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Development of a Rn-220 emanation-based generator for high-purity Pb-212 production:

Final Report

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the U.S. Department of Energy
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Executive Summary

This report summarizes the development and demonstration of a thorium-228/radium-224/radon-220 ($^{228}\text{Th}/^{224}\text{Ra}/^{220}\text{Rn}$) and radium-224/radon-220 ($^{224}\text{Ra}/^{220}\text{Rn}$) emanation-based generator for producing high-purity ^{212}Pb in a form suitable for targeted alpha therapy applications. The project was motivated by limitations of conventional wet-column $^{224}\text{Ra}/^{212}\text{Pb}$ generators, including the possibility of ^{224}Ra breakthrough and the need for post-elution chemical processing prior to biomolecule labeling. In contrast, the approach described here uses gas-phase transport of ^{220}Rn away from a ^{228}Th or ^{224}Ra -bearing source, followed by spatially separated decay to ^{212}Pb and aqueous recovery of the product into a radiolabeling-compatible buffer solution.

The work addressed the five original Specific Objectives, while accounting for the later revised scope in which no tasks were eliminated, but several activities were reduced in scale. The team identified practical ^{220}Rn emanation source configurations based on a suite of commercially available resins and specific carrier gas conditions. The project also evaluated multiple Rn collection strategies, including organic solvent capture, cryogenic deposition, organic nanocage media (CC3), and closed-loop decay chamber concepts. These studies established the basis for a simplified generator approach in which ^{220}Rn is transported from the source and ^{212}Pb is subsequently recovered from the collection region in small aqueous volumes.

A major outcome of the report is the demonstration that the generator can produce ^{212}Pb with high yields, purity, and chelation performance.¹ The decay chamber concept enabled recovery of most chamber-deposited ^{212}Pb into ammonium acetate or sodium acetate buffers. Generator testing used both ^{228}Th and ^{224}Ra emanation sources; the highest-activity generator testing reached approximately 18.7 mCi, exceeding the revised 10–15 mCi activity target. In these evaluations, ^{212}Pb recovery into sodium and ammonium acetate was typically near 90% of the decay chamber activity, with overall product yields (considering ^{220}Rn emanation fraction and ^{212}Pb collection fraction) reaching approximately 82% under the best conditions. Product purity was likewise strong: decay-based measurements showed no detectable ^{228}Th or ^{224}Ra contamination in selected high-activity product fractions, with calculated ^{212}Pb product decontamination factors greater than 10^8 .

Results also demonstrate that the recovered ^{212}Pb product is chemically useful, not merely radionuclidically pure. When ^{212}Pb was collected directly into ammonium acetate containing the TCMC (DOTAM) chelator, essentially quantitative complexation was observed, with 99.8–100.0% bound and 99.3–99.7% bound when assessed by two methods.² These results indicate that the product matrix did not contain a bindable-metal inventory sufficient to inhibit TCMC labeling under the evaluated conditions. We also demonstrated that radiolabeling onto TCMC chelator can happen concurrently with ^{212}Pb stripping with acetate salt solutions – thereby reducing ^{212}Pb collection and labeling to a single step.

¹ This report contains the results of work performed under Contract No. DE-AC05-76RL01830 from the United States Department of Energy. As such, this report may contain patented, patent pending, or other Intellectual Property. For a list of available technologies, please visit: <https://www.pnnl.gov/available-technologies/improved-lead-212-pb-212-bismuth-212-bi-212-generator-systems>.

² Instant thin layer chromatography (iTLC) and aminopropyl (NH2) cartridge methods, respectively.

Overall, the report shows that the revised project objectives were met: the team developed an automated, high-yield $^{228}\text{Th}/^{212}\text{Pb}$ and $^{224}\text{Ra}/^{212}\text{Pb}$ generator concept capable of producing high-purity, label-ready ^{212}Pb while substantially reducing the risk of parent-isotope breakthrough and opportunities for metals contamination.

Finally, the project trained future radiochemists by embedding students and Research Associates directly into the full development cycle of the generator system. Participants gained hands-on experience in alpha-emitting radionuclide handling, source preparation, gas-phase ^{220}Rn transport, generator assembly, automated fluidic operation, radiometric counting, decay correction, yield calculations, radionuclidic purity assessment, contamination control, and radiolabeling-relevant product evaluation. Because the work addressed a clinically relevant radioisotope production challenge, trainees learned to connect fundamental radiochemistry with practical requirements for high-purity, label-ready nuclide preparation. In this manner, the project satisfied the training Specific Objective by using the R&D effort itself as the training platform for developing the next generation of radiochemists.

Acknowledgments

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The authors would like to acknowledge PNNL's Office of STEM education for providing internship opportunities through Post-Bachelors, Post-Masters, and Post-Doctoral Research Associate (RA) positions.

Acronyms and abbreviations

ACS	American Chemical Society reagent grade
AG MP-50; MP-50	Bio-Rad AG MP-50 macroporous cation exchange resin
CC3	Metal-free organic nanocage
DOE	U.S. Department of Energy
DOE-IRP	DOE Isotope R&D and Production Program
DOTAM	See TCMC
EDTA	Ethylenediaminetetraacetic acid
EVA	Ethylene-vinyl acetate
FEP	Fluorinated ethylene propylene
FOA	Funding Opportunity Announcement
GMP	Good Manufacturing Practice
HCl	Hydrochloric acid
HNO ₃	Nitric acid
HPGe	High-purity germanium detector
ICP-MS	Inductively coupled plasma-mass spectrometer
iTLC	Instant thin-layer chromatography
M _B	Bindable metals; operational ²⁰⁸⁺²¹² Pb-equivalent metal burden determined by TCMC titration
MDA	Minimum detectable activity
NaI(Tl)	Thallium-doped sodium iodide scintillation detector
NaOAc	Sodium acetate buffer
NH ₂	Aminopropyl resin cartridge
NH ₄ OAc	Ammonium acetate buffer
NIDC	National Isotope Development Center
N ₂	Nitrogen carrier gas

PBS	Phosphate-buffered saline
PE	Polyethylene
PEEK	Polyether ether ketone
PFA	Perfluoroalkoxy alkane
PMMA	Polymethyl methacrylate
PNNL	Pacific Northwest National Laboratory
PP	Polypropylene
PTFE	Polytetrafluoroethylene
PVC	Polyvinyl chloride
RA	Research Associate
SO	Specific Objective
SPECT	Single-photon emission computed tomography
STEM	Science, technology, engineering, and mathematics
TAT	Targeted alpha therapy
TCMC	1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane; Pb chelator also referred to as DOTAM
UHP	Ultra-high purity

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1.0 Introduction

This report summarizes the principal accomplishments from the Pacific Northwest National Laboratory (PNNL) effort to develop a $^{228}\text{Th}/^{224}\text{Ra}/^{220}\text{Rn}$ and/or $^{224}\text{Ra}/^{220}\text{Rn}$ emanation-based generator for production of high-purity ^{212}Pb . This project [1] was a continuation of the original research into ^{220}Rn emanation-based generators [2]. The work was motivated by a simple premise: if ^{220}Rn can be efficiently released from a ^{228}Th or ^{224}Ra -bearing source, transported downstream as a gas, and captured away from that source, then the ingrown ^{212}Pb can be recovered from a location that is physically separated from the longer-lived parent isotope [3].³ This gas-phase separation is the central feature that distinguishes the present approach from conventional “wet-column”⁴ $^{224}\text{Ra}/^{212}\text{Pb}$ generators.

The wet column ^{212}Pb generator was originally conceived and designed in the 1980s by Atcher, Friedman, and Hines [4, 5], and the assembly has not changed appreciably in these ~40 years. The wet-column generators have enabled important $^{212}\text{Pb}/^{212}\text{Bi}$ research and the move towards clinical trials, but they also possess limitations that are inherent to the format. The product is milked from the same solid phase that contains ^{224}Ra ; therefore, even well-designed systems have a degree of parent nuclide breakthrough [4], along with possible metal contaminants originating from the column packing medium and/or eluting reagents. In addition, the eluted product matrix requires post-elution treatment before it is compatible with biomolecule labeling. This includes removal of the mineral acid eluent and transposition to a buffered solution, or a secondary column approach to bind the ^{212}Pb while the mineral acid is flushed through [6]. These steps complicate routine radiopharmaceutical workflows by adding processing time, increasing operator handling dose, and potentially introducing contaminants to the ^{212}Pb product.

