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Remotely-prepared $^{212}Pb/^{212}Bi$ generator columns: Process overview & early performance evaluation

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U.S. DEPARTMENT OF ENERGY BATTELLE
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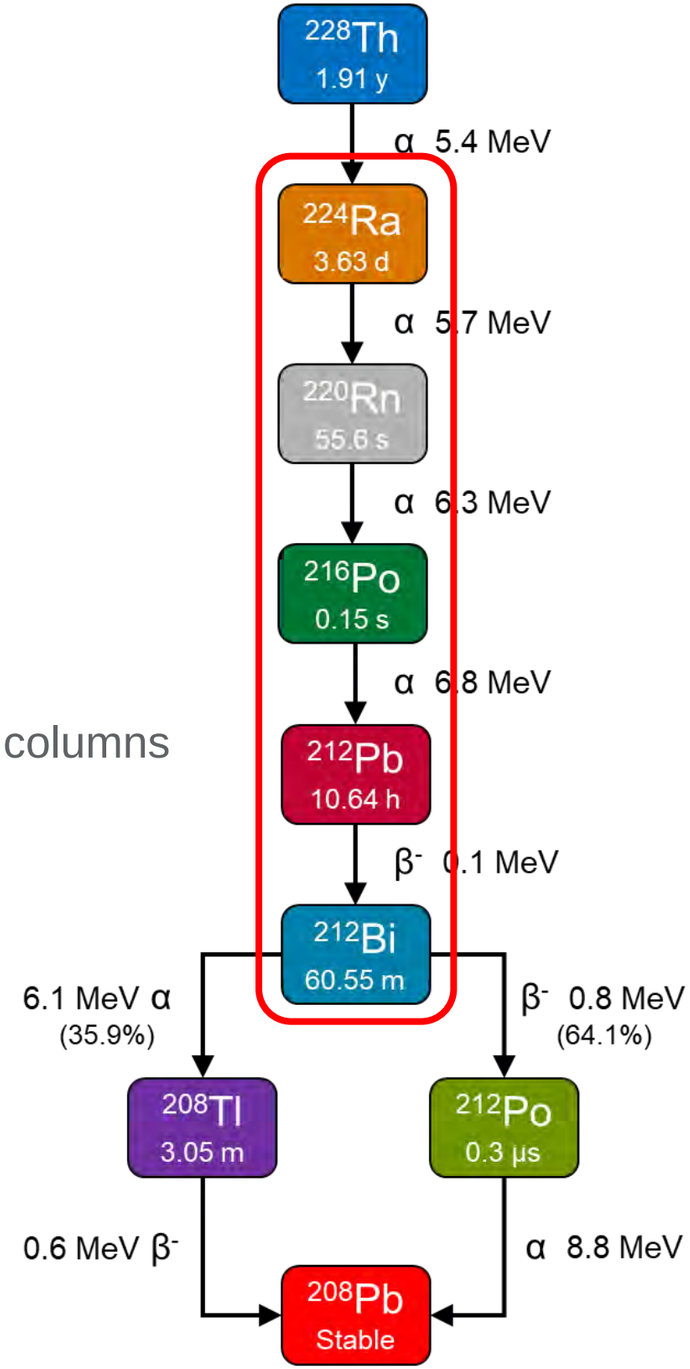
Purpose of Work

- Limited generator availability in the U.S.
  - NIDC presently supplies ≤ 20 mCi generators
  - Manual generator assembly process delivers high dose to staff
    - ✓ 1 mCi ^{224}Ra + progeny ≈ 90 mSv/h @ contact
- Generator demand is increasing
  - Requires improved assembly efficiencies w/ decreased staff dose
  - PNNL has developed a remote, automated system to prepare generator columns
    - ✓ In FY21, we demonstrated process efficacy up to ~3 mCi level
    - ✓ In FY22, anticipate demonstration at clinical levels



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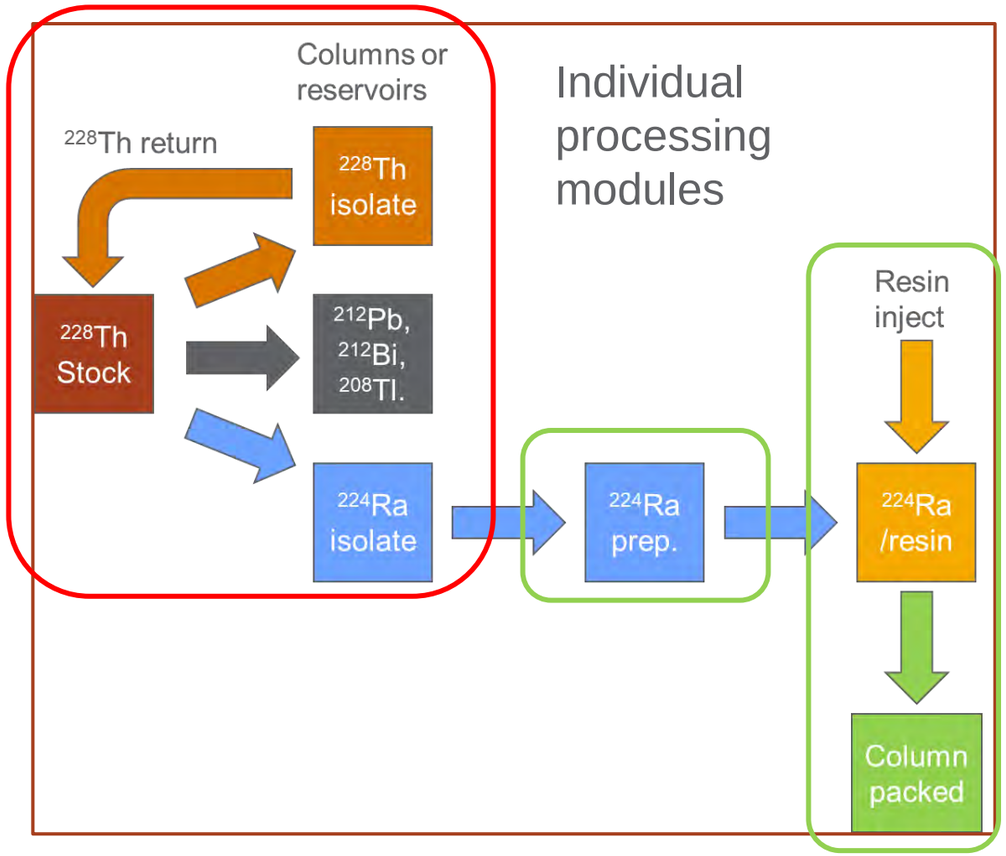
Part I.
Automated preparation of ^{224}Ra Generator

Research Objectives

- **Objective 1:** Develop the process chemistry for isolating ^{224}Ra from ^{228}Th, and the remote assembly of ^{224}Ra generator columns for ^{212}Pb milking

- Three fluidically-interlinked modules
  - Module 1: ^{224}Ra purification from ^{228}Th
    - ✓ Radionuclidicly pure ^{224}Ra
      - ✓ >5x10^5 decontamination from ^{228}Th
    - ✓ Removal of dose contributors (^{212}Pb, ^{212}Bi, & ^{208}Tl)
    - ✓ Recovery and reuse of ^{228}Th
      - ✓ >99% ^{228}Th recovery



