Production of [^{43,47}Sc] from [^{46,50}Ti]TiO_2 targets

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Introduction

The clinically used theranostic pair: ^{68}Ga and ^{177}Lu have shown how effective theranostic pairs are in medicine. Yet, these complexes can exhibit different pharmacokinetics. An elementally matched theranostic pair would allow for identical complexation chemistry, *in vitro* binding, and *in vivo* pharmacokinetics. These chemical characteristics allows scientists and physicians the ability to imaging treatment assessment, and determine the dosimetry of radiopharmaceuticals

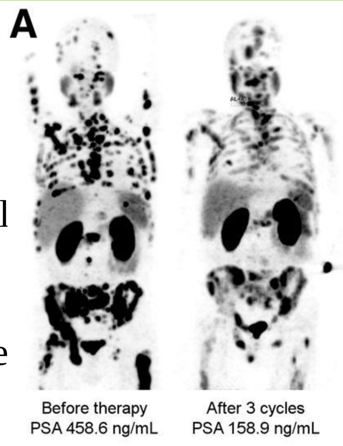
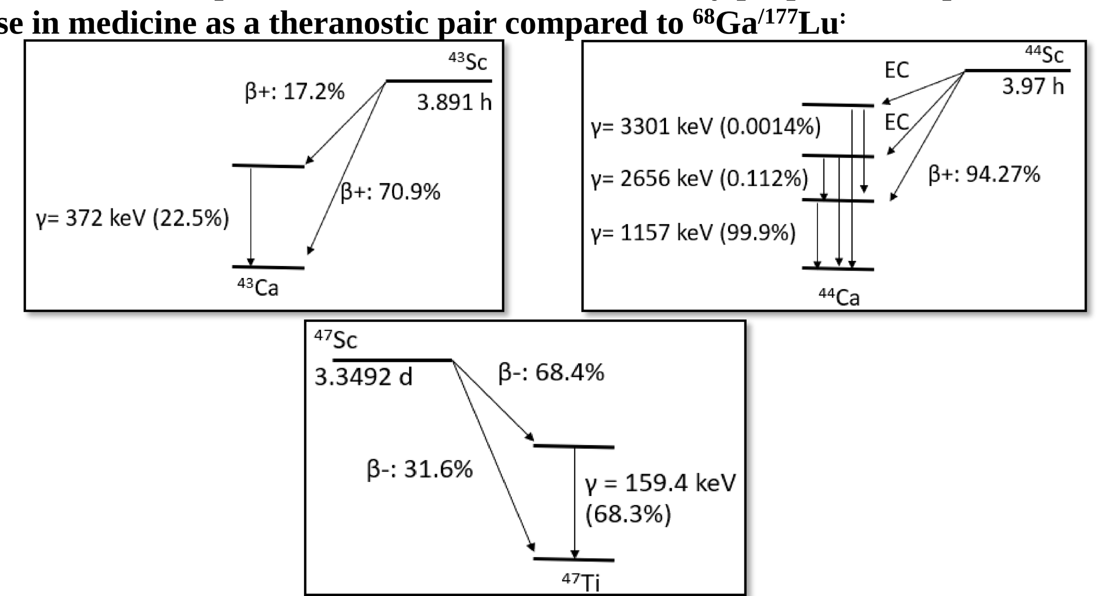


