST!