Radiochemical Separation

In Medical Radionuclide Production: Experiences and Challenges

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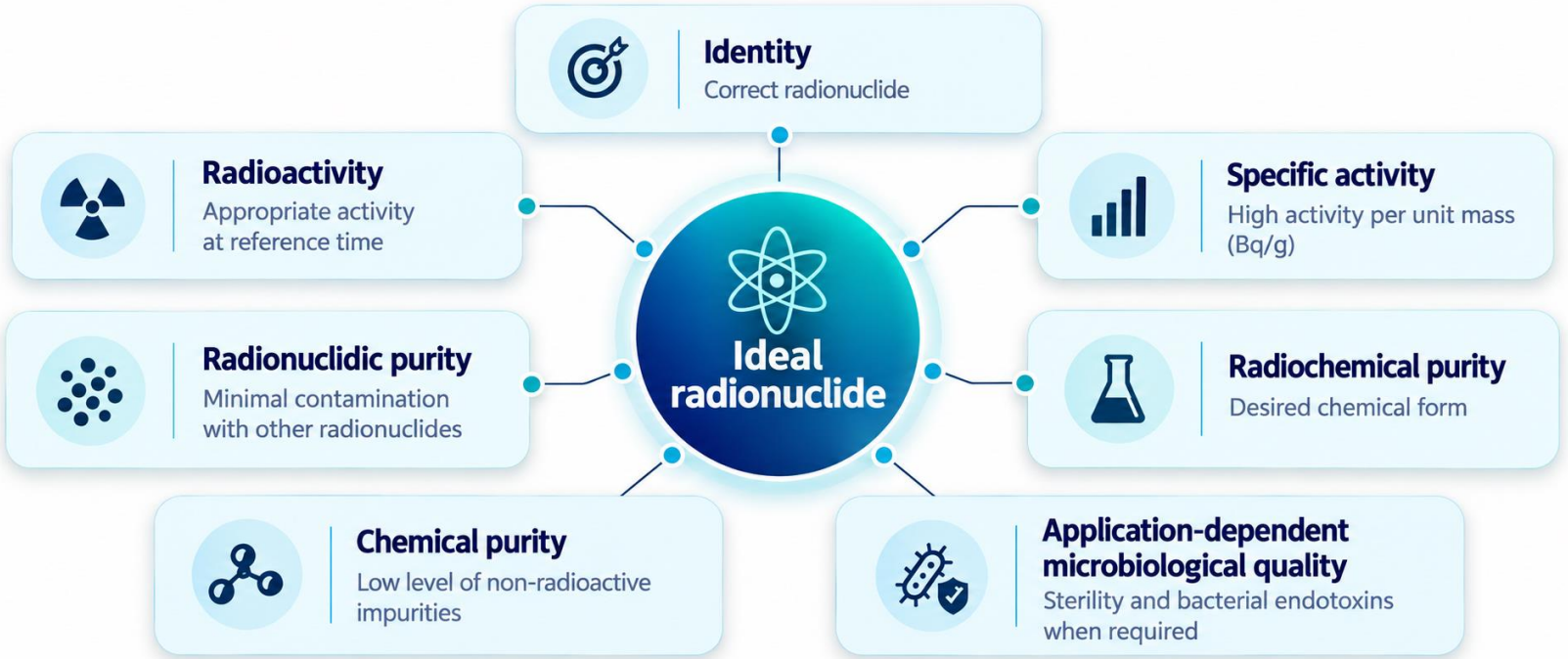
October 22 - 23, 2026,
Kraków, Poland



Perfect radionuclide for medical application

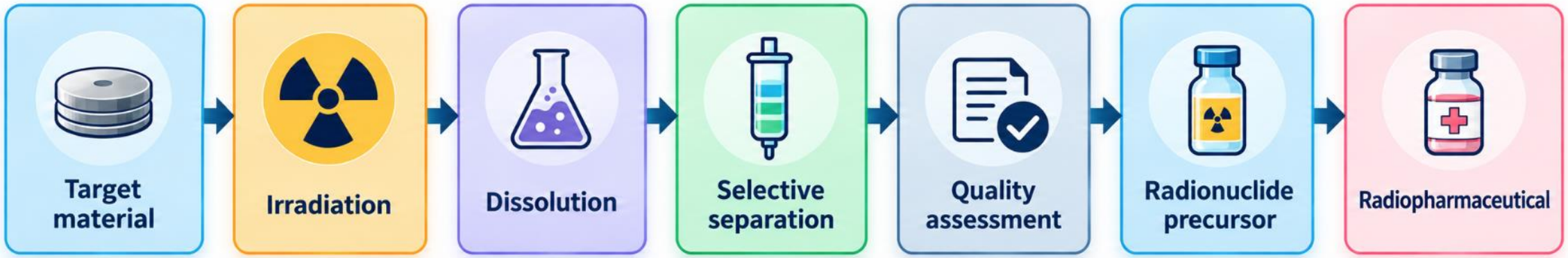
Key quality attributes of radionuclide precursors