Figure 1: [^{68}Ga]PSMA and [^{177}Lu]PSMA patient

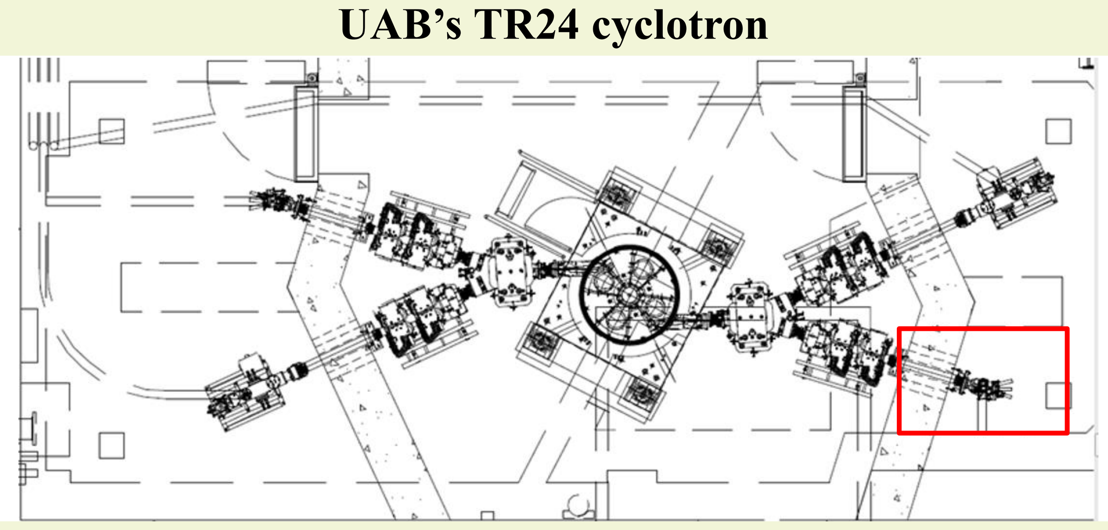
Three radioisotopes of scandium that have the decay properties for potential use in medicine as a theranostic pair compared to ^{68}Ga/^{177}Lu:



- Availability for high radionuclide purity scandium isotopes are limited due to lack of robust production techniques.
- Our goal is to develop a technique to produce high purity radioscandium isotopes from proton irradiation of enriched [^{46,50}Ti]TiO_2 targets.

Production

UAB's TR24 cyclotron



Production of radioscandium from titanium targets

Isotopes of ^{nat}Ti

- ^{46}Ti: 8.25%
- ^{47}Ti: 7.44%
- ^{48}Ti: 73.72%
- ^{49}Ti: 5.41%
- ^{50}Ti: 5.18%

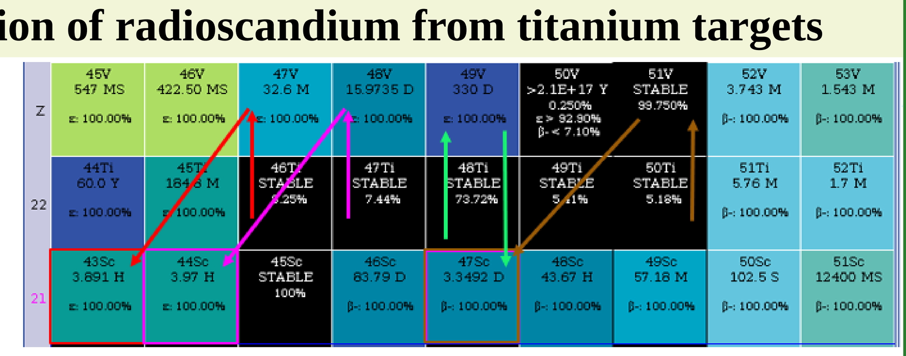


Figure 2: Production routes of radioscandium isotopes of medical interest from ^{nat}Ti