Research Objectives

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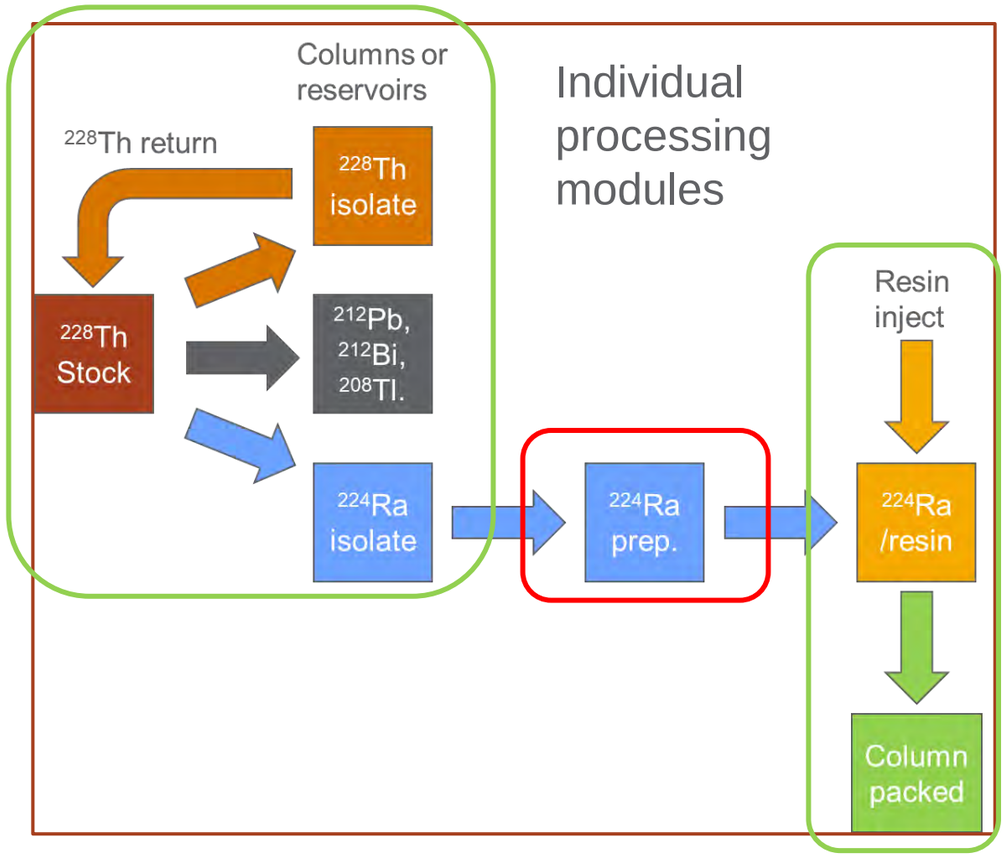
    - ✓ Radionuclidicly pure ^{224}Ra
    - ✓ Removal of dose contributors (^{212}Pb, ^{212}Bi, & ^{208}Tl)
    - ✓ Recovery and reuse of ^{228}Th
  - Module 2: ^{224}Ra preparation step
    - ✓ Convert ^{224}Ra form for optimal CatIX sorption



Research Objectives

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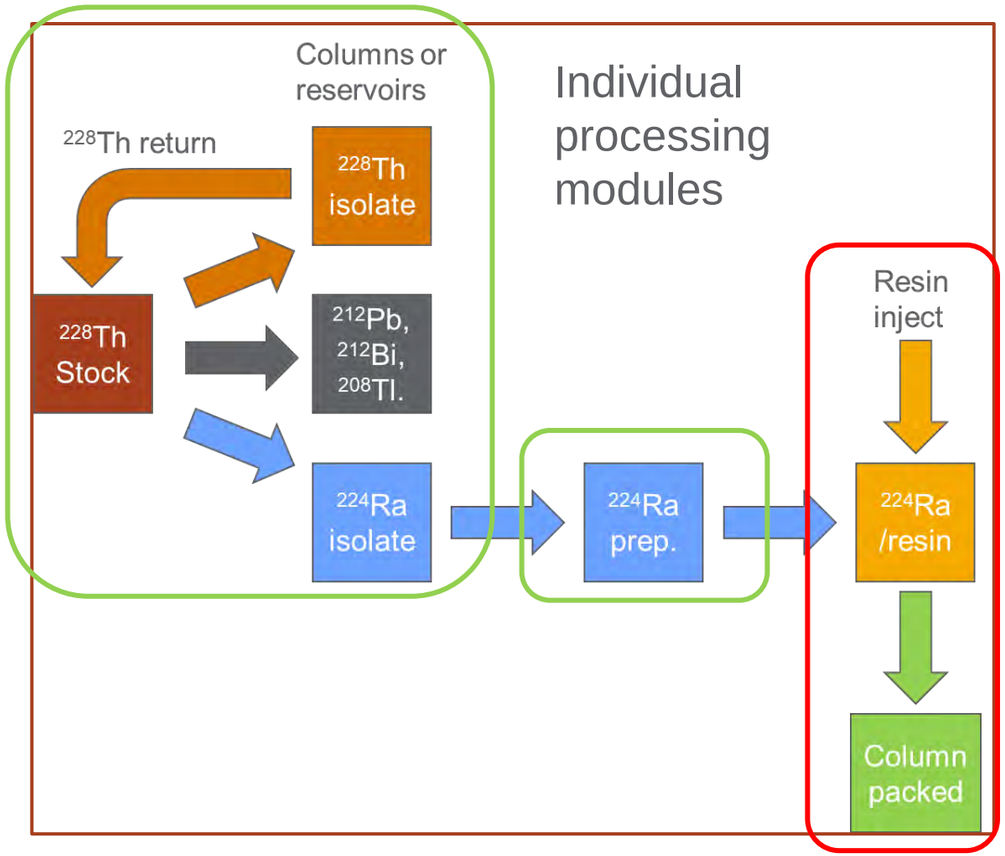
    - ✓ Removal of dose contributors (^{212}Pb, ^{212}Bi, & ^{208}Tl)
    - ✓ Recovery and reuse of ^{228}Th
  - Module 2: ^{224}Ra preparation step
    - ✓ Convert ^{224}Ra form for optimal CatIX sorption
  - Module 3: ^{224}Ra / resin binding and column packing
    - ✓ Homogenously loaded column beds
    - ✓ High ^{224}Ra binding yield



Research Objectives

- **Objective 2:** Develop fluidic systems for each module
  - System engineering (hardware & software development)
- **Objective 3:** Fully integrate into an in-line, end to end system
  - Gen II system constructed; Inter-linked modules; Assembled in glove-bag adjacent to hot cell; upgraded system control electronics & software
  - Process optimization & testing
    - ✓ <1 h end-to-end, from ^{228}Th stock insertion to packed ^{212}Pb generator column
    - ✓ Human intervention limited to ^{228}Th stock insertion (front end) & generator column disconnect (back end)

