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How recycled uranium could secure a sovereign UK supply of lead-212 for targeted alpha therapy

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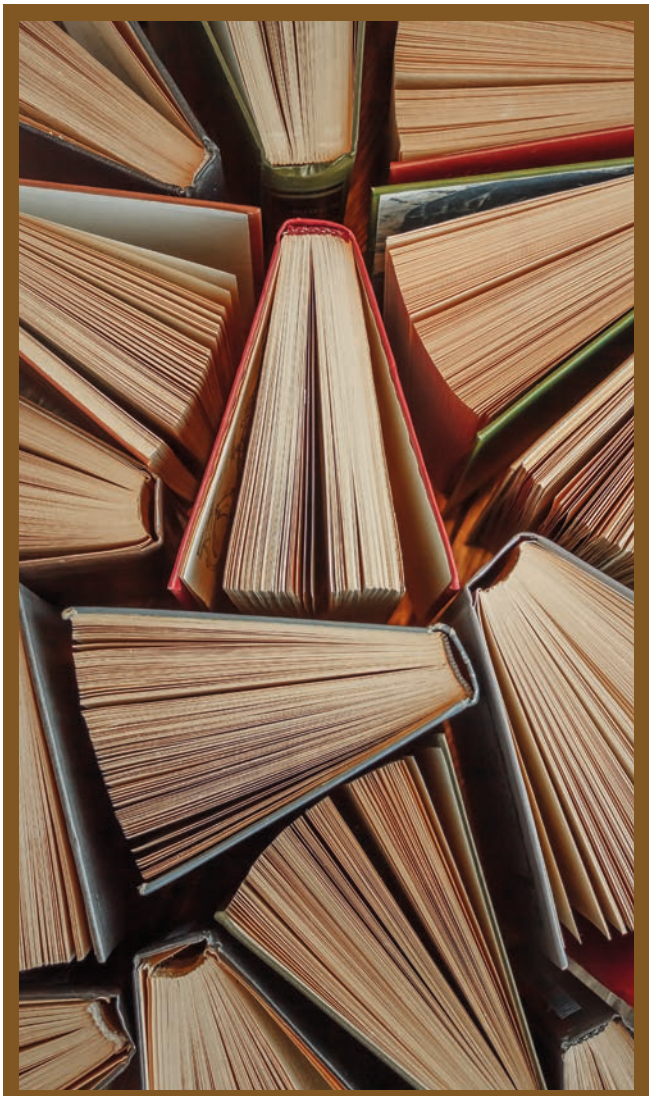

A production route for lead-212 for Targeted Alpha Therapy

Using the UK's nuclear legacy for cancer treatment

By **Howard Greenwood**, **Samantha Ree**, **Tim Tinsley**, **Rachel Roberts**, **Laura Maray**, **James Dinsley**

SUMMARY

- Targeted Alpha Therapy (TAT) is an up and coming cancer treatment with great potential to improve treatments for many types of cancer by delivering radioactive atoms directly to cancer cells where decay leads to cell death with minimal effect on surrounding healthy cells.
- Lead-212 (^{212}Pb) is recognised as a radionuclide likely to be effective for TAT. ^{212}Pb can be sourced from recycled (reprocessed) uranium (RU). The UK has significant stocks of RU; this could provide a sovereign source of ^{212}Pb for the UK.
- The United Kingdom National Nuclear Laboratory (UKNNL) has been developing a process to allow the extraction of ^{212}Pb from RU.

1. INTRODUCTION

Cancer is a condition where cells multiply uncontrollably; it is the second leading cause of death globally. Radiotherapy is a type of cancer treatment that uses radiation to kill cancer cells; approximately 50% of all cancer patients will receive radiotherapy during their course of treatment.[1] Targeted Radionuclide Therapy (TRT) is a form of radiotherapy where a radioactive atom is transported through the body gathering at tumour sites where decay of the atom then delivers a very high radiation dose to the cancer cells whilst minimising unwanted dose to healthy cells[2].

