The ^{44}Ti/^{44}Sc Generator: Current Status, Challenges, and Prospects

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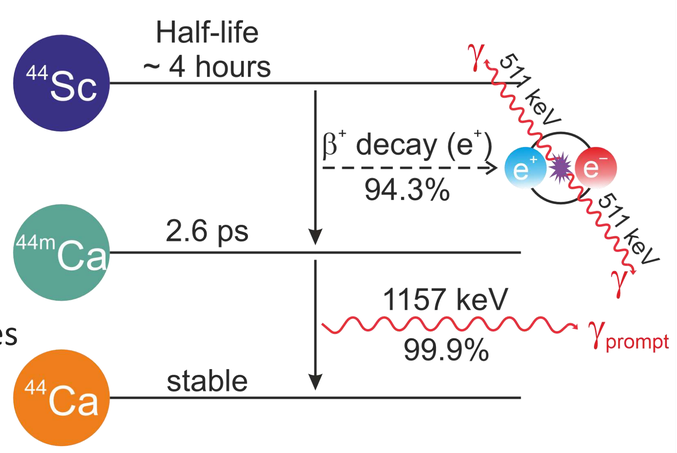
The ^{44}Ti/^{44}Sc generator is being developed as a long-term source of scandium-44 (^{44}Sc) for positron emission tomography (PET) and positronium lifetime imaging (PLI) [1, 2]. ^{44}Sc is attractive because it combines a suitable half-life for synthesis and imaging, positron emission for PET, and an additional prompt γ emission that can support advanced coincidence-based imaging approaches. The long half-life of the parent radionuclide, titanium-44 (^{44}Ti), makes it possible in principle to obtain ^{44}Sc repeatedly from a single generator system, reducing dependence on local cyclotron production [3].

However, practical implementation remains challenging. The production of ^{44}Ti is difficult and still limited by low yields, demanding irradiation conditions, and target-related constraints [4]. At the same time, Ti(IV) chemistry under generator conditions is complex: hydrolysis, variable speciation, pH sensitivity, and interactions with sorbent materials can affect both parent retention and the chemical quality of the ^{44}Sc eluate [5].

This poster presents the current concept and status of ^{44}Ti/^{44}Sc generator development, including first ^{44}Ti production at Heavy Ion Laboratory (HIL, Warsaw), the main technical bottlenecks, and the key requirements for a practical system. The broader use of this generator will depend not only on optimisation of individual steps, but on solving these production, chemistry, and design challenges.

Why Scandium?

- Ideal timescale for synthesis and imaging **($T_{1/2}$ ≈ 4 h)**
- **Hight β⁺ emission** (94.3%) for PET and positronium studies
- **Prompt γ** (1157 keV, 99.9%) → precise timestamp and localisation of positronium formation
- Sc^{3+} chemistry similar to lanthanides → **highly stable complexes** with DOTA-type chelators

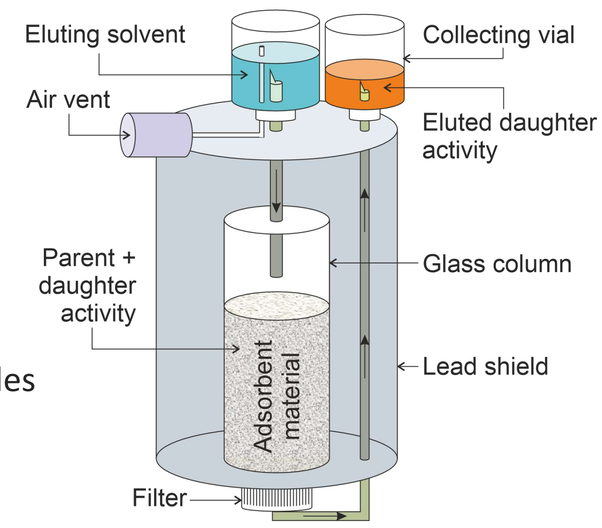


These features make ^{44}Sc a uniquely powerful radionuclide for advanced PET and positronium imaging

^{44}Ti/^{44}Sc Generator

- **Parent isotope (Ti)** fixed on adsorbent in a shielded glass column
- **^{44}Sc daughter** produced *in situ* by decay
- Selective **elution with solvent** releases pure ^{44}Sc into collecting vial
- Provides **on-demand supply** of ^{44}Sc without need for local cyclotron
- **Long-lived parent** (^{44}Ti, $T_{1/2}$ ≈ 60 years) → a single generator operates for decades