Cross-sections for ^{46}Ti(p,α)^{43}Sc and ^{50}Ti(p,α)^{47}Sc

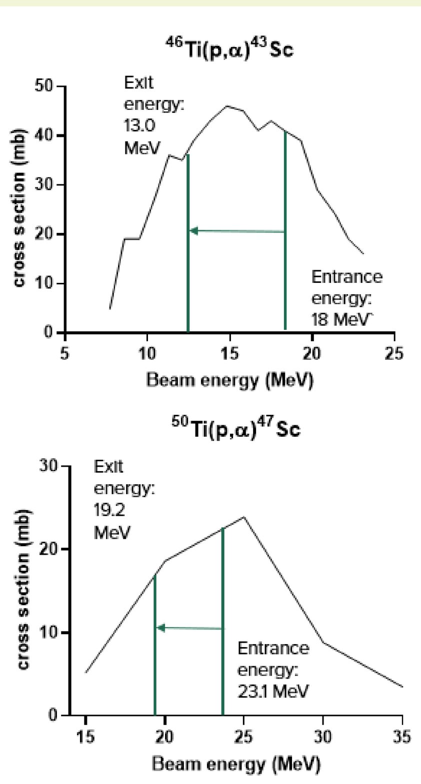


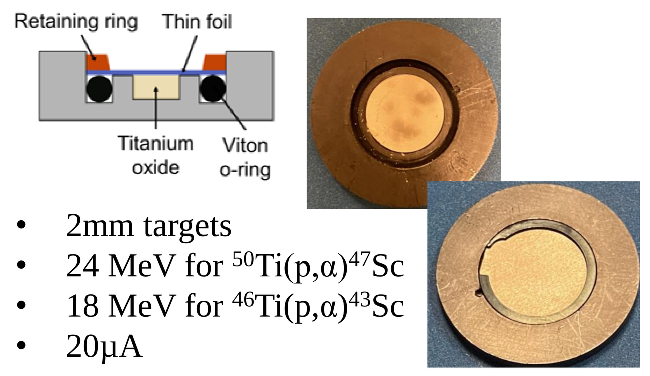
Figure 3:Cross sections for ^{47}Sc and ^{43}Sc on ^{46,50}Ti

Table 1: Products from ^{nat}Ti

Isotope	Nuclear reaction	Half-life	γ
^{43}Sc	^{46}Ti(p,α)^{43}Sc	3.9 hours	372 (22.5%)
^{44g}Sc	^{47}Ti(p,α)^{44g}Sc	3.9 hours	1157 (99.9%)
^{44m}Sc	^{47}Ti(p,α)^{44m}Sc	58.6 hours	271 (86.74%)
^{46}Sc	^{47}Ti(p,2p)^{46}Sc ^{49}Ti(p,α)^{46}Sc ^{50}Ti(p,n+α)^{46}Sc	83.7 days	889 (99.98)%) 1120(99.98 %)
^{47}Sc	^{48}Ti(p,2p)^{47}Sc ^{50}Ti(p,α)^{47}Sc	3.9 days	159(68.3%)
^{48}Sc	^{49}Ti(p,2p)^{48}Sc	48.6 hours	175 (7.48%) 983(100%) 1037(97.6%) 1212 (2.38%) 1312(100%)
^{48}V	^{48}Ti(p,n)^{48}V ^{49}Ti(p,2n)^{48}V	15.9 days	983(98.98%) 1312(98.2%)

Purification

Target



- 2mm targets
- 24 MeV for ^{50}Ti(p,α)^{47}Sc
- 18 MeV for ^{46}Ti(p,α)^{43}Sc
- 20µA

Table 2: Enrichment of $^{x}TiO_2$

Isotope	Atomic Percent for [^{46}Ti]TiO_2	Atomic Percent for [^{50}Ti]TiO_2
46	96.84	1.69
47	0.5	1.29
48	2.33	12.51
49	0.16	1.41
50	0.16	83.1

Dissolution process

1. Target removed and added PFA digestion vial
2. 300 mg NH_4HF_2; Heated at 250°C for 2 hours
3. Remove and added 5 mL 12.1M HCl
4. Heated at 160°C for 45 minutes
5. Diluted to 10 mL of 9M HCl

Separation

- FT
  - Dissolved added
  - Ti and ^{48}V should flow through
- E1
  - 20 mL 9M HCl
  - Wash out any Ti and ^{48}V
- E2
  - 10 mL 7M HNO_3
  - Wash out any contaminates
- E3
  - 3 mL 1M HNO_3
- E4-E6
  - 3 separately collected 3 mL 0.1M HCl
  - Collect ^{43,47}Sc