The generator concept evaluated in this project instead uses ^{220}Rn as a physical bridge between ^{224}Ra and ^{212}Pb . During the gas-phase collection mode, ^{220}Rn is emanated from a ^{228}Th - or ^{224}Ra -loaded source (Figure 1) and transported to a downstream collection chamber, where it decays (and accumulates) to non-gaseous ^{212}Pb (Figure 2). Assuming perfect ^{220}Rn emanation and collection from the source, the ^{212}Pb ingrowth rates are identical between a traditional (static) column and emanation generator.

³ This report contains the results of work performed under Contract No. DE-AC05-76RL01830 from the United States Department of Energy. As such, this report may contain patented, patent pending, or other Intellectual Property. For a list of available technologies, please visit: <https://www.pnnl.gov/available-technologies/improved-lead-212-pb-212-bismuth-212-bi-212-generator-systems>.

⁴ Generator columns that used hydrochloric acid to separate ^{212}Pb and ^{212}Bi from ^{224}Ra that is pre-loaded onto a cation exchange column.

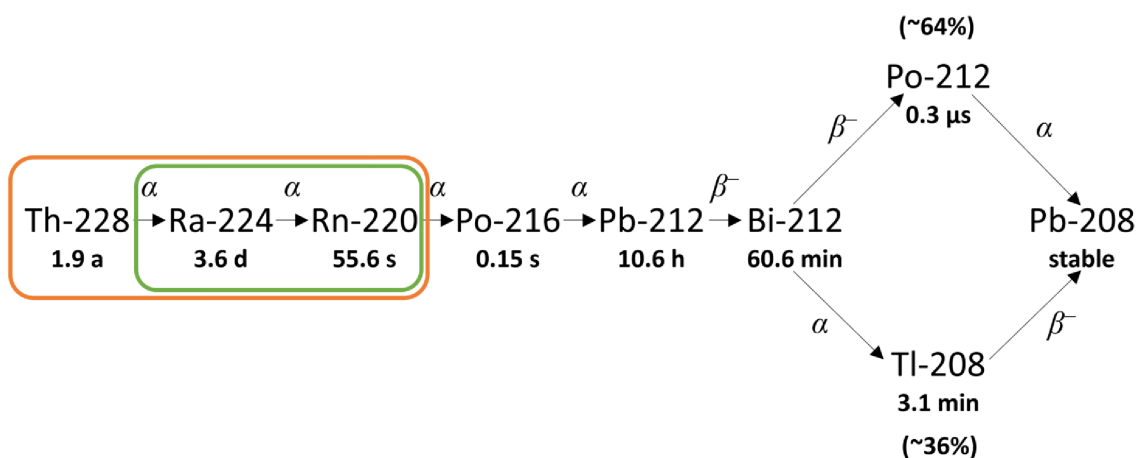


Figure 1. ^{228}Th decay scheme, showing ^{224}Ra (green) and ^{228}Th (orange) source nuclides used for ^{220}Rn emanation generators.

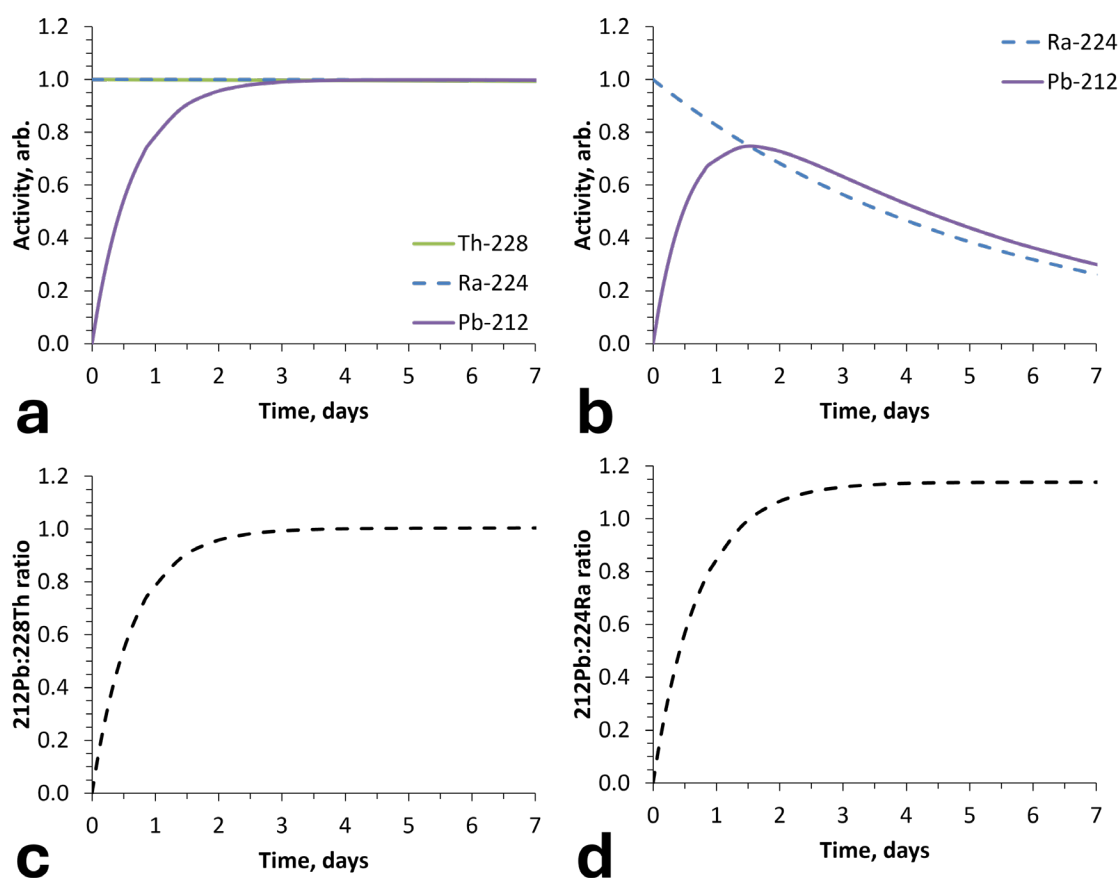


Figure 2. ^{212}Pb ingrowth schemes, with (a) $^{228}\text{Th}/^{224}\text{Ra}$, and (b) ^{224}Ra source nuclide across a 7 day interval. ^{212}Pb ingrowth fraction relative to grandparent or parent nuclide for $^{228}\text{Th}/^{224}\text{Ra}$ (c) and ^{224}Ra (d) source nuclides. Plots assume no loss of ^{220}Rn between ^{224}Ra decay and ^{212}Pb ingrowth.

Prior to initiating the aqueous ^{212}Pb recovery mode, the gas path is isolated and the accumulated ^{212}Pb is recovered into a buffered solution. This two-mode operation was envisioned from the beginning of the research and became the organizing principle for the experimental work, the automated platform architecture, and the final high-activity demonstrations [3].

The original proposal [1] defined five traits required for a practical emanation generator: 1) efficient Ra collection on a robust source material; 2) high ^{220}Rn emanation power; 3) efficient downstream Rn collection; 4) high-yield recovery of ingrown ^{212}Pb ; and 5) recovery of ^{212}Pb in a solution compatible with direct labeling. The revised scope [7] retained the five Specific Objectives (SOs) from the original proposal tasks, but reduced the breadth of several activities to fit the available budget. The resin survey was narrowed, the parallel test stand was reduced from three gas-delivery channels to one, CC3 optimization was scaled back, rad-controlled ICP-MS metals analysis was removed, and high-activity testing was limited to a small number of runs in the 10-15 mCi target range, with additional runs as budget allowed.

Despite those reductions, the essential deliverables were achieved. The work identified practical source materials and operating conditions for high ^{220}Rn emanation, established workable Rn collection approaches, developed aqueous recovery of ^{212}Pb into label-compatible solutions, and demonstrated automated generator operation at clinically relevant ^{224}Ra activity. Most importantly, the resulting ^{212}Pb product showed no detectable grandparent and/or parent isotope contamination in the evaluated high-activity runs – whether the source nuclide was ^{228}Th or ^{224}Ra . Additionally, ^{212}Pb product chelation titration experiments with TCMC (DOTAM)⁵ chelator indicated extremely low competing metals contamination levels.