Targeting can be achieved in two main ways, firstly by using the inherent chemistry of the radionuclide within the body (for example, radium which can replace calcium in the hydroxyapatite component of bone resulting in uptake of radium at areas of new bone growth such as cancers), and, secondly, by attaching the radionuclide to a targeting component that is selective for specific chemical species carried by the targeted cancer cells (for example, cell surface receptors). Figure 1 shows a typical targeting construct of the latter type.

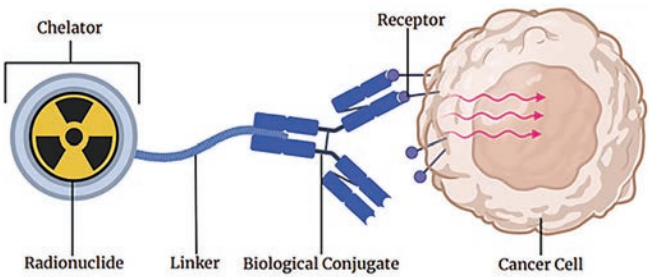

Figure 1. Components of a TRT radiopharmaceutical construct

Broadly speaking, there are two main types of TRT, one using alpha-emitting radionuclides (Targeted Alpha Therapy, TAT) and one using beta-emitting radionuclides (Targeted Beta Therapy, TBT).

TBT is perhaps more well established, currently, than TAT, but the latter offers considerable promise due to the high energy (typically 5-9 MeV) and very short range in vivo (40-100 µm) of an alpha particle which means it can deposit a huge amount of radiation energy in a small volume causing very heavy localised damage at the target site whilst minimising harm to surrounding healthy tissue. Hence, TAT is typically more suited to treating microscopic or small-volume diseases.

In terms of TAT, only a small number of radionuclides have suitable nuclear decay properties;[3] the most important factors are a high alpha energy and a suitable half-life (too short and bulk decay occurs during production, administration and in vivo transfer to the cancer cells, too long and patients excrete radioactivity for lengthy periods); generally, 45 mins to 30 days is considered the "Goldilocks" zone for radionuclides used in TAT. A recent study by the United Kingdom National Nuclear Laboratory (UKNNL) which also looked at some chemical aspects of the various nuclides with suitable half-lives, identified around 20 radionuclides of which terbium-149 (^{149}Tb), astatine-211 (^{211}At), ^{212}Pb/bismuth-212 (^{212}Bi), ^{223}Ra, thorium-227 (^{227}Th) and actinium (^{225}Ac)/^{213}Bi were considered among the most likely to be efficacious.[4]

1.1. Barriers to the use of TAT

Currently, the deployment of TAT in large scale treatment programmes is held back by a lack of supply of relevant radionuclides; indeed, even research and development suffers from a lack of access to these materials.

Typical routes to radionuclide production are irradiation of suitable targets in an accelerator or reactor (typically, though not exclusively, high neutron flux material test reactors). This is especially true in the UK where such accelerator/reactor infrastructure does not currently exist for large-scale industrial production of therapeutic radionuclides, especially those required for TAT.

Where the UK does have distinct advantages with regards the future of TAT are its industrial scale alpha handling facilities and access to a wide range of nuclear legacy materials, some of which contain radionuclides useful for TAT.

Recently, UKNNL has been investigating the recovery of radionuclides for both TAT and TBT from a variety of nuclear fuel cycle legacy materials which are under the charge of the Nuclear Decommissioning Authority (NDA).

1.2. Case Study: extraction and use of ^{212}Pb in TAT

One of the radionuclides identified as useful for TAT, and available from UK legacy material, is ^{212}Pb.

^{212}Pb is actually a beta-emitter with a half-life of 10.64 hrs, but it decays through two high energy alpha emitters, namely ^{212}Bi (half-life 1.009 hrs) and polonium-212 (^{212}Po) (half-life 0.3 µs) which have alpha energies of, respectively, approximately 6 and 9 MeV.