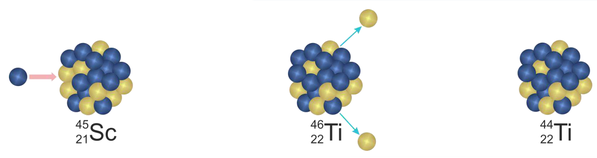
This simple, reusable system enables a sustainable and decentralised source of ^{44}Sc for PET and positronium imaging

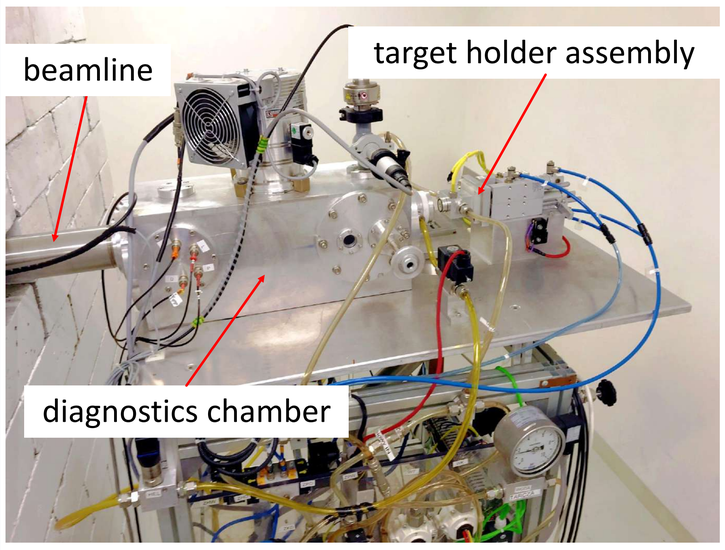


Bottlenecks

^{44}Ti Production	Ti(IV) Chemistry	Generator design
low cross-section	hydrolysis	parent breakthrough
low yield	variable speciation	long-term stability
prolonged irradiation	sorbent interactions	radiolysis
target overheating	pH sensitivity	no universal sorbent

First ^{44}Ti production at HIL





TARGET	
Material	**nat. Sc (metallic)**
Diameter	**10 mm (8 mm eff.)**
Thickness	**132.5 mg/cm²**
Cover	**5 µm Al**
IRRADIATION	
Energy	**16.5 MeV**
Current	**~5 µA (eff.)**
Duration	**103 h**
OUTCOME	
^{44}Ti activity	**~250 kBq**
Status	**proof of feasibility**

^{44}Ti/^{44}Sc generator prototypes

~1967 [6] — large volume
Dowex 1×8
yield: 60–70% | breakthrough: 0.02–0.1%
oxalic acid eluent; first concept

2010 [7] — oxalates
AG 1-X8
yield: 97% | breakthrough: low
oxalates inhibit radiolabelling

2016 [8] — inconsistent
TEVA resin
yield: 60–97% | breakthrough: variable
radiolysis; poor reproducibility

2022 [9] — no oxalates
Hydroxamate resin
yield: 80–85% | breakthrough: 0%
leaching; not yet scaled

2023 [10] — modular design
Modular ZR resin
yield: 82.9±5.3% | breakthrough: n/a (cartridge recovery)
clinical-scale; replaceable cartridge

2024 [11] — most robust
SnO_2 (inorganic)
yield: 85.3±2.8% | activity: 7.4 MBq
0.71% → DGA cleanup

Progress has moved from early ion-exchange concepts to more selective resin and inorganic systems, but no prototype yet combines high ^{44}Sc recovery, negligible ^{44}Ti breakthrough, scalable ^{44}Ti activity and directly radiolabelling-ready eluate [6–11].

Key requirements

- **High ^{44}Sc recovery** — yield after regrowth
- **Minimal ^{44}Ti breakthrough** — near-zero leakage
- **Clean eluate** — radiolabelling-ready
- **Stable Ti(IV) retention** — pH/speciation robust
- **Reproducible operation** — stable cycles

Conclusions

- The ^{44}Ti/^{44}Sc generator offers a promising route to a long-term source of ^{44}Sc for PET and positronium imaging.
- Practical implementation is still limited by ^{44}Ti production, Ti(IV) chemistry, and generator design.
- Further progress requires higher ^{44}Ti yields, stable Ti(IV) retention, minimal parent breakthrough, and radiolabelling-ready eluate.

Acknowledgements The authors acknowledge the support from the European Union within the Horizon Europe Framework Programme (ERC Advanced Grant POSITRONIUM no. 101199807), the National Science Centre of Poland through grants no. 2021/42/A/ST2/00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, the Sci-Mat and qLife Priority Research Areas budget under the program Excellence Initiative – Research University at Jagiellonian University.

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