1.1 $^{212}\text{Pb}/^{212}\text{Bi}$ in cancer therapy

Lead-212 is a 10.6 h beta-emitting radionuclide that serves as an *in vivo* generator for ^{212}Bi [8]. The ^{212}Pb half-life is long enough to support radiolabeling, formulation, and biological localization of peptides or antibodies [9], while the subsequent $^{212}\text{Bi}/^{212}\text{Po}$ decay sequence provides short-range alpha emissions appropriate for targeted alpha therapy. For that reason, reliable and high-purity ^{212}Pb production remains important to the continued development of targeted alpha-emitting radiopharmaceuticals [8]. The recent availability of ^{203}Pb , which decays via electron capture to ^{203}Tl and emits a 279 keV photon, has facilitated single-photon emission computed tomography (SPECT) imaging – thus forming a theranostic matched pair to the ^{212}Pb therapeutic nuclide [10].

For clinical translation, the ^{212}Pb product must be more than merely obtainable. It must be recovered reproducibly, with minimal parent breakthrough and metals contamination, in a chemical form that is compatible with subsequent chelation [6]. The present project was therefore focused not only on moving ^{220}Rn from a source to a collection chamber, but also on recovering the resulting ^{212}Pb in a form that could be directly useful for biomolecule-labeling chemistry [8, 11].

⁵ 1,4,7,10-Tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane

1.2 Historical and current status of ^{212}Pb generators

The conventional $^{224}\text{Ra}/^{212}\text{Pb}$ generator is based on cation-exchange retention of ^{224}Ra and periodic elution of ingrown ^{212}Pb and/or ^{212}Bi using hydrochloric acid. This approach, advanced by Atcher, Friedman, and Hines, remains a practical and important route for obtaining ^{212}Pb [4, 5]. The conventional generator preparation process has been recently adapted to an end-to-end, remotely operated fluidic system at PNNL for routine preparation [12-16]. The wet column generators are currently available through the National Isotope Development Center (NIDC) [17].

Earlier emanation-based ^{212}Pb generators confirmed the value of spatially separating Rn from its parent source, but they also revealed practical limitations. Published systems used Ba-stearate sources, ion-exchange media, aqueous emanation sources, decay chambers, solvent traps, and cryogenic capture approaches (see **Appendix A**). These systems generally supported the conclusion that parent breakthrough can be avoided by gas-phase separation, but many suffered from low overall yield, radiolytic degradation, cumbersome source preparation, difficult ^{212}Pb recovery, or reliance on complex low-temperature systems. The present project was designed to retain the purity advantage of emanation while developing a more practical, compact, and automatable generator format [3, 15].

1.3 Research objectives

The primary objective was to develop a $^{212}\text{Pb}/^{212}\text{Bi}$ isotope-production technology based on gaseous transport of ^{220}Rn away from a source containing a ^{220}Rn parent nuclide. The work was organized around five Specific Objectives (SOs):

- **SO1 (Tasks 1-2):** Refinement of the thoron emanation source form factor;
- **SO2 (Tasks 3-4):** Refinement of the emanated thoron collection chamber;
- **SO3 (Task 5):** Enhanced collection of ultra-high-purity ^{212}Pb in label-ready aqueous solution;
- **SO4 (Tasks 6-7):** Design and testing of an engineered emanation generator system; and
- **SO5:** Training of students and Research Associates in the radiochemical methods involved in ^{212}Pb production.

The revised project scope did not remove any of these SOs. Rather, it reduced the experimental breadth of several tasks. Task 1 focused primarily on AG MP-50 and closely related source configurations, but several additional commercially available resins were identified that exhibited high Rn emanation power. Task 2 retained a single-channel test stand rather than the originally proposed three-channel arrangement. Task 3 reduced the number of CC3 synthesis and optimization studies. Task 5 shifted product-quality assessment toward radionuclidic purity and chelation performance rather than ICP-MS metals analysis. Task 7 limited the planned high-activity demonstrations to the 10-15 mCi range, with the expectation that additional runs would be performed as budget allowed. Tasks 4 and 6 were retained as the chamber-engineering and integrated-system engineering components, respectively.

1.4 Research outcomes

The following lists the accomplishments made in each Specific Objective:

SO1: The project demonstrated high ^{220}Rn emanation from resin-based sources, defined the importance of carrier-gas humidity for source performance (where polystyrene divinylbenzene based resins were employed), and demonstrated that some classes of resins do not require humidity to exhibit high Rn emanation power.

SO2: We evaluated multiple Rn collection strategies. The organic nanocage material, CC3, was synthesized and was shown to exhibit excellent Rn capture performance across a range of material masses, carrier gas flow rates, etc. when packed into a column and exposed to emanated ^{220}Rn [18]. Additionally, we devised a “closed loop” generator system, whereby emanated ^{220}Rn was cycled through a continuous air-filled pathway (with the emanation source embedded within the path) via a compact air pump. Within the loop, the decay products were collected onto the surface of a collection chamber.

SO3: For the “closed loop” system described above, we assessed a range of materials to identify ideal collection chamber compositions. We documented a number of materials and surfaces that allowed for high ^{212}Pb recovery using simple buffered aqueous solutions that are compatible with radiolabeling of conjugated proteins. These were all metal-free materials that did not contribute to metals contamination of the ^{212}Pb product. See **SO4** for information on ^{212}Pb product purity.

SO4: We assembled and evaluated an automated closed-loop emanation generator platform that integrated the radionuclide source, gas circulation loop, decay chamber, and aqueous product-recovery steps into a compact end-to-end system. The platform operated in the intended two-mode format: gas-phase transport and decay of emanated ^{220}Rn , followed by aqueous recovery of ingrown ^{212}Pb from the decay chamber. The system was tested with both ^{228}Th - and ^{224}Ra -loaded emanation sources across increasing activity levels, culminating in a ^{224}Ra demonstration at approximately 18.7 mCi, which exceeded the revised 10–15 mCi high-activity target range.

In the high-activity ^{224}Ra configuration, the generator supplied ^{212}Pb in acetate buffer with calculated overall product yields as high as ~82%. This value is important because it reflects the combined performance of the entire process: ^{220}Rn emanation from the source, gas-phase transport, decay-chamber collection, and aqueous ^{212}Pb recovery. Delayed product measurements showed no detectable ^{224}Ra in the evaluated ^{212}Pb product fractions, with calculated parent nuclide decontamination factors greater than 10^8 ; similar parent-isotope decontamination performance was observed for ^{228}Th -supported generator testing.

The recovered product also demonstrated the chemical utility required for downstream radiopharmaceutical use. TCMC titration experiments across multiple ^{212}Pb milked products from generators across multiple activity scales showed low bindable metal (M_B)⁶ burden in the acetate product fractions. Even direct ^{212}Pb chelation into TCMC-containing ammonium acetate from the decay chamber produced essentially quantitative ^{212}Pb complexation by both iTLC and aminopropyl resin (NH₂) cartridge assessment. These results demonstrate that the automated closed-loop generator can produce high-yield, high-purity, label-ready

⁶ Where bindable metals (M_B) is the mole ratio between TCMC and bound $^{212+208}\text{Pb}$, with the perfect metric being unity (1:1 TCMC: $^{212+208}\text{Pb}$). See similar method described in [19].

^{212}Pb while avoiding detectable parent breakthrough and minimizing the need for extensive post-collection solution transposition.

SO5: The project facilitated the training and mentorship of a Post-Bachelors, a Post-Masters, and a Post-Doctoral Research Associate; two of these interns were later hired as full-time staff in the Radiochemical Separations Team of the Nuclear Sciences Division.

2.0 Experimental methods and instrumentation

2.1 Reagents, materials, and radionuclides

All reagent solutions were prepared using ≥ 18.0 M Ω -cm deionized water. ACS reagent grade HCl and HNO₃ were used for acid media, with Optima™ grade acids employed during emanation generator preparation. Sodium acetate/acetic acid (NaOAc) and ammonium acetate (NH₄OAc) buffers were used for ²¹²Pb recovery and product collection. Tetrasodium EDTA and TCMC (DOTAM) solutions were used for selected labeling and speciation checks. Key solid media included activated charcoal for quantitative ²²⁰Rn trapping, PNNL-synthesized CC3 organic nanocage material for room-temperature ²²⁰Rn collection [18], hydrogel desiccant for in-line humidity reduction, and a range of commercially available ion-exchange/extraction chromatographic resins for source and ²¹²Pb isolation studies. This included AG MP-50 (Bio-Rad Laboratories) macroporous cation exchange resin. Radionuclide parent source material (²²⁸Th) was obtained through the DOE-IRP's National Isotope Development Center (NIDC).