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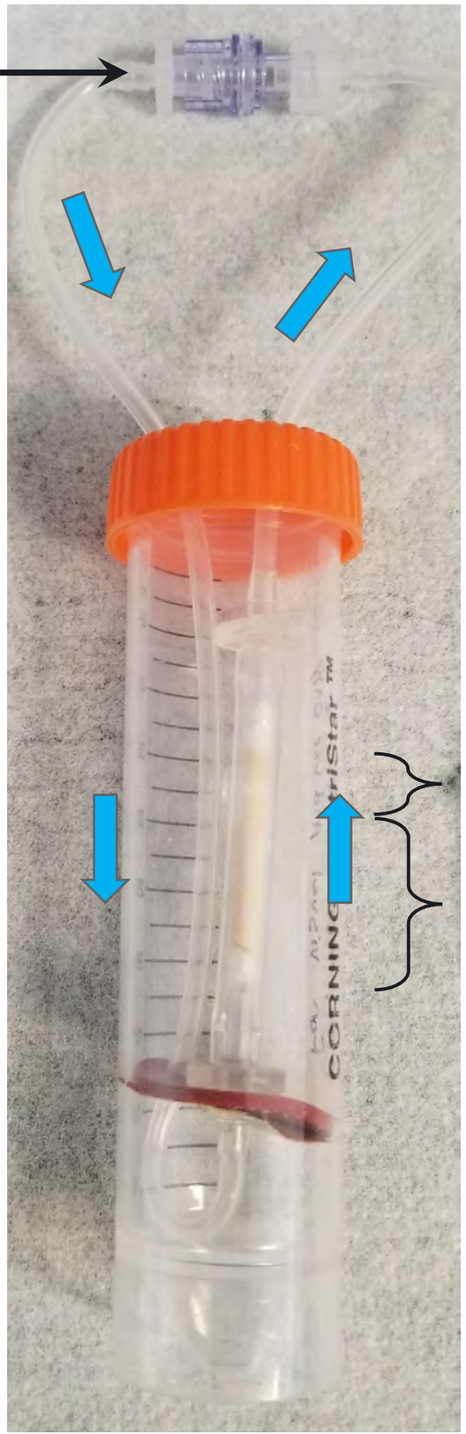
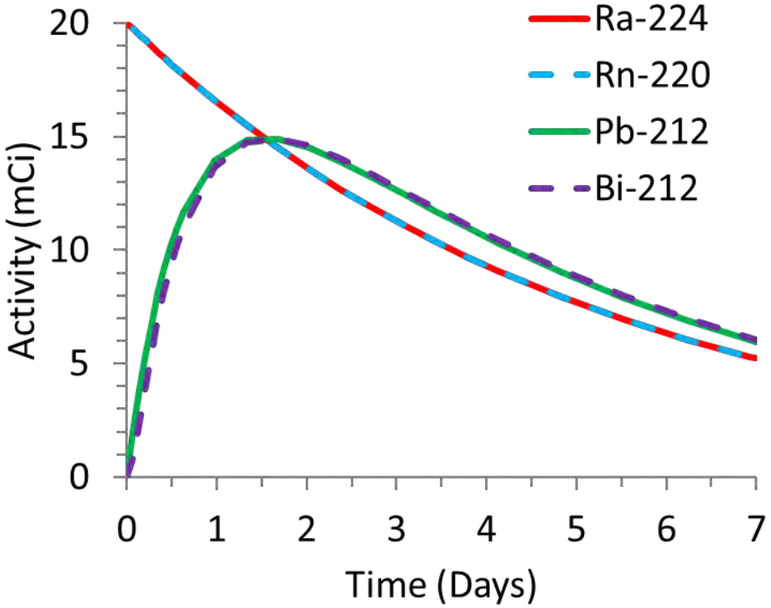


Part II.
Auto-packed ^{212}Pb generator performance

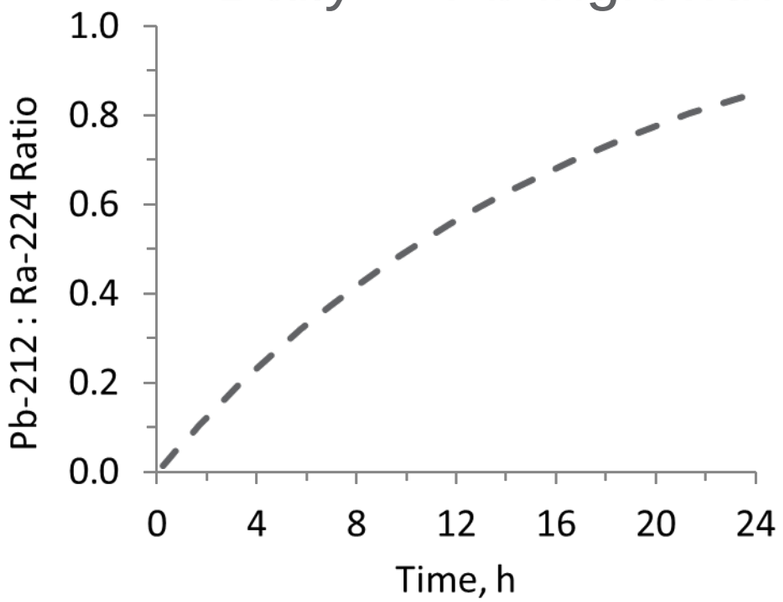
- Preliminary testing performed up to ~2.8 mCi

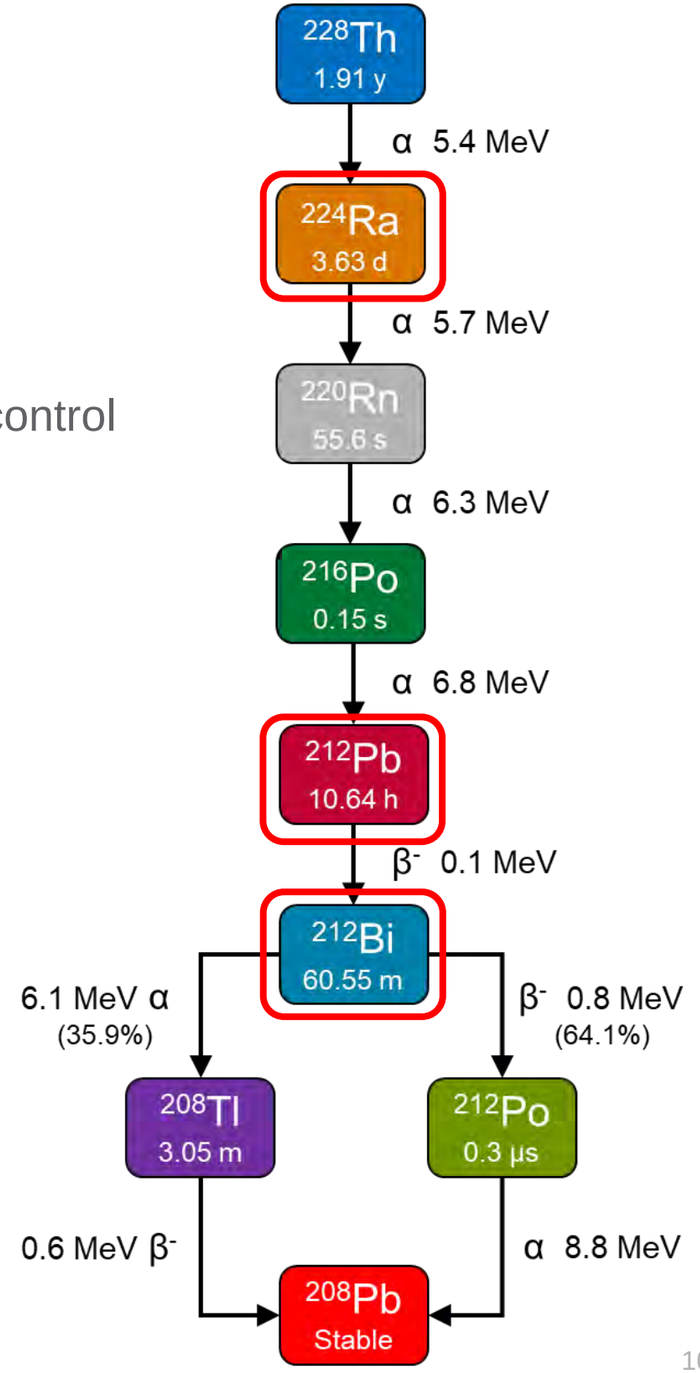
^{212}Pb / ^{212}Bi generator column performance

- Test generators are typically milked at 24 h intervals
  - Milkings performed using digital pumps for absolute volume & flow rate control
  - Conduct daily milking tests across ≥10 days
    - ✓ Evaluate ^{212}Pb + ^{212}Bi co-elution in HCl
    - ✓ Sequential ^{212}Bi then ^{212}Pb elution in HCl
    - ✓ In-line ^{212}Pb conversion to acetate buffer