The half-life of ^{212}Po is far too short to permit any chemical manipulation to make a radiopharmaceutical containing it, let alone use it directly in a patient, and although there is some interest in the direct use of ^{212}Bi, with half-life of only an hour, its use is not practical except in some extreme scenarios. Typically, therefore, a radiopharmaceutical is made with ^{212}Pb as part of the atom-chelator-linker-targeting moiety "construct", with the 10.64 hr half-life of the ^{212}Pb allowing radionuclide production, transport over a reasonable distance, binding of the radionuclide into the construct in a radiopharmacy and administering to a patient; used in this context, the ^{212}Pb is termed a "nano-generator" or "in vivo generator" for the actual alpha emitting ^{212}Bi/^{212}Po.

^{212}Pb, ^{212}Bi and ^{212}Po are part of the natural thorium (^{232}Th) and uranium-232 (^{232}U) decay chains, as shown in Figure 2.

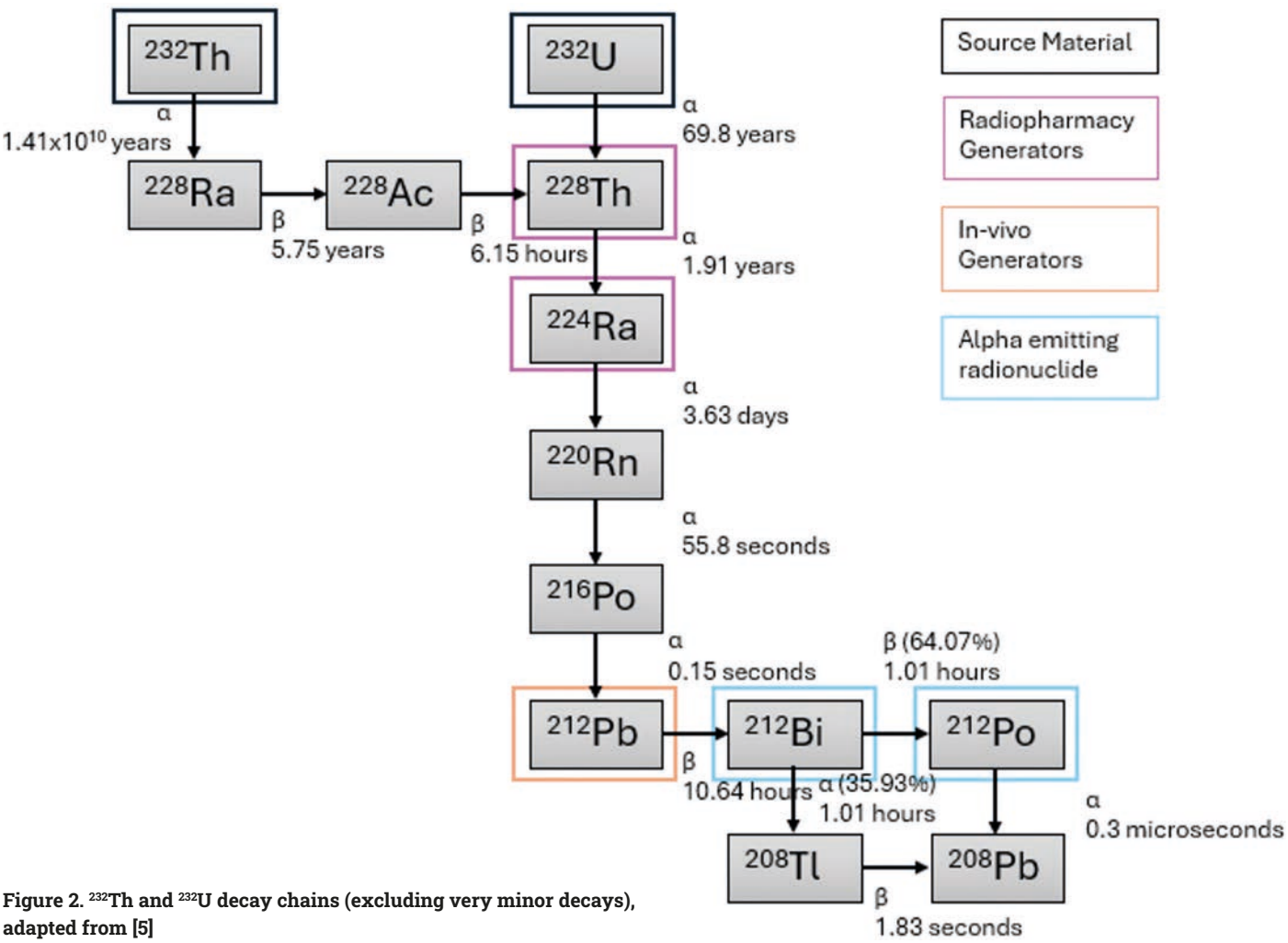

Figure 2. ^{232}Th and ^{232}U decay chains (excluding very minor decays), adapted from [5]

Orano-Med in France use large stocks of ^{232}Th to provide ^{212}Pb for use in TAT. [6] The UK has some small stocks of natural thorium that could usefully be employed to produce ^{212}Pb, but at nowhere near the scale of French production; the UK does, however, have large stocks of higher-burnup reprocessed (or recycled) uranium (RU) from THORP (THermal Oxide Reprocessing Plant) which contain ^{232}U (a uranium isotope which is not present in unirradiated uranium) at levels which are sufficient to supply tens of thousands of UK patient doses per annum.

In the case of natural thorium, the material must be sufficiently "aged" after a chemical purification, for grow-in of the decay chain (which is essentially controlled by the 5.75 year half-life of ^{228}Ra, the immediate decay daughter of ^{232}Th, meaning that a lengthy grow-in is required). In the case of RU, the ^{232}U content peaks about a decade after reprocessing, after which it decays with its almost 70 year half-life.