2.2 Gas delivery and humidity control

Nitrogen carrier gas was regulated and dried before flow control through a low-pressure digital mass flow controller. Flow rates were confirmed using a digital mass flow meter. Where humidified carrier gas was required, pre-dried nitrogen gas was passed through a small water-bubbler column and monitored with an in-line humidity sensor. Rn emanation and capture studies were performed within either a customized temperature-controlled box or heating block. In later generator tests, a compact diaphragm pump was used to circulate carrier gas through the ²²⁴Ra-loaded emanation source and ²²⁰Rn collection chamber. Hydrogel desiccant columns or other in-line moisture-removal hardware were used when humidified gas improved ²²⁰Rn emanation but impaired downstream collection.

2.3 Fluid delivery, automation, and radiometric measurements

The final prototype used digital syringe pumps, distribution valves, FEP/PEEK fluidic connections, and diaphragm air pumps. Auxiliary electronic control was used where required for pump and valve actuation. The in-house developed *FlowZilla*™ software provided automated sequence execution, enabling reproducible generator cycling between gas-phase ²²⁰Rn collection and aqueous-phase ²¹²Pb recovery.

Radiometric measurements were performed using a suite of detectors, including a 3-inch well style NaI(Tl) scintillation detector, a Wizard 2470 autogamma counter, a high purity germanium gamma spectrometer, and a dose calibrator. Radiometric data were corrected using geometry-specific detection efficiencies for columns, charcoal traps, and solution vials. The primary ²¹²Pb/²¹²Bi gamma emission region and the ²⁰⁸Tl 583 keV gamma emission were used as practical indicators of progeny activity, with ²⁰⁸Tl providing confirmatory data. When employing low-resolution NaI(Tl) scintillation detectors or the dose calibrator, measurements were taken under secular equilibrium conditions.

3.0 Results and discussion

The following subsections summarize the project accomplishments by Specific Objective. The emphasis is placed on the revised scope, because those revisions defined the practical success criteria for the completed effort [1, 7].

3.1 SO1. Refinement of thoron emanation source form factor

SO1 (Tasks 1-2) addressed the preparation and performance of $^{228}\text{Th}/^{224}\text{Ra}$ and ^{224}Ra based emanation sources. The sources needed to do two things simultaneously: retain the Th and/or Ra under practical handling conditions and release the short-lived Rn daughter efficiently into a carrier gas stream. Macroporous cation-exchange resins were therefore evaluated because they combine strong Th and Ra affinity, defined particle and column formats, and a pore structure that can facilitate Rn escape. Additionally, numerous other commercially available resins were evaluated, and several additional candidates possessing the two essential traits were identified.

Bio-Rad AG MP-50 strongly acidic cation exchange resin emerged as a convenient source material for the generator. This is because MP-50 resin is already employed in the preparation of the traditional wet column generator. As such, the generators in this study could be prepared using PNNL's existing automated generator production line [12-16, 20], which is currently used to supply ^{212}Pb wet column generators on behalf of the NIDC.

We also cataloged a number of alternate commercially available resins that could strongly retain either ^{228}Th or ^{224}Ra , and exhibited excellent ^{220}Rn emanation power. Our work showed that resin form factor, loading configuration, carrier-gas flow, temperature, and humidity all influence emanation performance. For polystyrene divinylbenzene-based resins (including AG MP-50), dry carrier-gas operation generally produced low emanation coefficients from resin beds, while humidified carrier gas substantially increased ^{220}Rn release (Figure 3). Depending on resin type and configuration, humidified conditions produced emanation powers near or above 90%, with several macroporous cation-exchange resin configurations approaching approximately 95-98% under optimized conditions. Other resins exhibited very high Rn emanation power without requiring moisture-rich carrier gas conditions.

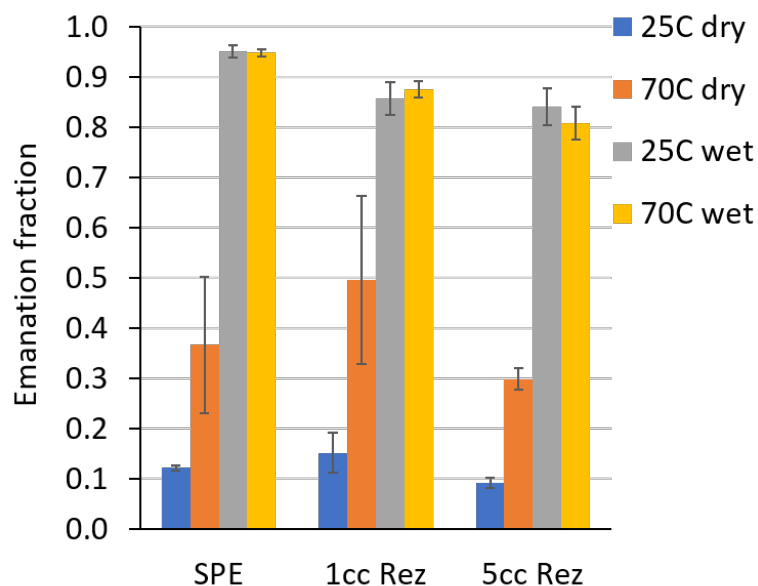


Figure 3. Measured Rn-220 emanation coefficients for three polypropylene column types packed with AG MP-50 macroporous cation exchange resin. Columns were operated at 25 °C and 70 °C, with (“wet”) and without (“dry”) the use of humidified N₂ carrier gas. The three columns are: SPE = 1 cm³ solid phase extraction tube kit; 1cc Rez = 1 cm³ Rezorian tube kit; 5cc Rez = 5 cm³ Rezorian tube kit (all supplied from Millipore Sigma, St. Louis, MO).

The project also addressed the practical issue of source containment. As activity increased, the team identified removable contamination associated with ²²⁰Rn leakage from early source housings, which has been observed elsewhere [21]. This observation led to a redesign of the generator housing using a solvent-welded polymethyl methacrylate (PMMA) enclosure and use of ²²⁰Rn-impermeable fluorinated ethylene propylene (FEP) / polyvinyl chloride (PVC) tubing [20]. The combined changes reduced ²²⁰Rn leakage and removable contamination by roughly three orders of magnitude relative to the early configuration. This was an important engineering step because the work scope required testing at multi-mCi ²²⁴Ra levels.

Task 2 was reduced from the originally proposed three-channel test stand to a single-channel capability. That reduction decreased testing throughput, but it did not prevent the project from generating the needed performance data. The single-channel configuration was sufficient to evaluate source behavior, carrier-gas conditioning, humidity effects, trap performance, and activity distributions across the source and downstream traps.

3.2 SO₂. Refinement of emanated thoron collection material and chamber

SO₂ (Tasks 3-4) focused on collection of the emanated ²²⁰Rn after it left the source. This step was a central design challenge because the same humidity that improves ²²⁰Rn emanation from the source can reduce Rn capture efficiency for some downstream media. The project therefore evaluated several possible capture approaches before converging on a practical room-temperature collection strategy.

Early experiments showed that simple pressure-gradient transport and collection across an evacuated distance were not productive, even when combined with a cooled collection surface. Carrier-gas transport was substantially more reliable and was therefore retained as the preferred Rn movement mechanism. Organic solvent capture and cryogenic collection were also evaluated. These approaches provided useful information and demonstrated that ^{212}Pb recovery from captured Rn was possible, but they were not ideal for a compact production generator because they introduced disadvantages such as flammability hazards, cost, complexity, and ^{212}Pb product recovery challenges.

3.2.1 Organic nanocage

A useful collection medium was the CC3 organic nanocage material. CC3 is a metal-free porous organic cage material whose cavity dimensions are well matched to heavy noble gases [18, 22, 23]. The project demonstrated that CC3 can collect ^{220}Rn from a flowing N_2 carrier gas at room temperature [18]. Capture performance depended on flow rate, CC3 mass, temperature, humidity, and residence time. As expected from the source studies, humidified carrier gas created a process conflict: it improved Rn release from the source but diminished CC3 Rn capture. Inline drying with a simple desiccant column was sufficient to restore CC3 capture behavior toward dry-gas performance and was much simpler than a chilled condenser approach.

The outcome of SO₂ was therefore not merely selection of a material. The project established the operating logic for the coupled source-and-collector system: humidify the carrier gas to maximize emanation from the ^{228}Th - or ^{224}Ra -bearing resin, then remove enough moisture before CC3 exposure to preserve high Rn capture. This balance between source performance and collection performance became one of the key process insights of the project.