European Pharmacopoeia in the general monograph on Radiopharmaceutical Preparations (Ph.Eur. 0125) defines a **radiopharmaceutical precursor** as any radionuclide produced for radiolabeling of another substance before administration



High specific activity / no-carrier-added radionuclides enable lower administered masses of radiolabelled compounds.

The central challenge: from an irradiated target to a usable precursor



What we want

High radionuclidic and chemical purity, high specific activity, useful activity concentration, and suitability for radiolabelling.

What we actually handle

Large excess of target material, activation by-products, trace metal impurities, and time-dependent radioactive decay.

Radiochemical separation is one of the most critical steps because it directly affects the purity, recovery yield, and quality of the final product.

Radiochemical techniques for separating radionuclides from irradiated targets



Precipitation

- Based on differences in solubility
- Useful for bulk target separation
- Risk of losses by occlusion / entrainment



Solvent extraction

- Selective transfer into an immiscible organic phase
- Simple and adaptable to remote operation
- Generates organic radioactive waste



Extraction chromatography

- Extractant fixed on a solid support
- Fast and highly efficient
- Lower sorption capacity than solvent extraction



Ion exchange

- Separation based on ion affinity / charge interactions
- High efficiency and reproducibility
- Limited selectivity for very similar ions



Electrolysis & electrodeposition

- Based on differences in electrode potential
- Can concentrate the product; easy to automate
- Applicable only to suitable electrochemical systems



Thermal separation

- Uses differences in volatility
- Effective for volatile radionuclides
- Requires precautions to prevent radioactive losses

There is no universal separation method. The choice depends on the radionuclide, target material, production route and final application.

In practice, separation processes are often combined into multistep protocols: primary separation, fine purification, and pre-conditioning

^{99m}Tc from low-specific-activity ^{99}Mo

Why a conventional $^{99}Mo/^{99m}Tc$ generator cannot simply accommodate a much larger mass of Mo?

Fission ^{99}Mo

> 370 TBq/g > 10,000 Ci/g

^{235}U fission → **high specific activity ^{99}Mo**

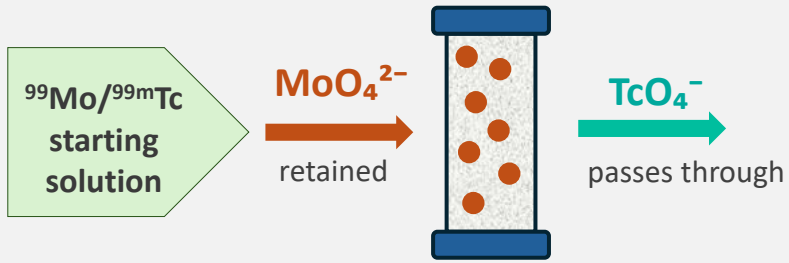
Alternative ^{99}Mo

~ 370 GBq/g ~ 10 Ci/g

$^{98}Mo(n,\gamma)^{99}Mo$
$^{100}Mo(\gamma,n)^{99}Mo$

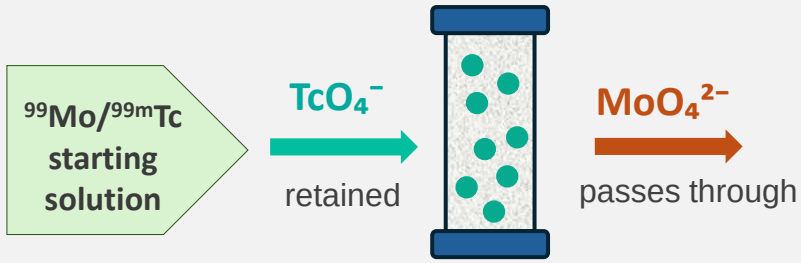
→ **low specific activity ^{99}Mo**

Conventional $^{99}Mo/^{99m}Tc$ generator



Capacity only ~2–20 mg Mo/g Al_2O_3 → impractical columns for LSA ^{99}Mo

Reverse $^{99}Mo/^{99m}Tc$ generator



Retention of trace ^{99m}Tc instead of bulk Mo → no need for high Mo sorption capacity