Direct production of ^{212}Pb from aged ^{232}Th or RU is not economically feasible at scale, since, given the concentration of ^{212}Pb at secular equilibrium (4000 Bq/g ^{232}Th and typically not more than 1500 Bq/g RU), large masses of thorium or uranium would need to be processed to recover a single patient dose (with repeated such processing after the ^{212}Pb has grown-back in).

^{224}Ra, which is further up the two decay chains also has potential for use in TAT, in two possible ways. Firstly, as an alpha emitting radionuclide in its own right, where it could be used as a simple solution of radium chloride for bone cancer treatment, and secondly as a "local generator" (or "radiopharmacy generator") for ^{212}Pb. In this latter context, recovery of the 3.63 day half-life ^{224}Ra and its transport to a point-of-use allows the radium based generator to be extracted ("milked"), repeatedly, for a week or two before decay reduces ^{212}Pb production to below useful levels. As with ^{212}Pb, direct recovery of ^{224}Ra is not practical from either ^{232}Th or RU (in the ^{232}Th case, ^{228}Ra would also be extracted).

^{228}Th can be used as a local generator in similar fashion, and with its much longer half-life forms long-lived generators that require many less radioactive transports, in a full scale treatment scenario, than in the cases of direct supply of ^{212}Pb or ^{224}Ra as a local generator. The disadvantage of a ^{228}Th based local generator, in the UK at least, is that the Radiation (Emergency Preparedness and Public Information) Regulations 2019 (REPPIR) restrict, in most practical scenarios, the amount of ^{228}Th that can be held at sites such as hospital radiopharmacies to levels likely too low for efficient use.