3.2.2 Decay chamber

We also evaluated a ^{212}Pb collection method that had no reliance on engineered nanoporous media. We assessed a “decay chamber” in which ^{220}Rn would be pushed out of the emanation source via the N_2 carrier gas in low-volume tubing and then enter a significantly larger void space (chamber) before the carrier gas / ^{220}Rn was directed out of the space. The “residence time” of the ^{220}Rn in the decay chamber is dictated by the carrier gas flow rate and the volume of the decay chamber by the simple equation: $t_r = v \cdot R_f^{-1}$.⁷ As residence time increases, the fraction of the short-lived ^{220}Rn that decays inside the chamber likewise increases.

Inside the decay chamber, a fraction of the ^{220}Rn alpha decays to short-lived (144 ms) polonium-216 (^{216}Po) and then alpha decays to longer-lived ^{212}Pb . As these recoiling “hot” daughter atoms are non-gaseous, they quickly associate with the nearest surface – that being the chamber walls. The ^{212}Pb ends up on the chamber wall whether the ^{220}Rn atom decayed within the chamber void space or had associated itself on the chamber surface. Note that it is possible for ^{220}Rn atoms to diffuse into the chamber material and subsequently decay to ^{212}Pb – in this case, the ^{212}Pb is trapped within the material and is rendered unrecoverable.

⁷ Where t_r is residence time, v is decay chamber volume, and R_f is the rate of flow.

We assessed a range of materials to determine their viability as a decay chamber. Cylindrical candidate chamber materials were configured to receive a stream of ^{220}Rn in N_2 carrier gas for a sufficient duration to have substantial ^{212}Pb build-up. Next, we sequentially rinsed the surfaces with phosphate buffered saline, ammonium acetate, and finally hydrochloric acid to determine the ^{212}Pb yield with each leachate. The tested materials included quartz, polypropylene, polyethylene, fluorinated ethylene propylene (FEP) / perfluoroalkoxy alkane (PFA)-type fluoropolymer surfaces, polyether ether ketone (PEEK), PVC, acrylic, polycarbonate, ethylene-vinyl acetate (EVA), and a clear resin material produced by a 3D printer. The results showed that leachate-recoverable ^{212}Pb was strongly dependent on material composition, with fluoropolymer and polyethylene-type materials retaining less residual activity than several harder polymer or resin surfaces. These observations guided selection of lower-sorbing, lower-permeability materials for the closed-loop decay chamber design, with the goal of maximizing the fraction of ingrown ^{212}Pb that could be recovered into the product solution rather than lost to chamber-wall diffusion or sorption. Ultimately, we found that commercially available sterile / disposable polypropylene syringes (slightly modified for system use) were an excellent compromise between cost / simplicity and recoverable ^{212}Pb .

3.3 SO3. Enhanced collection of UHP ^{212}Pb in label-ready aqueous solution

3.3.1 Organic nanocage

SO3 (Task 5) addressed recovery and product quality. Once ^{220}Rn decays in or on the collection material, the desired ^{212}Pb must be transferred into a solution matrix suitable for radiolabeling. The project found that simple aqueous leaching was not sufficient for CC3-based collection, because much of the decay-generated ^{212}Pb was associated with the nanocage material. Complete dissolution of the CC3 collection bed was therefore required to release ^{212}Pb into solution.

When employing CC3 as the ^{220}Rn getter, the resulting aqueous process used automated fluid delivery, heated and oscillatory dissolution of the CC3 media using mineral acid, followed by lead-selective column isolation. The dissolved CC3 solution was passed through the column, which retained Pb while dissolved organic components and short-lived daughters were eluted to waste. The retained ^{212}Pb was then eluted using sodium acetate or ammonium acetate buffer. This approach preserved the fundamental advantage of gas-phase parent separation while yielding a practical aqueous product stream. However, this process was cumbersome and risked introducing metal contaminants into the ^{212}Pb product.

3.3.2 Decay chamber

Using the (modified) polypropylene syringe as a decay chamber, we demonstrated that high-purity ^{212}Pb could be recovered directly into either ammonium acetate or sodium acetate buffer solutions. For the ~ 2 mCi ^{228}Th -supported generator, three sequential 0.4 mL rinses of the chamber surfaces recovered an average of $88.0 \pm 2.2\%$ of the chamber-deposited ^{212}Pb into 1 M NH_4OAc at pH 7 and $87.0 \pm 2.9\%$ into 1 M NaOAc at pH 6, respectively.⁸ A subsequent ~ 6 mCi ^{228}Th -supported generator gave similar recoveries, with

⁸ A separate study demonstrated that recoverable ^{212}Pb from the polypropylene syringe across three consecutive 0.4 mL rinses using 1 M NH_4OAc (pH 5) was distributed at $\sim 78\%$ / $\sim 19\%$ / $\sim 3\%$.

88.6±3.9% in 1 M NH₄OAc and 86.1±1.7% in 1 M NaOAc, while decay-based purity measurements showed no detectable ²²⁴Ra or ²²⁸Th in the product fractions.

The revised scope removed the originally planned rad-controlled mass spectrometry-based metals-purity measurements of the collected ²¹²Pb product fraction. Product-quality assessment therefore focused on radionuclidic purity and chelation performance. The radionuclidic purity results were strong. In high-activity ²²⁸Th and ²²⁴Ra generator runs, delayed measurements of the product fractions showed no detectable parent nuclide. The resulting calculated decontamination factors were greater than 10⁸, with product radionuclidic purity of at least 99.9999975% for the evaluated product fractions.⁹

Metals purity was assessed by ²¹²Pb chelation performance via titration with TCMC. Aliquots of each ²¹²Pb product were added to acetate buffer solutions containing increasing amounts of chelator (typically in the nmole to pmole range).¹⁰ The ²¹²⁺²⁰⁸Pb content was calculated based on the time elapsed since the ²²⁰Rn emanation run initiation and the total ²¹²Pb activity in the product. The mixture was incubated at 38 °C for 40 minutes. The bound ²¹²Pb fraction was then evaluated by two independent methods. The first was iTLC, where TCMC-bound Pb remained at the origin while unbound Pb migrated with the mobile phase. The second used an aminopropyl (NH₂) resin cartridge method [19], where TCMC-bound Pb passed through the cartridge while unbound Pb was retained and later recovered with HCl.

Across three milkings of the highest activity (~18.7 mCi) ²²⁴Ra based emanation generator, the ²¹²Pb product (in acetate buffer) was titrated with TCMC. In assessing the bindable metals (M_B:²⁰⁸⁺²¹²Pb) ratio [19], we found that the TCMC titrations yielded values between 1.9 and 5.7. With the ideal ²⁰⁸⁺²¹²M_B:Pb ratio being “1”, we conclude that the ²¹²Pb product emerging from the polypropylene decay chamber is highly pure. Minute metal contamination can accumulate from reagent impurities, pipette tips, vials, and decay chamber walls; these impurity sources are difficult to avoid.

We also demonstrated that ²¹²Pb/TCMC chelation can happen concurrently with decay chamber nuclide product collection. Here, 10⁻⁶ M concentrations of TCMC were added to the acetate buffer used to remove ²¹²Pb from the decay chamber walls. The presence of TCMC did not enhance the recovery of ²¹²Pb from the polymer walls – it remained constant at 86.5% (Figure 5b). The interesting observation, however, was that the ²¹²Pb emerging from the acetate + TCMC mixture was bound at 99.8–100.0% by the iTLC method and 99.3–99.7% by the NH₂ cartridge method. These results are consistent with the separate bindable-metals titration assessments, which showed low Pb-equivalent bindable-metal inventories in the acetate product fractions. However, the direct-collection TCMC experiment went one step further by demonstrating that a fixed 10⁻⁶ M TCMC concentration was sufficient to complex essentially all recovered ²¹²Pb without a separate / subsequent labeling step.

3.4 SO4. Engineered emanation generator system for UHP ²¹²Pb

SO4 (Tasks 6-7) integrated the source, gas handling, ²²⁰Rn collection, and ²¹²Pb recovery components into a compact (approximately 9 x 12 inch footprint) automated generator platform. The final system operated in the intended two modes: gas-phase ²²⁰Rn transport and build-up of ²¹²Pb between an emanation source and a decay chamber in a “closed-loop”

⁹ Based on calculation of the minimum detectable activity (MDA) via the Currie Equation Currie [24].