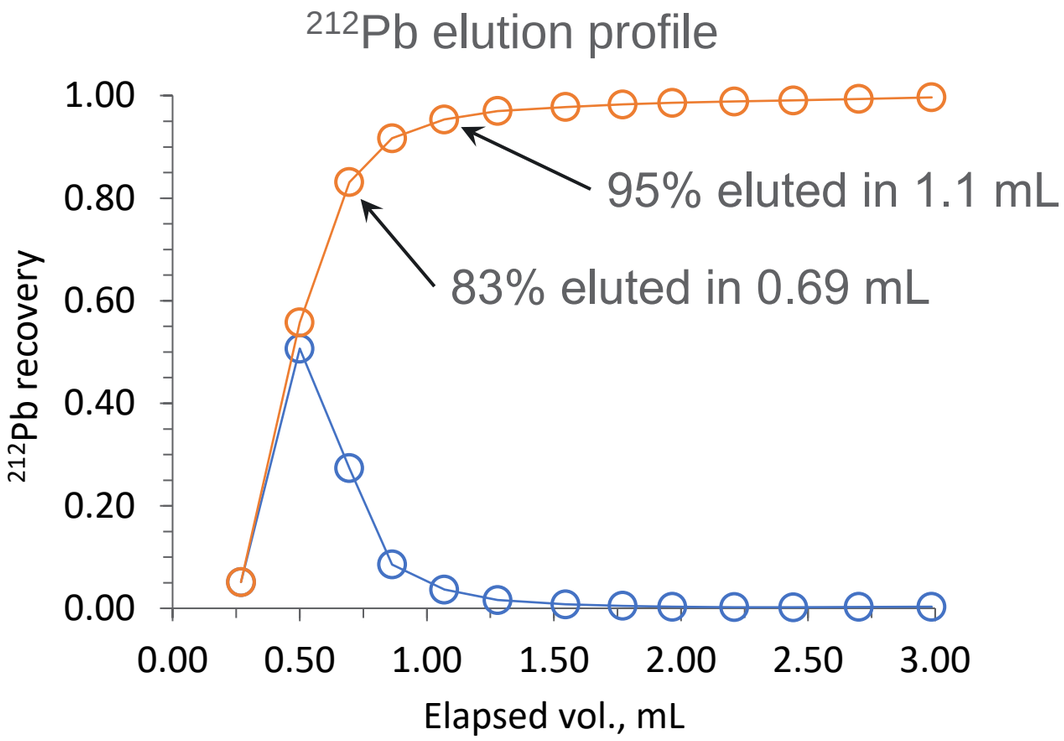
Daily ^{212}Pb ingrowth

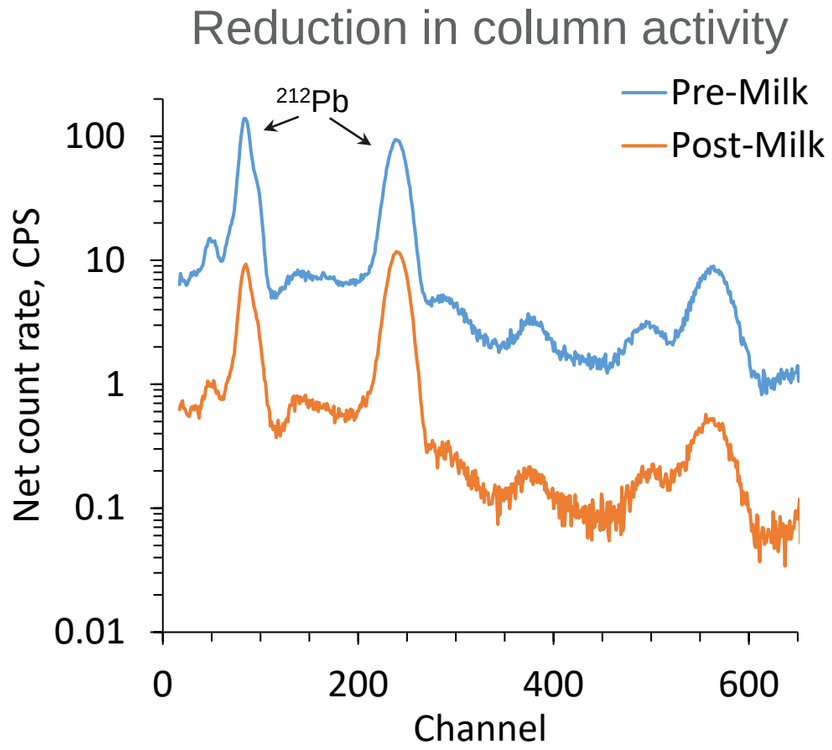




^{212}Pb / ^{212}Bi generator column performance

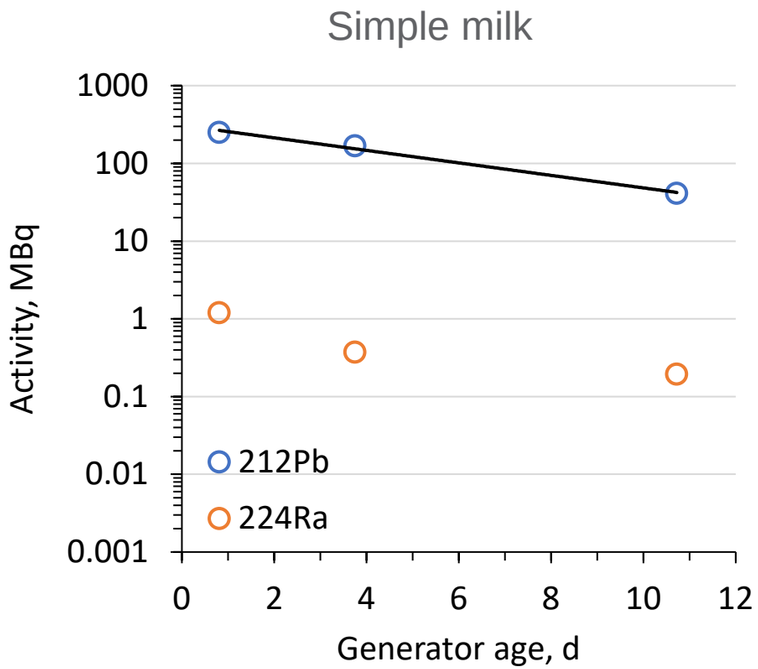
- Simple generator column milking process:
  - 1 mL 2 M HCl, followed by 1 mL H_2O flush & air for storage
    - ✓ Elutes ^{212}Pb & ^{212}Bi together
  - Flow rate = 1 mL/min





Evaluation of ^{224}Ra breakthrough performance

- Aged the milked products to determine ^{224}Ra content
  - **Simple** milking = 1 mL 2M HCl
  - Observed consistent ^{224}Ra fraction (~0.45%) in ^{212}Pb product