Extraction of ^{228}Th from ^{232}Th or RU does however offer a practical route to ^{212}Pb and/or ^{224}Ra recovery, by production of a ^{228}Th based "Thorium Cow" which can be milked, for considerable periods of time, for either or both desired radionuclides. Given the high specific activity of ^{228}Th, only very small masses of ^{228}Th are required to yield patient scales doses of ^{212}Pb, greatly reducing processing scales compared to those required for direct extraction from starting materials.

Extraction of ^{228}Th from ^{232}Th, directly, requires a difficult isotope separation and such is generally not considered practical for thorium; chemical separation of radium from the thorium (^{232}Th/^{228}Th) recovers both ^{228}Ra and ^{224}Ra which are then held (the latter decays away quite quickly) for some time until sufficient ^{228}Th has grown-in to the decaying ^{228}Ra, at which point a second chemical separation of radium and thorium yields pure ^{228}Th.

In the case of RU, chemical separation of thorium from uranium recovers ^{228}Th plus ^{234}Th (immediate daughter (i.e. decay progeny) of ^{238}U, at approximately 10x the ^{228}Th activity), ^{231}Th (immediate daughter of ^{235}U) and ^{230}Th (from the ^{238}U/^{234}U decay chain). ^{231}Th has a half-life of only 1.063 days and quickly decays away, whilst the very long half-life ^{230}Th is present only at undetectably low concentration having been separated from uranium during ore processing/ore concentrate refining and, due to its 75600 year half-life, it does not grow-in to any significant amount on the timescales involved in human processing of uranium.

^{234}Th (half-life 24.1 days) largely decays away across 6 months or so, but, since it decays via the very short half-life protactinium-234m (^{234}mPa) to the very long half-life ^{234}U, no detectable grow-in of additional ^{230}Th (or its daughters such as ^{226}Ra, ^{214}Pb, ^{210}Pb, ^{210}Po etc occurs (as with ^{230}Th, almost all of each of these daughters would also have been removed on initial processing of uranium ore/concentrate).

Thus, the recovered ^{228}Th can be repeatedly milked for ^{212}Pb and/or ^{224}Ra without confounding isotopes of either being present in any remotely meaningful concentration.

It is worth noting that, as ^{208}Pb (a stable lead isotope) is the end product of the ^{232}Th and ^{232}U decay chains, that ^{208}Pb competes with ^{212}Pb for incorporation to the radiopharmaceutical construct and such stable bound "cold" lead competes with bound "hot" lead for binding sites on tumours; this essentially means that as ^{212}Pb and ^{208}Pb grow-in to a Thorium Cow or ^{224}Ra based local generator there is a period where the ^{212}Pb/^{208}Pb ratio is optimal. Grow-in of 1 day (which is very convenient operationally) produces a near optimal ^{212}Pb/^{208}Pb ratio.[7]

^{212}Pb administered to a patient can potentially be tracked using its gamma emissions (at 75-91 keV and 238.6 keV) and Single-Photon Emission Computed Tomography (SPECT) imaging; this allows clinicians to apply "theranostics" (imaging 212Pb distribution during treatment.[8]

2. UK PRODUCTION ROUTE FOR ^{212}PB FROM RECYCLED URANIUM

Whilst fission based nuclear power is the main concern of UKNNL, Health and Nuclear Medicine (H&NM) is one of the organisation's "Focus Areas"; this has arisen since the UK nuclear power programme has produced a number of materials from which radionuclides useful in H&NM can be extracted. Additionally, UKNNL has facilities and expertise useful in helping establish a supply chain for these radionuclides.

UKNNL have been developing a process to recover ^{212}Pb for TAT from RU. The process, which can be operated in a variety of ways, depending on the desired aim, essentially, in the first instance, makes use of the well-known fact that thorium (as a small, highly charged Th^{4+} ion which is only poorly hydrolysed in acidic solution) is more strongly absorbed onto certain ion exchange resins than almost any other species.