Reverse the selectivity: capture trace ^{99m}Tc instead of retaining bulk ^{99}Mo

TK202 resin reverse generator: selective Tc retention and Mo reuse

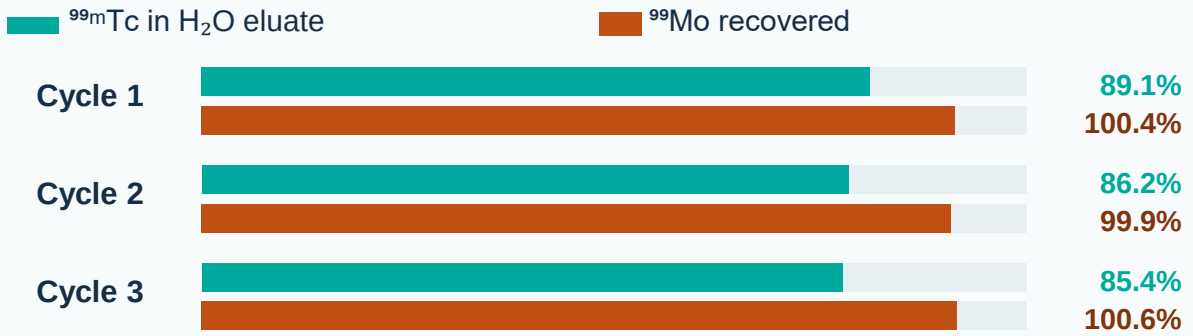
An example of single-step extraction chromatography

Experimental conditions:

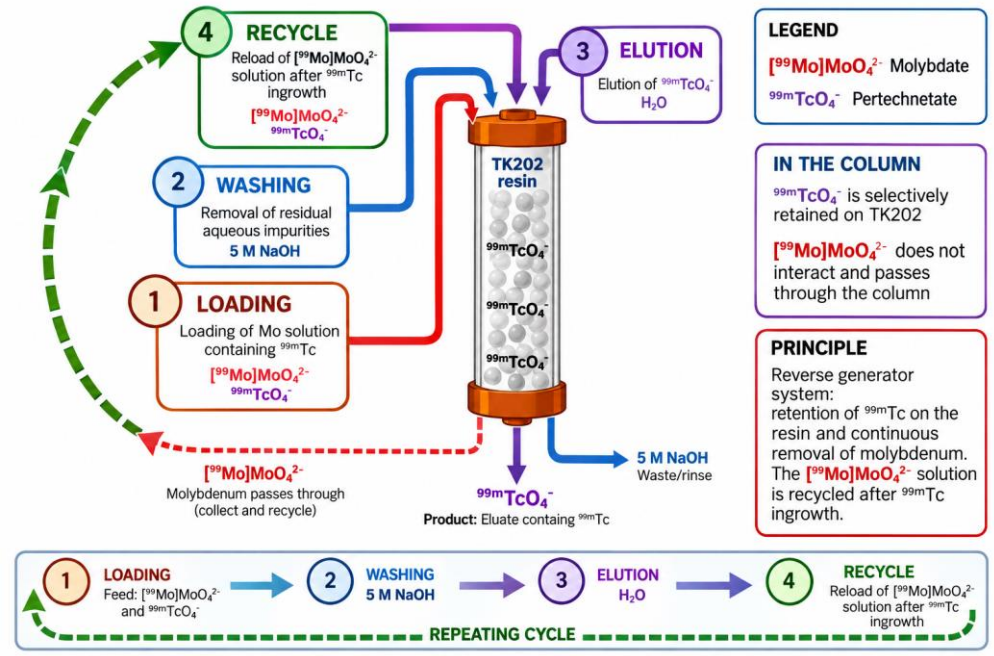
- ^{99}Mo activity: ~20 MBq
- Stable Mo mass: 220 mg
- TK202 resin mass: 200 mg
- Medium: 5 M NaOH