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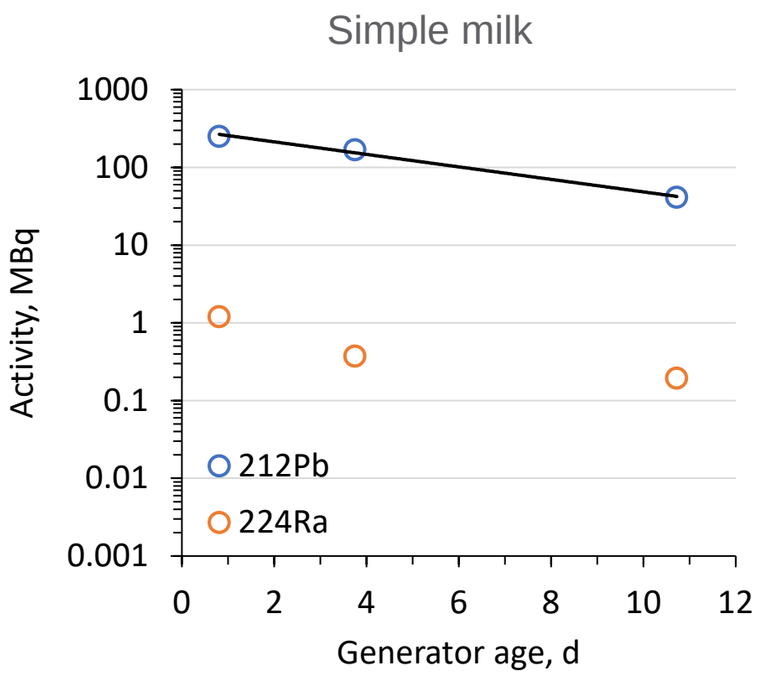
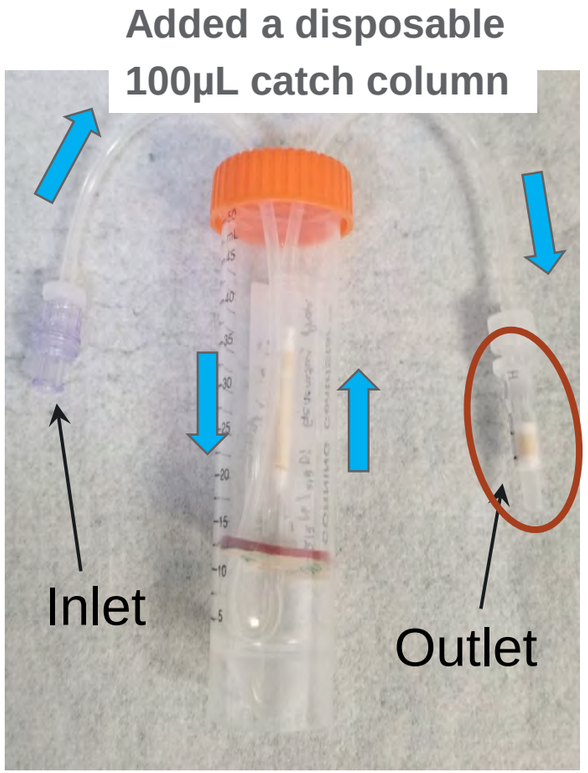
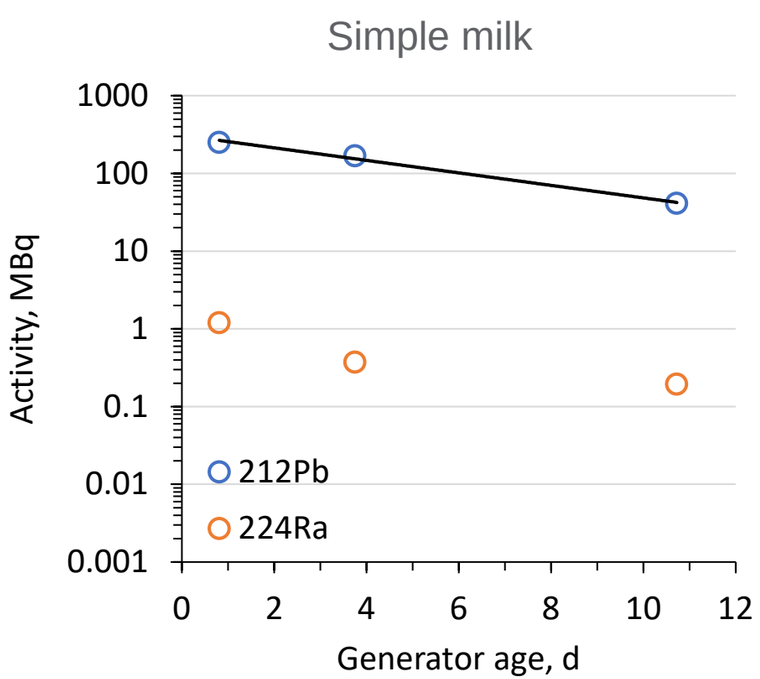


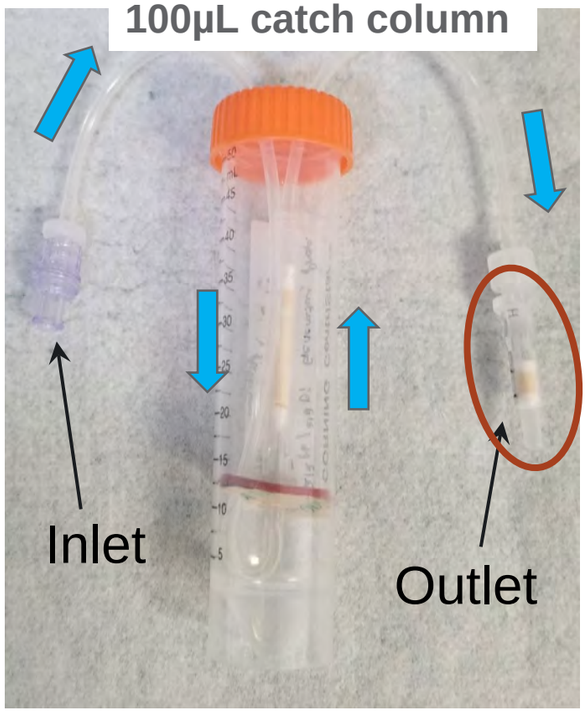


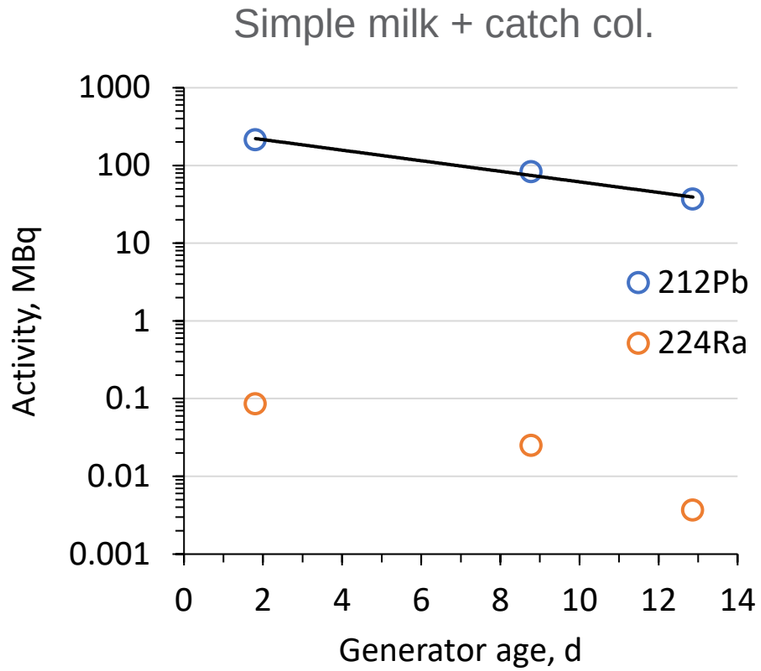
Evaluation of ^{224}Ra breakthrough performance

- Aged the milked products to determine ^{224}Ra content
  - **Simple + Catch** milking = 1 mL 2M HCl
  - Observed >10x increase in ^{212}Pb product purity