¹⁰ Generally TCMC:²¹²⁺²⁰⁸Pb mole ratios across the titrations ranged from 0.1:1 to 100:1.

configuration (Figure 4a), followed by aqueous recovery of accumulated ^{212}Pb (Figure 4b). Automated pumps, valves, and scripted fluidic operations were used to improve repeatability and virtually eliminate direct worker interaction. The system was operated in closed-loop mode to build up ^{212}Pb in the decay chamber for ~24 h before ^{212}Pb collection was performed. As described in Section 3.3.2, ^{212}Pb was collected in three consecutive 0.4 mL rinses comprising either ammonium or sodium acetate solution.

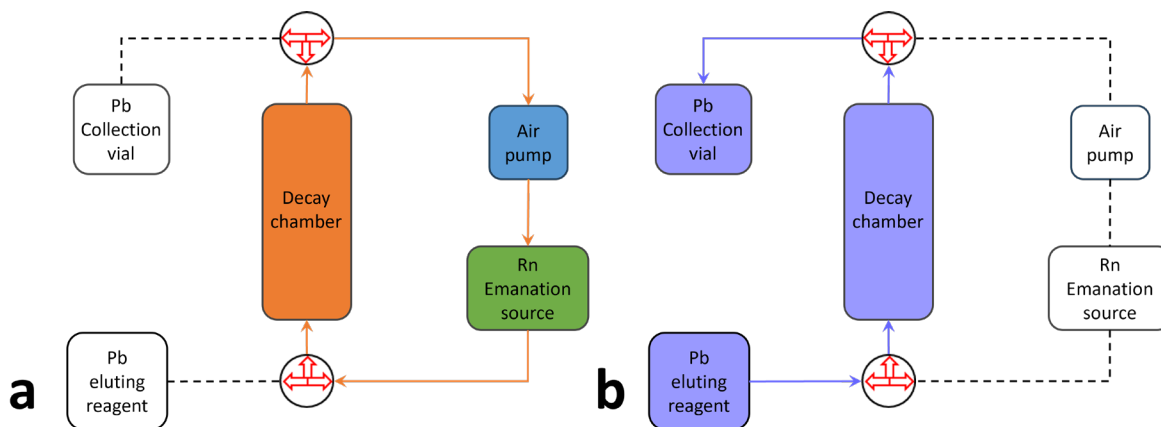


Figure 4. (a) Closed-loop collection of ^{212}Pb in a decay chamber by continuously cycling air (via an in-line pump) through a ^{220}Rn emanation source. (b) Recovery of ^{212}Pb in aqueous solution by passing Pb eluting reagent to a collection vial via the decay chamber.

Generator performance was evaluated across a range of source configurations and activities. ^{228}Th -supported sources were useful because they provided a longer-lived supply of ^{220}Rn for repeated testing and process debugging. These experiments showed repeatable ^{212}Pb recovery into buffered liquid fractions, with typical liquid recoveries around 87-90% of removable activity for approximately 0.2 mCi ^{228}Th configurations and about 86-88% for approximately 2 mCi ^{228}Th configurations. A larger ~6 mCi ^{228}Th -supported system produced similar liquid recovery fractions over longer collection intervals (extending over ~60 days).

The principal revised-scope demonstration used ^{224}Ra as the source nuclide; a generator prepared with 18.7 mCi ^{224}Ra exceeded the revised 10-15 mCi target activity. In ammonium acetate collection runs (Figure 5a), the liquid fraction averaged approximately 90.1% of recovered ^{212}Pb activity, and TCMC-containing ammonium acetate runs (Figure 5b) averaged approximately 86.5%.

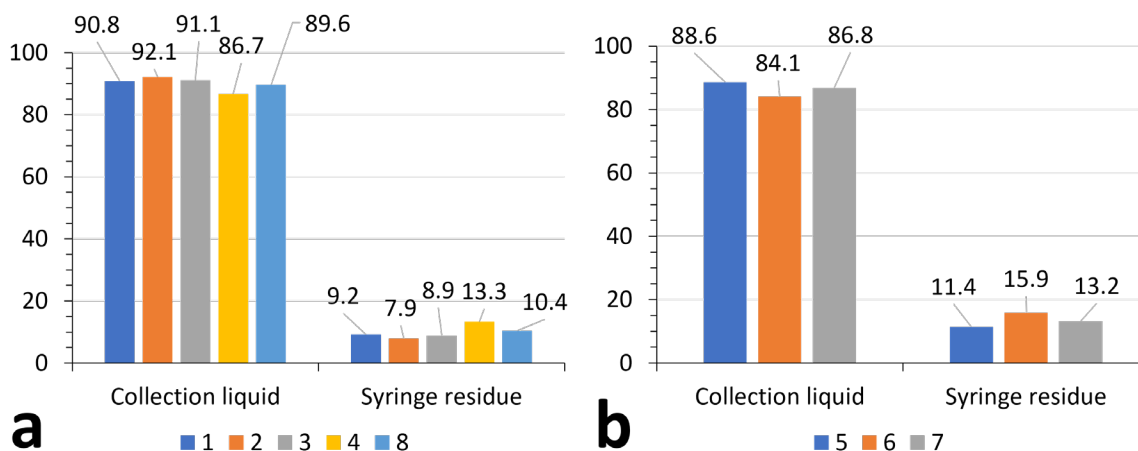


Figure 5. ^{212}Pb recoveries observed in collection liquid and what remained on the PP syringe decay chamber for an 18.7 mCi ^{224}Ra -based emanation generator. (a) 1 M ammonium acetate (pH 7) collection liquid. (b) Same ammonium acetate solution, but prepared with 10^{-6} M TCMC. The legend represents the ^{212}Pb collection day after the generator was prepared.

Details of the ^{212}Pb product quality (radionuclidic and metals purity) obtained by this system are described in Section 3.3.2. Calculated emanation rates across all the high-activity (^{224}Ra and ^{228}Th source) runs ranged from about 70.6% to 90.4%, and calculated overall ^{212}Pb product yields ranged from about 64% to 82%. The best observed overall ^{212}Pb yield was 81.8%.

These high-activity results compare favorably with the historical emanation-generator literature and demonstrate that the integrated PNNL platform can produce high-yield ^{212}Pb at relevant source activities. The result is especially important because the final yield reflects the product of many independent processing elements: source emanation, gas transport, ^{220}Rn collection / ^{212}Pb build-up, chamber recovery, and product transfer. The automated platform did not simply demonstrate an isolated material property – it demonstrated an end-to-end generator process.

3.5 SO5. Training and overall success against revised scope

SO5 was accomplished through direct participation of students and Research Associates in the experimental program. Their work was embedded across source preparation, gas and fluidic testing, radiometric measurement, automated-system operation, and data interpretation. This satisfied the proposal objective of providing hands-on training in isotope production, radiochemical purification, radioanalytical measurements, and generator-system development. The project facilitated the conversion of two Research Associates to junior staff members in the Nuclear Sciences Division of PNNL.

4.0 Conclusions

Overall, the project was successful against the revised scope. No Specific Objective was eliminated, and each was advanced to a defensible technical endpoint. The project demonstrated high ^{220}Rn emanation, practical Rn collection, recovery of ^{212}Pb into biomolecule-compatible solution, automated, end-to-end generator operation, and high-activity ^{224}Ra testing above the revised target range. The most important outcomes were the preparation of ^{212}Pb product with no detectable ^{228}Th or ^{224}Ra breakthrough in the evaluated high-activity product fractions (indicating high radionuclidic purity), and low bindable metals content – as determined by TCMC chelator titrations (indicating high purity from metal contaminants). These observations reinforce the original hypothesis that a “gas bridge” approach to ^{212}Pb production may be the ideal route to obtain an ultra-high purity radionuclide product.

In moving the emanation generator from concept towards routine utility, two important accomplishments are to be highlighted. First, one form of the emanation generator employs the same cation exchange resin employed in the traditional wet column format. As PNNL has previously established a fully automated ^{212}Pb generator production line to supply these traditional generators through the NIDC, we are likewise capable of producing the ^{220}Rn emanation version on the same line. Second, the automated “closed loop” ^{212}Pb dispensing system prototype that was designed and tested under this funding opportunity offers a clear path towards routine at-site ^{212}Pb generation via a simple, compact gas/fluid delivery platform.