In this process, shown in outline in Figure 3, RU is dissolved in nitric acid to a specific composition of uranyl nitrate and nitric acid and passed through a preconditioned ion exchange column; uranium, which is present at concentrations many orders of magnitude higher than thorium, occupies most of the ion exchange sites very quickly but as thorium can displace uranium,

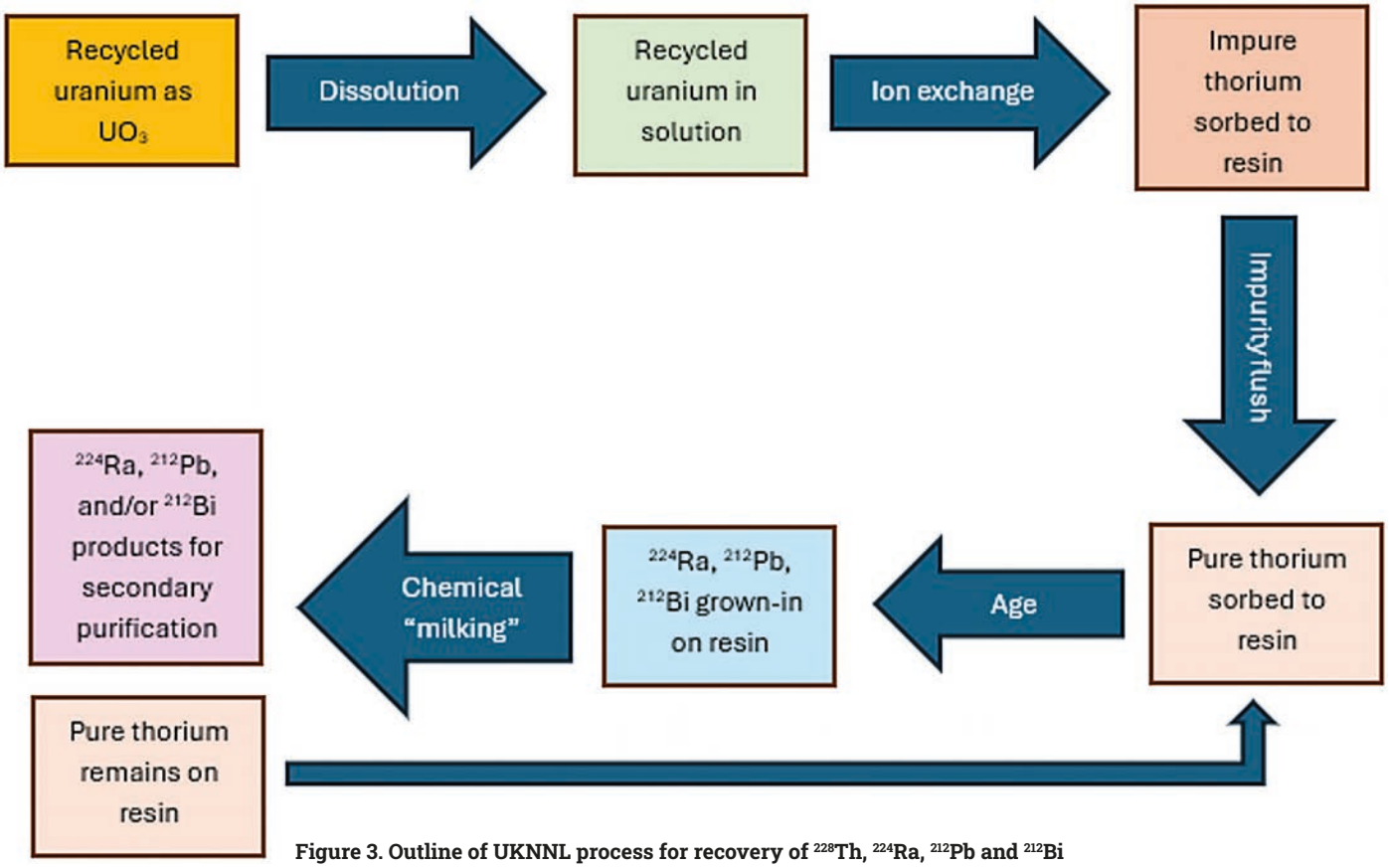

Figure 3. Outline of UKNNL process for recovery of ^{228}Th, ^{224}Ra, ^{212}Pb and ^{212}Bi

this does not prevent a high level of thorium uptake.