Added a disposable 100µL catch column





Evaluation of ^{224}Ra breakthrough performance

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  - **Simple + Catch** milking = 1 mL 2M HCl
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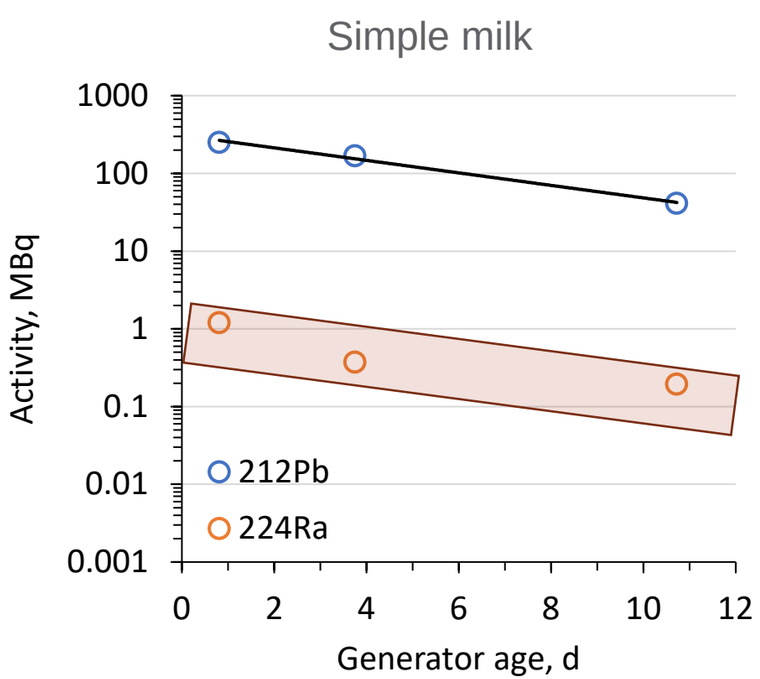

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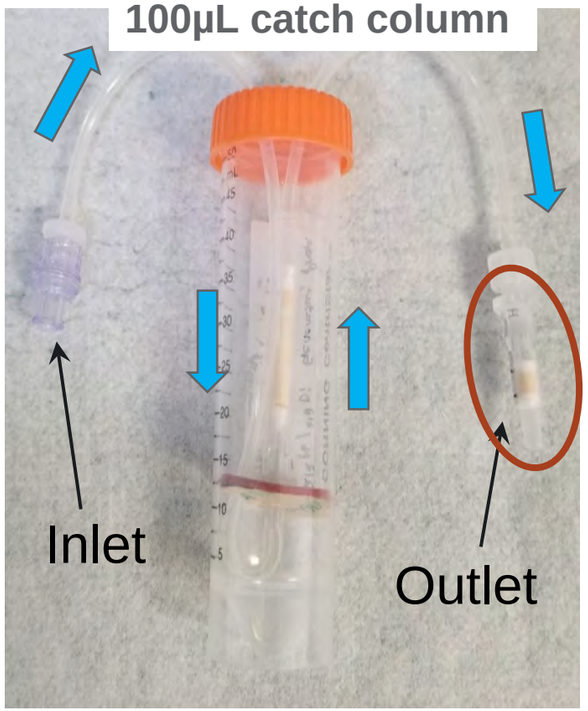
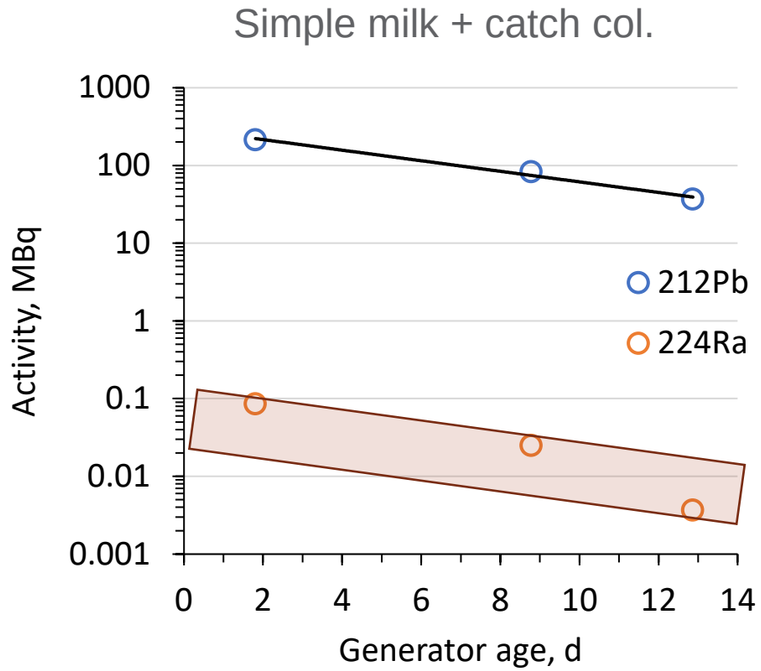
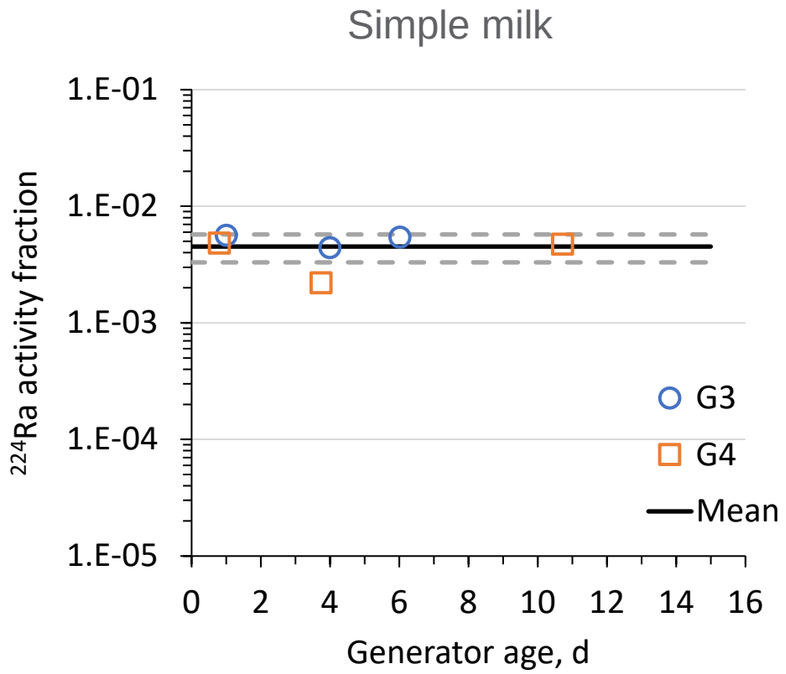
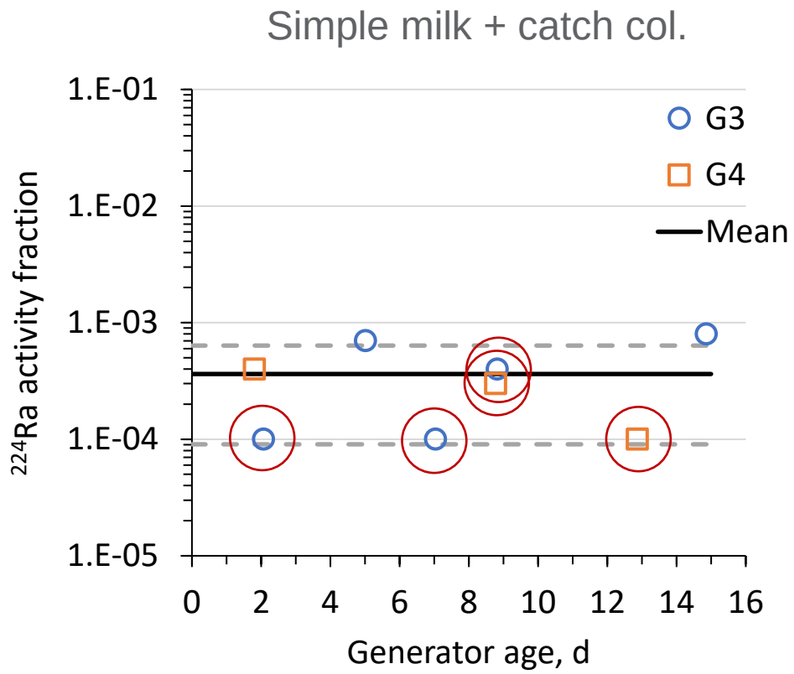