Three consecutive separation cycles

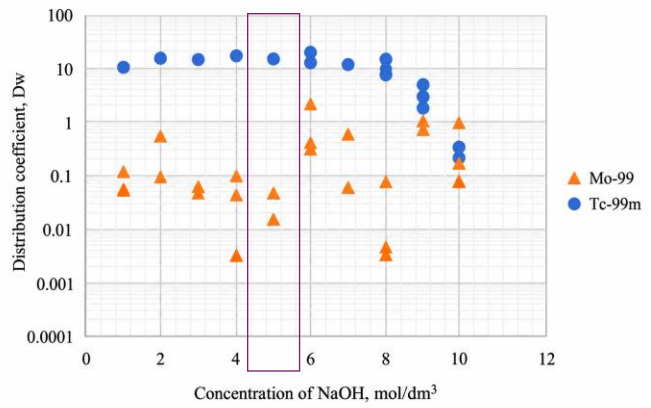
Activity recovered (% of loaded activity)



Repeated ^{99m}Tc recovery from the same recycled molybdenum solution

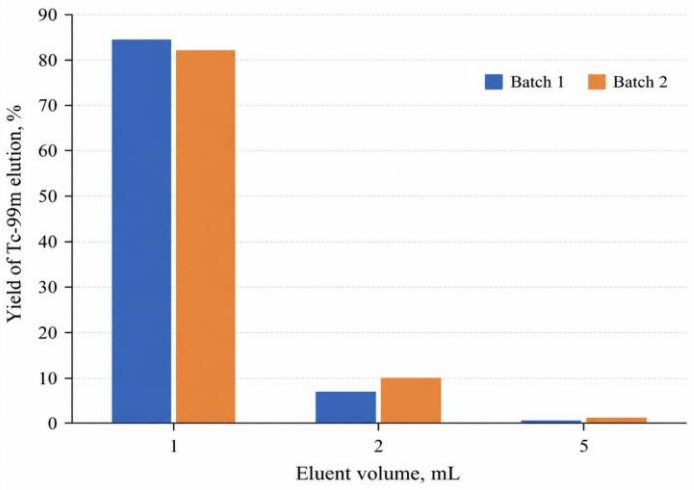


Distribution coefficients of ^{99m}Tc and ^{99}Mo on TK202 resin as a function of NaOH concentration



5M NaOH

Elution profile of ^{99m}Tc from TK202 resin using water as eluent



Cieszykowska et al., J Radioanal Nucl Chem (2026), DOI: 10.1007/s10967-026-11003-x

T½ = 3.97 h | β⁺ emitter | γ emission | PET imaging | Theranostic pair with ^{47}Sc

^{44}Sc separation from calcium targets

^{44}Ca (p,n) ^{44}Sc

Two routes to isolate trace Sc(III) from a large excess of Ca(II)

ROUTE A — $Sc(OH)_3$ precipitation

1	Target dissolution	3 M HCl
2	Precipitate $Sc(OH)_3$	pH 8.2–9.0
3	Filter + re-dissolve	0.5 M HCl
4	Cation-exchange purification	AG50W-X4

89 ± 9% recovery; n = 6

ROUTE B — UTEVA extraction chromatography

1	Target dissolution	11 M HCl
2	Retain Sc(III) on UTEVA	Ca passes
3	Elute retained ^{44}Sc	H_2O
4	Cation-exchange purification	AG50W-X4