Further optimization and investigation are warranted. Future work should focus on refining the “closed loop” gas/fluid delivery platform design to maximize simplicity and minimize construction cost and footprint. Additionally, it would be valuable to obtain expanded high-activity run statistics, evaluate long-duration system reliability, document ^{212}Pb labeling yield across a range of radiopharmaceutical products, and seek NIDC end user feedback on system performance and overall ease of use.¹¹ Also of interest is a formal evaluation of ^{228}Th source activity thresholds – to map performance degradation against activity level and time. Recyclability of spent ^{228}Th sources (elution of ^{228}Th from spent sources and transfer to fresh sources) should be evaluated. These needs represent the next step in maturing the technology. Despite these remaining needs, the central deliverable - an automated $^{228}\text{Th}/^{224}\text{Ra}/^{220}\text{Rn}$ and/or $^{224}\text{Ra}/^{220}\text{Rn}$ emanation generator concept capable of producing high-purity ^{212}Pb in a biomolecule-compatible solution - was achieved.

¹¹ To include an independent assessment of ^{212}Pb yield and radiolabeling performance vs. generator initial activity level and age.

5.0 References

- [1] M.J. O'Hara. "FOA LAB 20-2301 Proposal: Development of a $^{224}\text{Ra}/^{220}\text{Rn}$ emanation-based generator for high-purity ^{212}Pb production". PNNL. Richland, WA. 2020. p. 51.
- [2] M.J. O'Hara. "FOA LAB 16-1588 Proposal: Production of high-purity $^{212}\text{Pb}/^{212}\text{Bi}$ via gaseous transport of thoron: A $^{224}\text{Ra}/^{220}\text{Rn}$ emanation generator". PNNL. Richland, WA. 2016. p. 32.
- [3] M.J. O'Hara. System, emanation generator, and process for production of high-purity therapeutic radioisotopes. USA Patent US 11348702B2, May 31, 2022.
- [4] R.W. Atcher, A.M. Friedman, et al., An improved generator for the production of ^{212}Pb and ^{212}Bi from ^{224}Ra , Appl Radiat Isotop, 39 (1988) 283–286. 10.1016/0883-2889(88)90016-0
- [5] R.W. Atcher, A.M. Friedman, et al. Isotopic generator for bismuth-212 and lead-212 from radium. USA Patent US 4,663,129 A, May 5, 1987.
- [6] M. Li, X. Zhang, et al., Automated cassette-based production of high specific activity [$^{203/212}\text{Pb}$]peptide-based theranostic radiopharmaceuticals for image-guided radionuclide therapy for cancer, Appl Radiat Isotop, 127 (2017) 52–60. 10.1016/j.apradiso.2017.05.006
- [7] M.J. O'Hara. "Summary of changes to Proposal 76931 "Development of a $^{224}\text{Ra}/^{220}\text{Rn}$ emanation-based generator for high-purity ^{212}Pb production", under LAB 20-2301". April 4, 2022. PNNL. Richland, WA. 2022. p. 2.
- [8] J.M. Scaffidi-Muta, A.D. Abell, ^{212}Pb in targeted radionuclide therapy: a review, EJNMMI Radiopharmacy and Chemistry, 10 (2025) 34. 10.1186/s41181-025-00362-7
- [9] R. Zimmermann, Is ^{212}Pb Really Happening? The Post- $^{177}\text{Lu}/^{225}\text{Ac}$ Blockbuster?, J Nucl Med, 65 (2024) 176. 10.2967/jnumed.123.266774
- [10] Y. Berckmans, J. Kleynhans, et al., Lead radionuclides for theranostic applications in nuclear medicine: from atom to bedside, Theranostics, 16 (2026) 2887–2917. 10.7150/thno.126086
- [11] K.V. Kokov, B.V. Egorova, et al., ^{212}Pb : Production Approaches and Targeted Therapy Applications, Pharmaceutics, 14 (2022) 189. 10.3390/pharmaceutics14010189
- [12] M.J. O'Hara. Systems and Methods for Separating Radium from Lead, Bismuth, and Thorium. USA Patent US 11925879 B2, March 12, 2024.
- [13] M.J. O'Hara, G.B. Hall, et al. Systems and Methods for Producing Elements from Mixtures, Storage/Generation Vessels, and Storage/Generation Vessel Assemblies. USA Patent US 11999628 B2, June 4, 2024.
- [14] M.J. O'Hara, L.P. Boron-Brenner, Remotely-prepared $^{224}\text{Ra}/^{212}\text{Pb}$ generator columns: Process overview & recent performance evaluations, in: 2022 Lead-203/212 User Group Meeting - DOE Isotope Program, DOE Isotope Program, Virtual, 2022.
- [15] M.J. O'Hara, L.P. Boron-Brenner, et al., Recent activities in ^{212}Pb generator development at PNNL, in: 2020 Lead-212 User Group Meeting - DOE Isotope Program, DOE Isotope Program, Virtual, 2020.
- [16] M.J. O'Hara, L.P. Boron-Brenner, et al., Remotely-prepared $^{224}\text{Ra}/^{212}\text{Pb}$ generator columns: Process overview & recent performance evaluations, in: 2021 Lead-212 User Group Meeting - DOE Isotope Program, DOE Isotope Program, Virtual, 2021.
- [17] National Isotope Development Center. "Radium-224/ Lead-212 Generator". 2026 Available from: <https://www.isotopes.gov/products/lead>, Accessed May 25, 2026.
- [18] B. Scheibe, K. Krishnan, et al., Capturing the short-lived radon isotope Rn-220 with the porous organic cage CC3 – a potential sorbent for emanation-based Pb-212 generator systems [Manuscript submitted for publication], (2026)

- [19] M.J. O'Hara, N.J. Murray, et al., Hydroxamate column-based purification of zirconium-89 (^{89}Zr) using an automated fluidic platform, *Appl Radiat Isotop*, 132 (2018) 85–94. 10.1016/j.apradiso.2017.10.048
- [20] M.J. O'Hara, L.P. Boron-Brenner, et al., An automated triple-column method for the isolation of high-purity ^{224}Ra for use in ^{212}Pb generators; and development of an end-to-end remote ^{212}Pb generator packing station, in: 21st Symposium on Separation Science & Technology for Energy Applications, Knoxville, TN, 2023.
- [21] M. Pretze, H. Hartmann, et al., Different ^{212}Pb Generators and Its Radiation Safety Concerning ^{220}Rn (Thoron) Emanation, in: *Toxics*, 2025, pp. 462.
- [22] G. Zhu, C.D. Hoffman, et al., Engineering Porous Organic Cage Crystals with Increased Acid Gas Resistance, *Chemistry – A European Journal*, 22 (2016) 10743–10747. 10.1002/chem.201601659
- [23] L. Chen, P.S. Reiss, et al., Separation of rare gases and chiral molecules by selective binding in porous organic cages, *Nature Materials*, 13 (2014) 954–960. 10.1038/nmat4035
- [24] L.A. Currie, Limits for qualitative detection and quantitative determination. Application to radiochemistry, *Analytical Chemistry*, 40 (1968) 586–593. 10.1021/ac60259a007
- [25] F. Strassmann, Untersuchungen über den Zusammenhang zwischen Gitterstruktur und Gasdurchlässigkeit organischer Salze nach der Emaniermethode von Hahn, *Z. Physik. Chem. B*, 26B (1934) 362–372.
- [26] J.N. Gregory, J.F. Hill, et al., The diffusion of thoron in solids. Part 3-Diffusion and recoil in multimolecular films of barium stearate by emanating power measurements, *Transactions of the Faraday Society*, 48 (1952) 643–651. 10.1039/TF9524800643
- [27] J.N. Gregory, S. Moorbath, The diffusion of thoron in solids. Part II-the emanating power of barium salts of the fatty acids, *Transactions of the Faraday Society*, 47 (1951) 1064–1072. 10.1039/TF9514701064
- [28] J.B. Hursh, A.I. Lovaas, Preparation of a dry ^{228}Th source of thoron, *J Inorg Nucl Chem*, 29 (1967) 599–600. 10.1016/0022-1902(67)80312-9
- [29] S.P. Hassfjell, P. Hoff, A generator for production of ^{212}Pb and ^{212}Bi , *Appl Radiat Isotop*, 45 (1994) 1021–1025. 10.1016/0969-8043(94)90170-8
- [30] W. Wrasidlo, K.J. Mysels, Generation of lead-212 and radioimmunoconjugates for use in cancer therapy and the 'emanating power' of stearates, *Colloids & Surfaces A*, 186 (2001) 123–128. 10.1016/S0927-7757(00)00768-8
- [31] J.H. Norman, W.A. Wrasidlo, et al. Method and generator for producing radioactive lead-212. USA Patent US 5,038,046 A.
- [32] S. Hassfjell, A ^{212}Pb generator based on a ^{228}Th source, *Appl Radiat Isotop*, 55 (2001) 433–439. 10.1016/S0969-8043(00)00372-9
- [33] A.A. Artyukhov, P.N. Ivliev, et al., Developing a Prototype Diffusion Generator of the ^{212}Pb Radionuclide Based on the Emanation of ^{220}Rn from a ^{228}Th -Containing Ion-Exchange Resin, *Russian Journal of Physical Chemistry A*, 96 (2022) 1794–1799. 10.1134/S0036024422080039
- [34] P.P. Boldyrev, B.V. Egorova, et al., Physical and chemical processes on the ^{212}Pb radionuclide production for nuclear medicine, *Journal of Physics: Conference Series*, 1099 (2018) 012003. 10.1088/1742-6596/1099/1/012003
- [35] D.Y. Chuvilin, P.P. Boldyrev, et al. Method to produce radionuclide bismuth-212. Russia Patent RU2498434C1, Nov. 10, 2013.
- [36] A.A. Artyukhov, A.A. Artyukhov, et al., Development of a Prototype of a ^{220}Rn Gas Generator for Producing Radionuclide ^{212}Pb , *Nanobiotechnology Reports*, 18 (2023) 591–597. 10.1134/S2635167623600220
- [37] A.A. Artyukhov, A.A. Artyukhov, et al., Development of a ^{220}Rn Emanation Source Based on a Thin-Layer ^{228}Th Sorbent, *Nanobiotechnology Reports*, 18 (2023) 585–590. 10.1134/S2635167623600219