The loaded column (which can be loaded to different levels for different purposes) is then subjected to chemical flushing to remove uranium (and any other sorbed metal ions, such as trace actinides and fission products, and grown-in uranium daughters such as radium, polonium, lead, bismuth, thallium and so on) leaving a highly pure "Thorium Cow".

The Thorium Cow can then be held and "milked" regularly and repeatedly for grown-in ^{212}Pb and/or ^{224}Ra (and, if desired, ^{212}Bi).

A UKNNL laboratory rig set up for four MBq scale individual Thorium Cows is shown in Figure 4.

Column eluates from this process containing ^{212}Pb or ^{224}Ra are then typically evaporated to dryness, the (tiny mass) of dry solid treated to oxidise and remove organic material, and then the remaining (inorganic solid) redissolved in a very small volume of liquor (0.5-2 cm^3 is typical) for "secondary purification" (generally also carried out by ion exchange using analytical type resins) and/or local generator production with the aim that 99.9 % of the radioactivity present in the final lead product is due to ^{212}Pb and that "stable metals" (zinc, copper, non-radioactive lead, etc (uranium is also included)) are not present at more than 1 $\mu g/cm^3$ each.

Figure 4. Ion exchange rig based on four individual "Thorium Cows" used for the recovery of ^{228}Th, ^{224}Ra, ^{212}Pb and ^{212}Bi

The final ^{212}Pb product can be supplied as a solid, or as a solution ready for radiolabelling (typically weak hydrochloric acid or ammonium acetate is used for this latter).

GMP (Good Manufacturing Processes) suitable for the production of medical radionuclides can be introduced post-evaporation at much smaller scale than at the initial semi-industrial RU treatment and eluate evaporation stages.

Thorium Cows can be produced and operated in "large, dilute" forms which are long-lived in terms of use, but which require relatively large volumes of eluate, or in more concentrated forms but where radiation damage to resins may shorten the operational life of the Thorium Cow. UKNNL has operated "large, dilute" Thorium Cows in a laboratory setting to approaching 2 years of age before seeing evidence of resin degradation (resins are deliberately selected for durability).

The process could also be used to produce ^{228}Th as a relatively long-lived product for transfer to locations away from the initial production site, allowing Thorium Cows (or thorium based local generators) to be produced elsewhere.

An important part of the process is that the uranyl nitrate liquor (UNL) can be repeatedly recycled to recover additional ^{228}Th since, after extracting thorium, storing the liquor allows the 1.912 year half-life ^{228}Th to grow back in; combining this grown-in thorium with thorium remaining undecayed on any Cows made from it means that only a small top-up of "fresh" RU (to compensate for slight loss of ^{232}U due to its nearly 70 year half-life) is required to allow a fresh Cow to be made. Current UKNNL work is using RU based UNL on its third recycle through the ion exchange process.

2.1. Current UKNNL operations

UKNNL are part of a consortium carrying out a 3.5 year United Kingdom Research and Innovation (UKRI) Sustainable Medicines Manufacturing project (Project Alpha 10.6); this project aims to supply, regularly, ^{212}Pb, initially directly, and later via ^{224}Ra local generators, to the Medicines Discovery Catapult (MDC) who will use it to test targeting agents produced by various companies within the consortium. Under this project UKNNL will also work with Cyclife Aquila Nuclear to develop a ^{224}Ra based generator. This production will mean that UK sourced material can be used in TAT research and development, easing supply issues for radiopharmaceutical development. The UKNNL process is considered highly scalable to levels that could produce large numbers of patient doses using techniques and equipment already familiar to the UK nuclear industry.