93% recovery

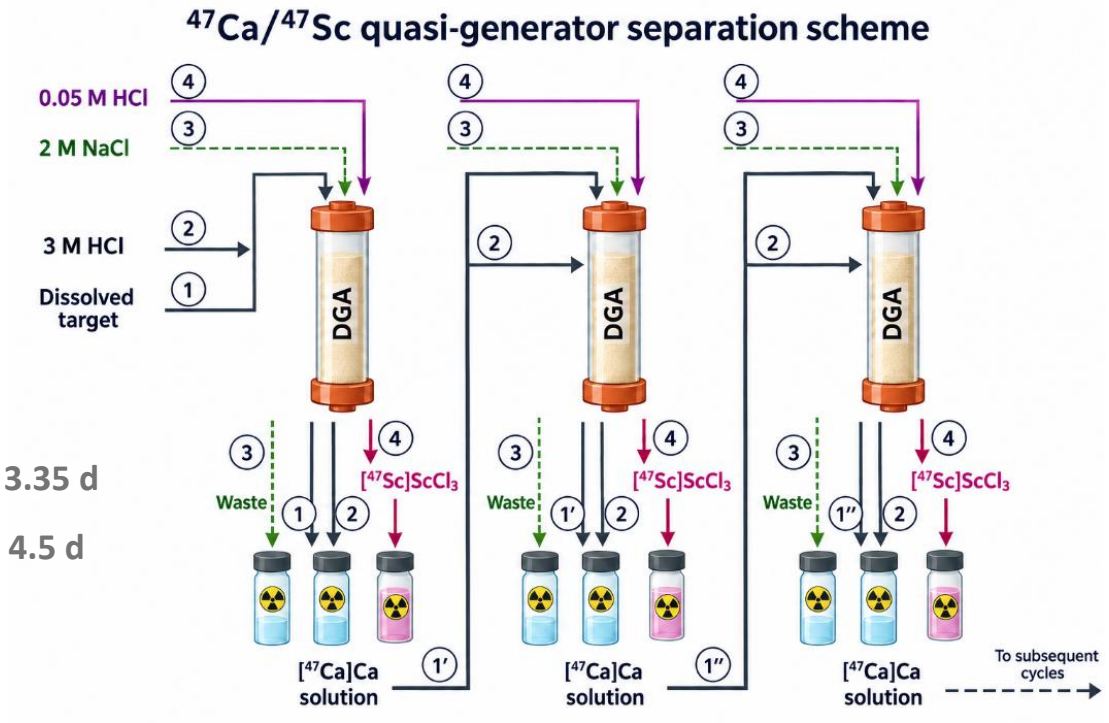
COMPARISON OF SEPARATION METHODS: Precipitation offers milder chemical conditions (3 M HCl) but variable recovery (89 ± 9%), while UTEVA provides 93% recovery but requires highly concentrated HCl (11 M).

T½ = 3.35 d | β⁻ emitter | SPECT imaging | Targeted radionuclide therapy | Theranostic pair with ^{44}Sc

Radionuclide quasi-generator system ^{47}Ca/^{47}Sc

Isolation of trace Sc(III) from a large excess of Ca(II)

^{46}Ca (n,γ) → ^{47}Ca (β⁻) → ^{47}Sc



^{47}Sc $T_{½}$ = 3.35 d

^{47}Ca $T_{½}$ = 4.5 d

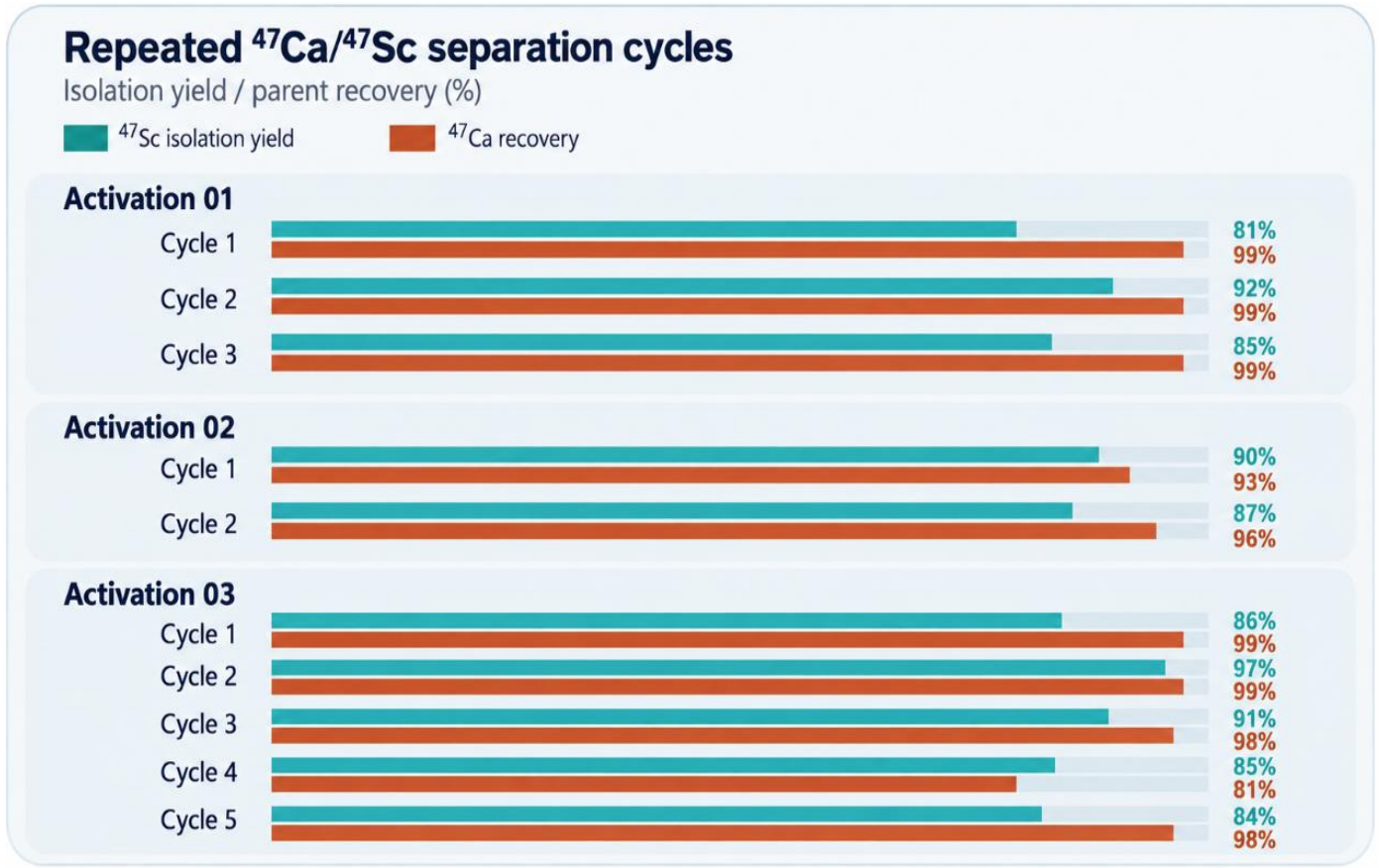
Why is this system challenging?