- [38] D.Y. Chuvilin, A.A. Artyukhov, et al. Method for producing radionuclide Pb-212 and device for its implementation. Russia Patent RU2784484C1, Nov. 28, 2022.
- [39] P.P. Boldyrev, A.I. Bortash, et al., $^{212}\text{Pb}/^{212}\text{Bi}$ Generator for nuclear medicine, Atomic Energy, 111 (2012) 422–427. 10.1007/s10512-012-9513-x
- [40] J.F. Kelly. Materials and processes for generating radioisotope. International Patent WO2023023731A1, Mar. 2, 2023.
- [41] R.H. Larsen. Production of highly purified ^{212}Pb . International Patent WO2021110950A1, Jun. 10, 2021.
- [42] R.G. Li, V.Y. Stenberg, et al., An Experimental Generator for Production of High-Purity (212)Pb for Use in Radiopharmaceuticals, J Nucl Med, 64 (2023) 173–176. 10.2967/jnumed.122.264009
- [43] A.A. Abbasi. Method for production of lead-212 isotope. USA Patent US 11383204 B1.
- [44] P.J. Nieuwland, D. Van Der Born, et al. System and method of the production and isolation of charged radionuclides. International Patent WO2023017122A1.

Appendix A

Table 1. Matrix of historical and current ^{220}Rn emanation generators in the published literature. See Table 2 for concise description of generator type.

Generator type		Source / Rn transport	^{212}Pb capture / recovery approach	Citation
1	Early Ba/Ra stearate thoron emanation sources	Ra or Th incorporated into Ba stearate films, precipitates, fatty-acid salts, or dry source assemblies; ^{220}Rn released by diffusion and/or recoil, with or without carrier gas	Source-material and thoron-source demonstrations rather than complete ^{212}Pb recovery generators	[25-28]
2	Static Ba stearate diffusion generators	^{228}Th coprecipitated with Ba stearate; passive ^{220}Rn diffusion into a spatially separated collection region	^{212}Pb deposited on a PE bottle surface or captured in a removable powder/sorbent region, followed by rinsing, dissolution, or removal of the collection medium	[29-31]
3	Carrier-gas Ba stearate generators with liquid Rn capture	^{228}Th /Ba stearate source; active carrier-gas transport	Low-temperature organic solvent capture followed by acid back-extraction and subsequent solution processing	[32]
4	Resin-supported emanation generators	^{228}Th or ^{224}Ra on ion exchange resin; passive or active ^{220}Rn transport	Downstream decay volume, tubing, or collection geometry, followed by rinsing or daughter-product recovery depending on design	[3, 33-35]
5	Hydrophilic membrane / thin-layer sorbent generators	^{228}Th impregnated into hydrophilic MFFK-3G fluoropolymer membrane or related thin-layer sorbent; active ^{220}Rn transport	Downstream decay or collection chamber, with ^{212}Pb recovered by rinsing or collection solution	[36-38]
6	Aqueous ^{228}Th -source generators	^{228}Th or mixed thorium isotopes dissolved in aqueous solution; active sparging / carrier gas	^{220}Rn allowed to decay in a long PTFE tube or downstream collection region, followed by solution rinsing / product recovery	[39]
7	Solid sorbent / dissolvable Rn-capture generators	^{220}Rn generated from an upstream source and captured in or on a solid collection medium	Urea, sugar, polystyrene beads, or low-temperature urea sorbent; sorbent dissolved or washed to recover ^{212}Pb	[3, 30, 31]

8	Porous inorganic / ceramic-support generators	^{224}Ra or ^{228}Th sorbed onto porous quartz wool or ceramic substrate; passive or active ^{220}Rn transport	Glass or other decay chamber rinsed with acid or other collection solution; product purity and recovery depend strongly on source immobilization and chamber design	[40-42]
9	Emerging commercial / patent decay-chamber systems	^{228}Th or ^{224}Ra source; active or passive ^{220}Rn transport depending on design	Decay chamber, electric-field-assisted collection, collection liquid, or other proprietary collection geometry intended to spatially separate source and product	[3, 40, 41, 43, 44]

Table 2. Generalized approaches across several ^{220}Rn emanation generator types summarized in Table 1.

Generator type	Summary of approach
1	These studies established Ba/Ra stearate and related long-chain fatty-acid salts as unusually effective thoron emanation materials. The work was primarily mechanistic or source-focused, demonstrating the importance of diffusion, recoil, crystal structure, and source preparation rather than providing a complete ^{212}Pb generator with defined product recovery.
2	These early proof-of-principle generator systems used the high emanating power of Ba stearate and passive diffusion of ^{220}Rn into a spatially separated collection region. They demonstrated the basic purity advantage of emanation-based ^{212}Pb production, but yields were limited by passive transport, collection geometry, and, in some cases, radiolytic degradation of the Ba stearate source.
3	Carrier gas was used to sweep ^{220}Rn from Ba stearate into a chilled organic solvent. This approach gave comparatively high Rn transfer and ^{212}Pb recovery, but the required liquid-liquid extraction, acid treatment, evaporation, and solution transposition made the product-recovery process operationally cumbersome.
4	These systems replaced Ba stearate with resin-supported ^{228}Th or ^{224}Ra , simplifying source preparation and potentially improving handling. Reported emanation performance was generally lower than Ba stearate or strongly dependent on water content, source geometry, and whether ^{220}Rn was transported passively or actively.
5	Thin, surface-loaded hydrophilic membranes or sorbents can provide short Rn diffusion paths and good immobilization of the parent isotope. Reported emanation efficiencies were high in several low-activity demonstrations, but the examples were generally at microcurie-level source loadings and therefore do not, by themselves, establish high-activity clinical scalability.
6	Liquid-source systems can reduce some solid-source radiolysis concerns and allow ^{220}Rn release by sparging. However, they introduce source-leakage concerns and may require long decay tubing, large rinse volumes, and additional solution processing before the ^{212}Pb product is suitable for use.
7	These systems capture ^{220}Rn or its decay progeny within a solid phase that is later dissolved or washed to recover ^{212}Pb . The approach can provide useful recovery, but the capture medium may introduce non-radioactive impurities or require additional purification to obtain a label-ready product.
8	Porous inorganic supports offer a potentially more radiolytically robust alternative to organic Ba stearate sources. Reported systems demonstrated moderate emanation or

	generator performance, but recovery and purity depend strongly on how well the parent isotope remains immobilized and how efficiently ^{212}Pb can be removed from the collection chamber.
9	Recent patent activity indicates renewed interest in emanation-based ^{212}Pb production. These concepts generally emphasize spatial separation of source and product, engineered decay chambers or collection fluids, simplified product recovery, and compatibility with automated or GMP-oriented production.

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