HOWARD GREENWOOD

Howard is a Principal Scientist at UKNNL with over 40-years' experience in radiochemical separations across the uranium fuel cycle, including fuel production operations and effluent, waste, and residue treatment at theoretical and laboratory stages, though pilot plant operation to design, commissioning and operation of full scale plant.

SAMANTHA REE

Samantha is a radiochemist within the Waste and Residue Processing team at UKNNL and largely focuses on the treatment of legacy materials pertinent to the production of radionuclides for nuclear medicine. Samantha was awarded an Industrial Fellowship with the Royal Commission of the Exhibition 1851 where she has received financial support to complete a PhD at the University of Manchester.

TIM TINSLEY

Tim is a chartered Chemical Engineer with over 30-years' experience working in the nuclear industry. He leads two developing areas for UKNNL: nuclear systems for space power, and radioisotopes in support of health & nuclear medicine, where he provides innovative thought leadership to establish new applications of the fuel cycle.

REFERENCES

[1] Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and Radiation Therapy: Current Advances and Future Directions. Int J Med Sci. 2012;9(3):193–9.

[2] "In Conversation with Jane Sosabowski", Nuclear Future, Volume 18, Issue 4, July-August 2022, pages 34-42.

[3] "Selection of radionuclide(s) for targeted alpha therapy based on their nuclear decay properties", Ree SM, Greenwood H, Young JD, Roberts RFC, Livens FR, Heath SL, et al. Nuclear Medicine Communications [Internet]. 2024 Mar 11; available from: https://journals.lww.com/10.1097/MNM.0000000000001832

[4] "Overview of the Most Promising Radionuclides for Targeted Alpha Therapy: The 'Hopeful Eight'", Eychenne R, Chérel M, Haddad F, Guérard F, Gestin JF. Pharmaceutics. 2021 Jun 18;13(6):906.

[5] "Minimising the impact of stable 208Pb on recovery of 212Pb from a generator", Rachel Roberts, Tim Carthy, Jennifer Young, Temi Awogboro, Howard Greenwood, Jane Sosabowski, Scott Heath, and Francis Livens, EJNMMI Radiopharmacy and Chemistry, 30th July2025.

[6] https://www.oranomed.com/en/industrial-platform

[7] Plompen AJM, Cabellos O, De Saint Jean C, Fleming M, Algora A, Angelone M, et al. The joint evaluated fission and fusion nuclear data library, JEFF-3.3. Eur. Phys. J. A. 2020 Jul;56(7):181

[8] Griffiths MR, Pattison DA, Latter M, Kuan K, Taylor S, Tieu W, et al. First-in-Human 212Pb-PSMA-Targeted α-Therapy SPECT/CT Imaging in a Patient with Metastatic Castration-Resistant Prostate Cancer. J. Nucl. Med. 2024 Apr 1;65(4):664.

RACHEL ROBERTS

Rachel is a radiochemist with over 10-years' experience in carrying out R&D within the nuclear industry, currently focussed on the extraction of alpha emitters from legacy materials. Rachel is a Technical Lead in Health and Nuclear Medicine at UKNNL, leads the UKNNL Core Science Theme for research into medical radionuclides, and has been the UKNNL lead within the EU SECURE programme.

LAURA MARAY

Laura is a radiochemist within the Health & Nuclear Medicine team at UKNNL, with experience in novel drug development from her PhD. Laura works on the extraction of medicinal radionuclides from legacy materials, in particular taking the lead on the ^{224}Ra based generator work associated with the UKRI Project Alpha 10.6.

JAMES DINSLEY

James is a radiochemist within UKNNL's Health & Nuclear Medicine team, specialising in the separation and quantification of radionuclides from legacy nuclear materials for use in the medical sector. James is the lead gamma spectroscopist of the team and also provides technical expertise towards radioecology projects at UKNNL.