1. Trace daughter ^{47}Sc in a large excess of parent ^{47}Ca
2. Repeated daughter recovery over multiple cycles
3. Preservation of the ^{47}Ca parent fraction for further ingrowth
4. High ^{47}Sc recovery with minimal ^{47}Ca breakthrough
5. Eluate suitable for radiolabeling

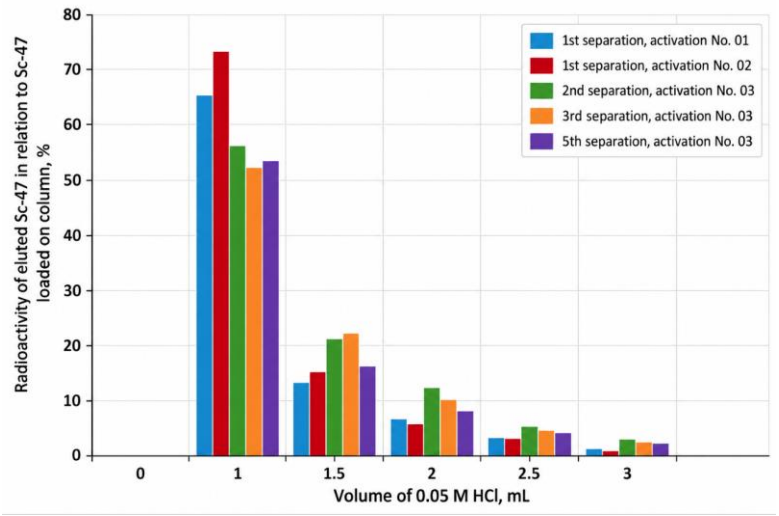
The daughter radionuclide is repeatedly recovered, while the parent radionuclide must be recovered quantitatively to allow further daughter ingrowth.

CASE STUDY 3: ^{47}Ca / ^{47}Sc

One irradiated target. More than one useful harvest



Elution profile of $[^{47}Sc]ScCl_3$



Quality control of $[^{47}Sc]ScCl_3$

Identity	confirmed by γ-ray spectrometry (159 keV) and ITLC (Rf ≈ 0.55)
Radionuclidic purity	>99.9% ^{47}Ca impurity: 0.009–0.076%
Radiochemical purity	95–96% first separations, ITLC
Chemical purity	Ca: 11.5–87.3 µg/mL | Fe: 0.7–5.9 µg/mL Zn: 0.2–2.5 µg/mL; Cu/Pb below or near detection limits
Radiolabelling performance	>98% RCP with DOTA-TATE up to 20 MBq/nmol (best batch); suitable for radiolabelling up to 4 days post-elution

These results demonstrate the feasibility of repeated Sc-47 recovery from a single irradiated target, while maintaining high separation efficiency and obtaining Sc-47 suitable for radiolabelling.