Evaluation of ^{224}Ra breakthrough performance

- Replicate generator comparison: Activity fraction of ^{224}Ra in milked ^{212}Pb
  - Simple milk mean: (4.5 ± 1.2)x10^{-3} (n=6)
  - Simple milk + catch col. mean: (3.6 ± 2.7) x10^{-4} (n=8)

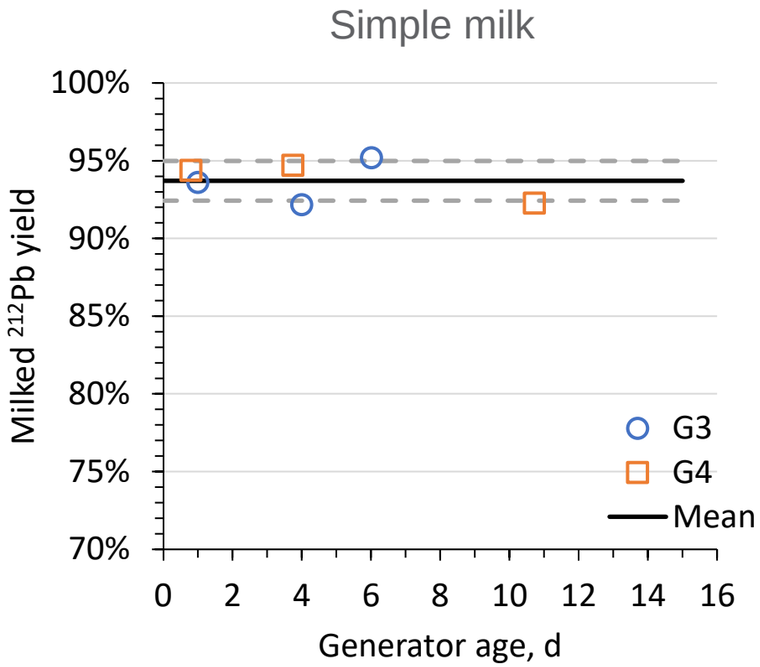


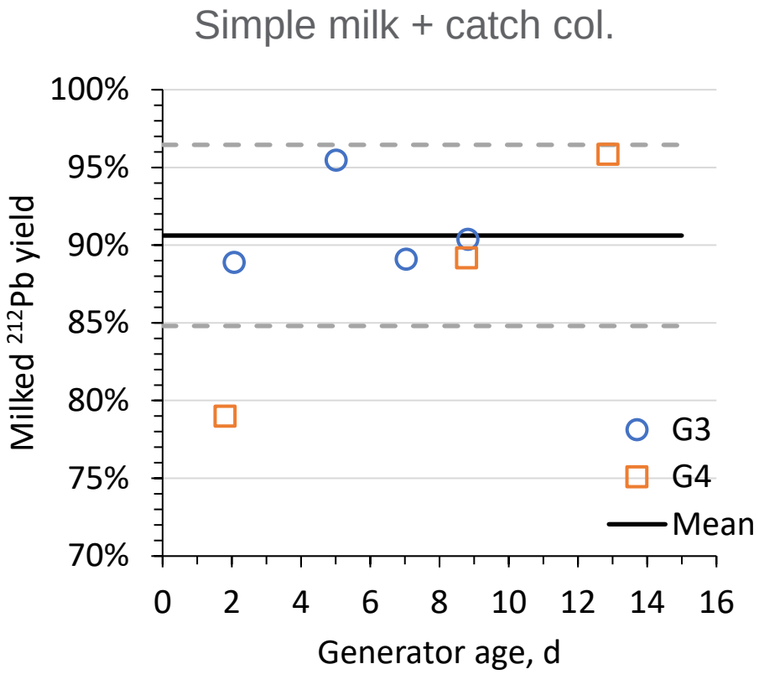


< determination limit

^{212}Pb yield in 1mL milked fraction

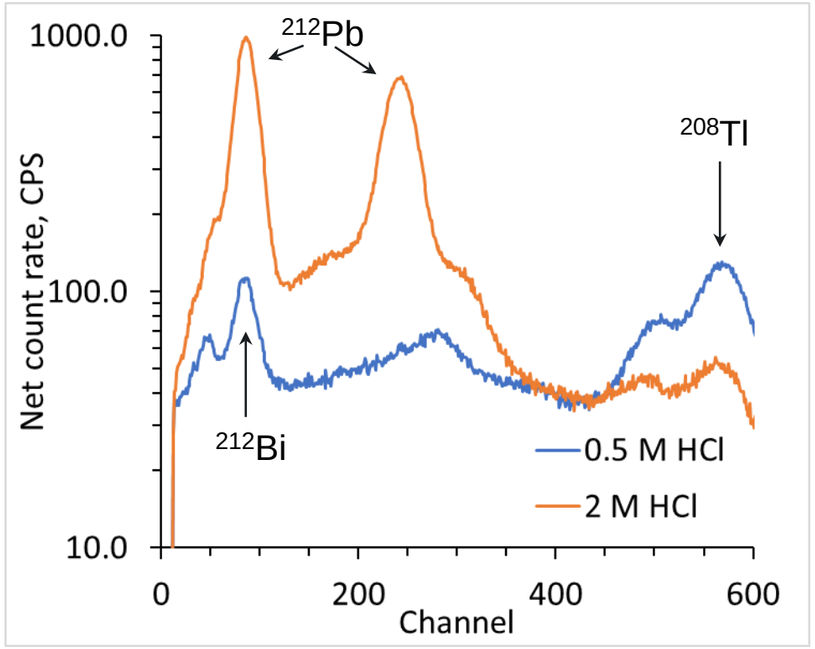
- ^{212}Pb yield in 1 mL 2 M HCl milking aliquot
  - Simple milk yield = 93.7 ± 1.3% (n=6)
    - ✓ (2M HCl / (2M HCl + DIW rinse)
  - Simple milk + catch col. yield = 90.6 ± 5.8% (n=8)
    - ✓ (2M HCl / (2M HCl + DIW rinse + catch col.)