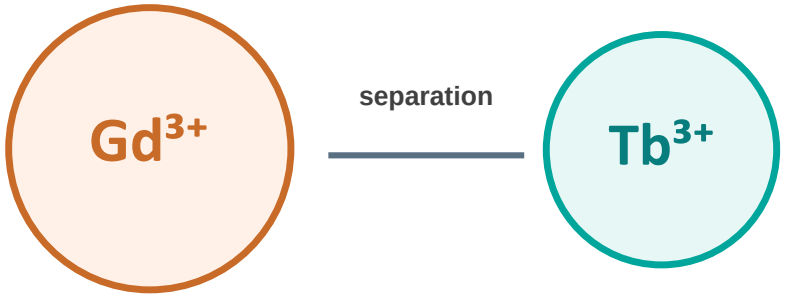
T½ = 6.95 d | β^- emiter + Auger and conversion electrons | Targeted radionuclide therapy | Theranostic pair with ^{155}Tb

Separation of ^{161}Tb from a large excess of Gd

Extreme Chemical Similarity

^{160}Gd (n,γ) → ^{161}Gd (β^-) → ^{161}Tb

Neighbouring lanthanides — almost the same chemistry

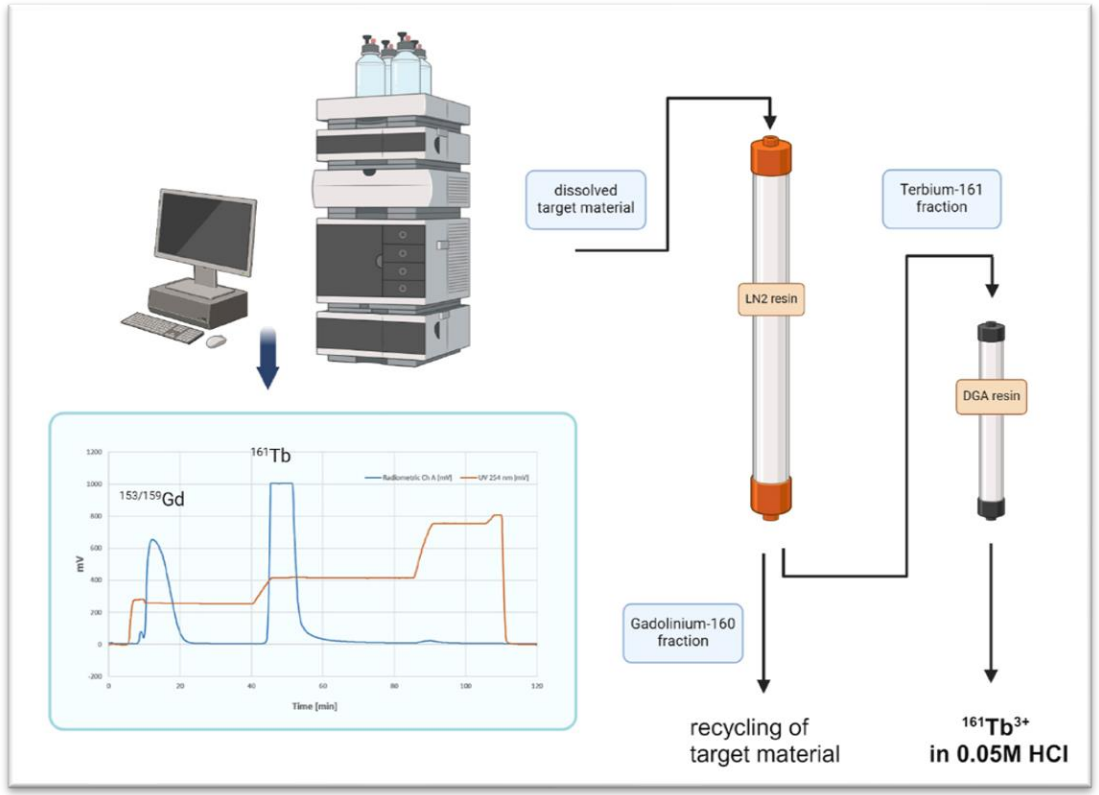


Both behave mainly as M^{3+} ions in aqueous radiochemistry

HIGH SELECTIVITY REQUIRED

Gd^{3+}	PROPERTY	Tb^{3+}
64	Atomic number	65
0.938 Å	**Ionic radius (coordination VI)**	0.923 Å
Lower	Charge density	Higher
Weaker	**Affinity to LN2 resin**	Stronger
First	Elution order	Second