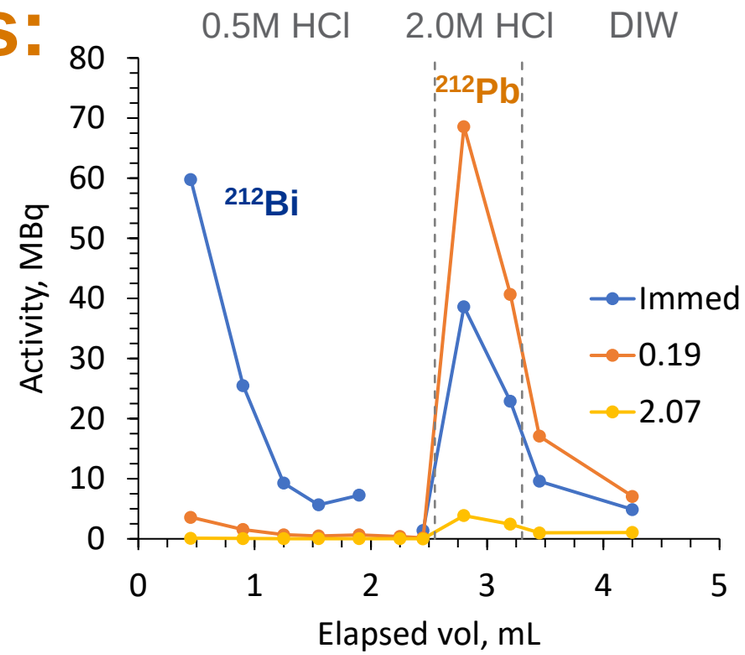


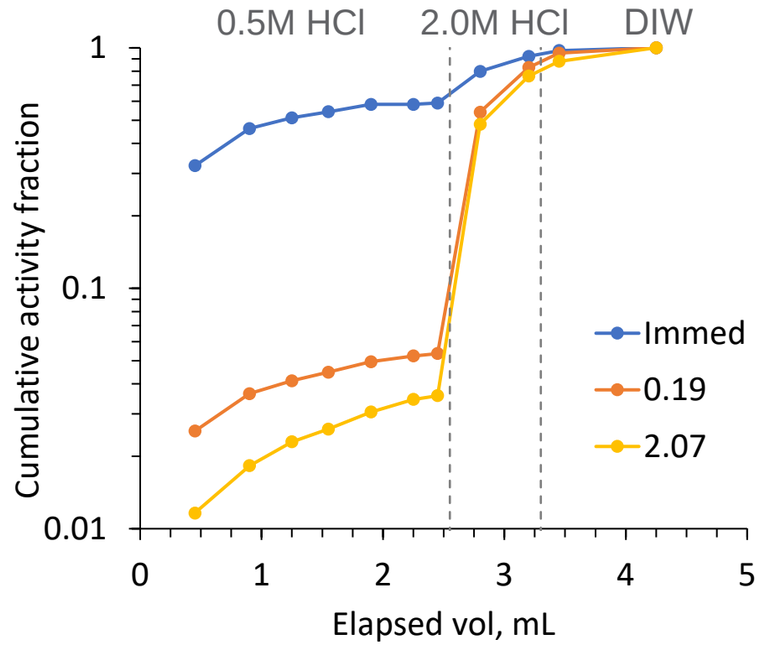


Sequential ^{212}Bi / ^{212}Pb elutions: Simple milking

- ^{212}Bi eluted in 0.5 M HCl prior to ^{212}Pb elution
  - ^{212}Bi / ^{212}Pb re-equilibrium in ~0.17 days (~4 h)

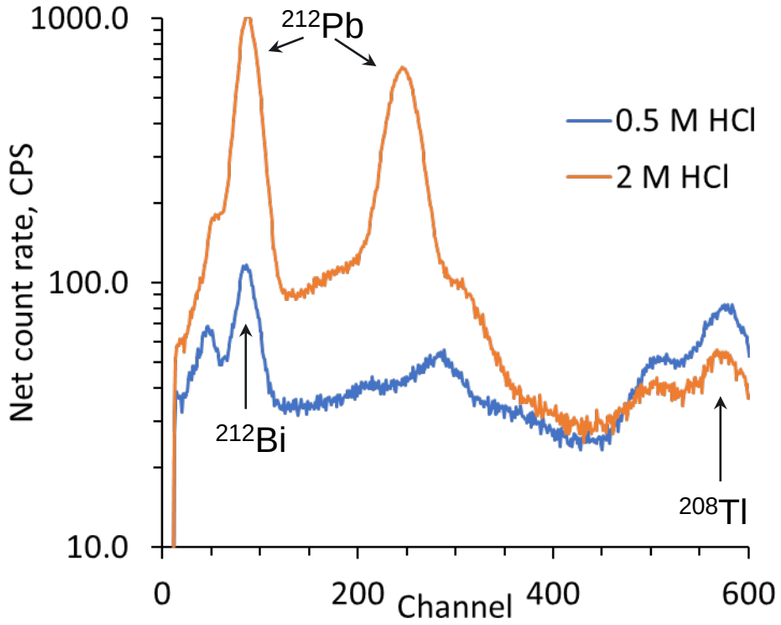


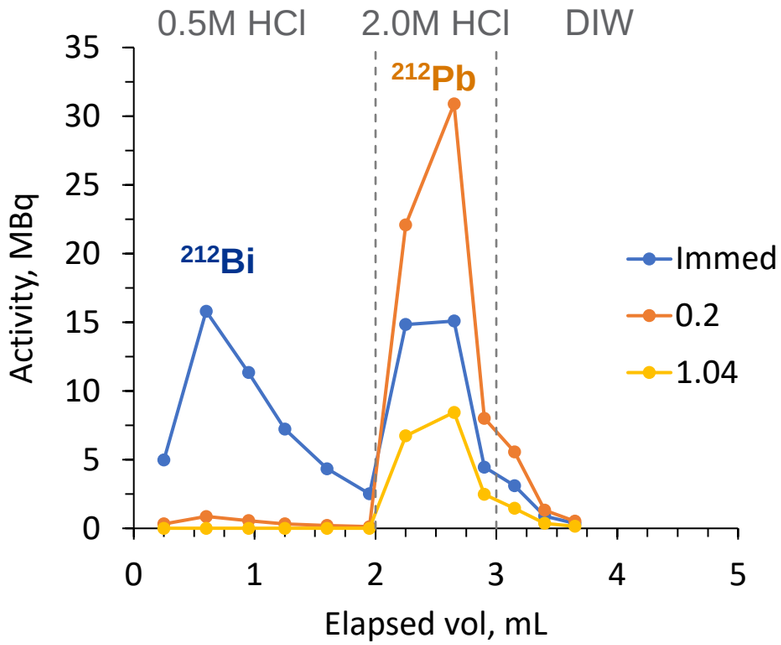


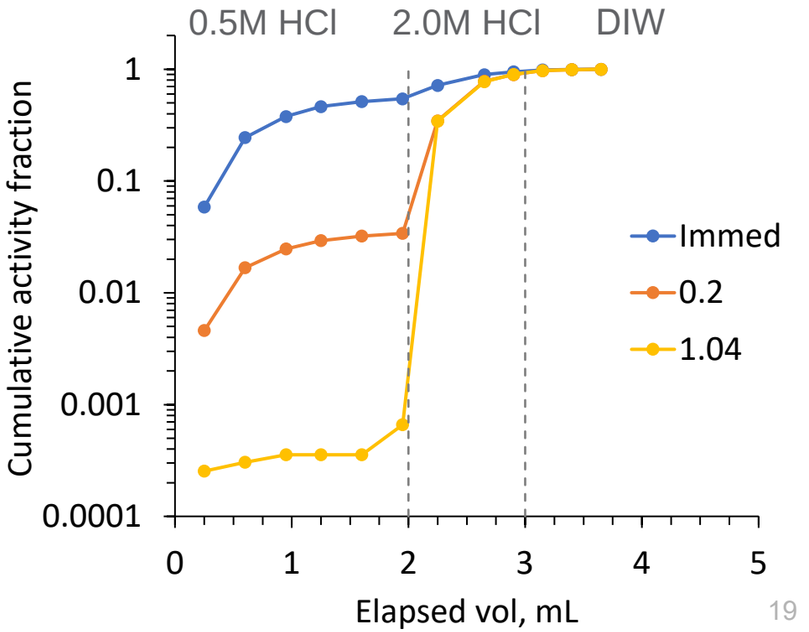


Sequential ^{212}Bi / ^{212}Pb elutions: Simple + catch col. milking

- ^{212}Bi eluted in 0.5 M HCl prior to ^{212}Pb elution
  - ^{212}Bi / ^{212}Pb re-equilibrium in ~0.17 days (~4 h)







Summary

- New fluidic system for auto-preparation of generators
  - System starts with ^{228}Th stock; ends with packed generator column
  - Elapsed end-to-end time of ~1 h
  - Dramatic reduction in dose to staff
- Current low-mCi test generators are indicating good performance to date
  - ^{228}Th decontamination factor >5x10^{5} (ongoing evaluation)
  - Pb yields (>90% in 1mL 2M HCl)
  - Sequential Bi (0.5M HCl) / Pb (2M HCl) elutions
  - Radionuclidic purity (~0.04% ^{224}Ra breakthrough)
  - Dispensation of ^{212}Pb product in pH 6 NaOAc buffer (not shown)
- In FY22, anticipate process scale-up to at least 20 mCi
  - Will continue milking performance testing
  - May seek end-user evaluations via NIDC

Acknowledgements

- This research was supported by the U.S. Department of Energy Isotope Program, managed by the Office of Science.

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Thank you!

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Questions