Two-step extraction chromatography



>98%

^{161}Tb recovery on LN2

>99%

^{161}Tb elution from DGA

99.3–99.9%

[^{161}Tb]$TbCl_3$ radiochemical purity

LN2 — Separation of Tb^{3+} from Gd^{3+}

Selective separation of adjacent lanthanides based on differences in their affinity for the extractant.

↓

DGA — Concentration and final purification of ^{161}Tb

Reduction of fraction volume, removal of metallic impurities (Al, Ca, Fe), and recovery of [^{161}Tb]$TbCl_3$ in 0.05 M HCl.

Żółtowska et al., Applied Radiation and Isotopes 226 (2025) 112144

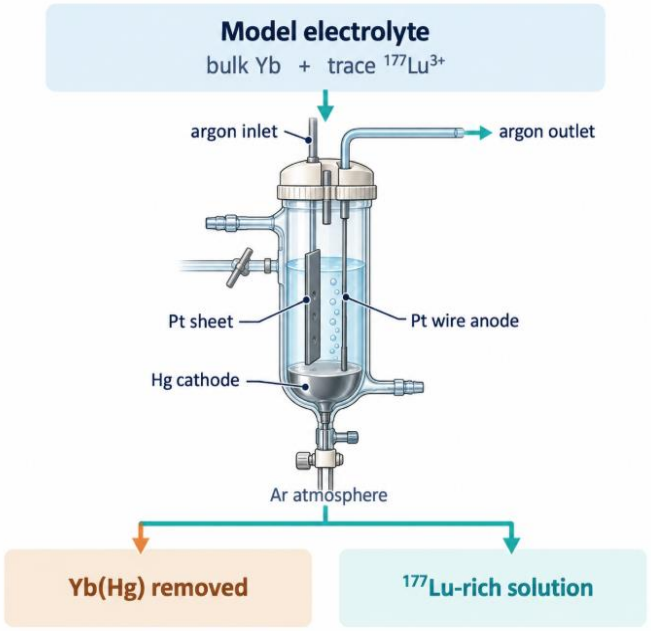
T½ = 6.65 d | β^- emitter | SPECT imaging | Targeted radionuclide therapy | Theranostic pairing with ^{68}Ga-labelled analogues

Electrochemical separation of Yb from a ^{177}Lu/Yb mixture

^{176}Yb (n,γ) → ^{177}Yb (β^-) → ^{177}Lu

A fast pre-purification step for no-carrier-added ^{177}Lu production

1. Separation scheme



2. Separation mechanism

1 Selective reduction

$$Yb^{3+} + e^- \rightarrow Yb^{2+}$$

Yb^{3+} is reduced at the mercury-pool cathode; Lu^{3+} is largely retained in solution.

2 Amalgamation with Hg

$$Yb^{2+} + Hg \rightarrow Yb(Hg)$$

Yb^{3+} forms an amalgam with mercury; Yb(Hg) is removed from the cell

3 Lu^{3+} remains in solution

Lu^{3+} is not reduced and stays in the electrolyte

3. Experimental results

Yb:Lu mass ratio during 3-step treatment

Initial	3,323
Step 1	1,290
Step 2	555
Step 3	224

94% Yb removal

14.8× lower Yb:Lu ratio

Electro-amalgamation removes bulk Yb; final chromatographic purification is still required for n.c.a. ^{177}Lu

Cieszykowska et al., SOP Transactions on Applied Chemistry 1 (2014)

Take-home messages

Radiochemical separation is an essential part of medical radionuclide production

A nuclear reaction becomes a practical production route only when the subsequent separation and purification processes are selective, reproducible, and suitable for the intended application.

RADIOCHEMICAL SEPARATION

NUCLEAR REACTION

MEDICAL APPLICATION

Thank you for your attention!



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