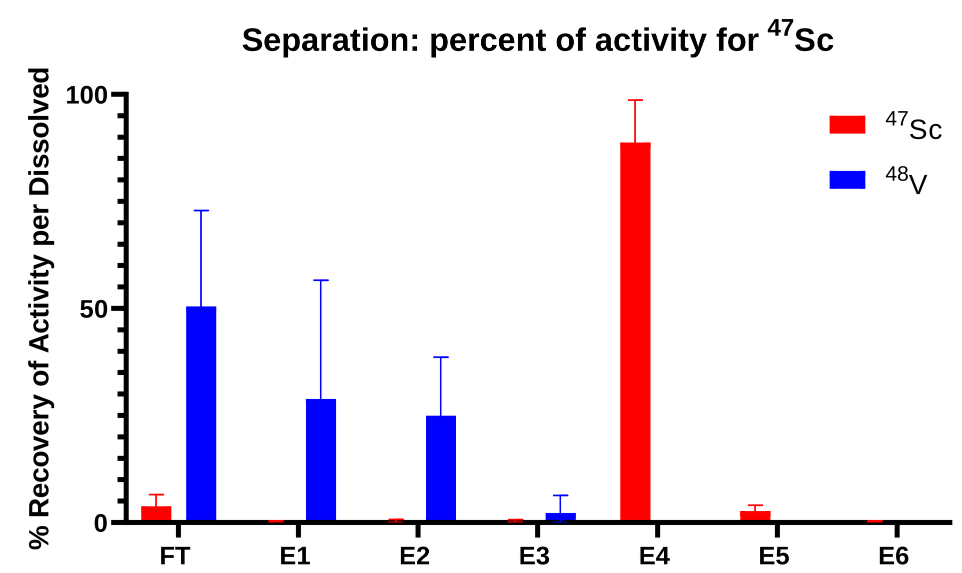


Figure 5: Elution profile for enriched [^{50}Ti]TiO_2 productions. FT is the flow through, followed by the elutions discussed in the separations section.

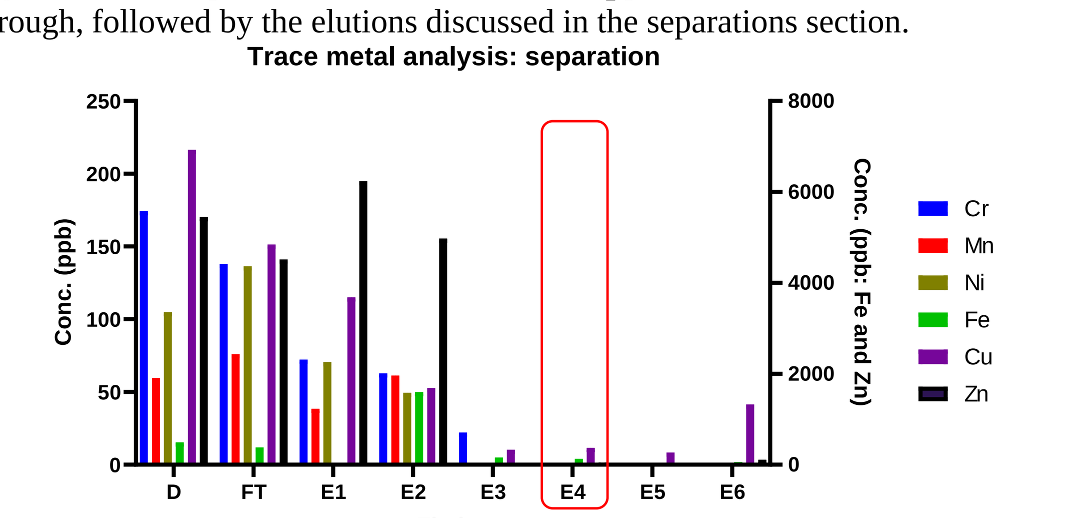


Figure 6: ICPMS elution profile of trace metal contaminants of an enriched [^{50}Ti]TiO_2 productions. FT is the flow through, followed by the elutions discussed in the separations section.

Table 3: Elution profile for ^{43}Sc

	^{43}Sc(mCi)			^{48}V(µCi)		
Starting	13.5	20.1	14.6	59.9	75.3	77.2
FT	.576	0	.924	27.3	22.7	35.6
E1	.174	0	.037	26.2	57.5	59.1
E2	.807	0	.010	26.2	37.8	35.9
E3	.032	.077	.075	0	0	0
E4	12.6	16.9	12.8	0	0	0
E5	.024	.371	.182	0	0	0
E6	.134	.027	0	0	0	

Table 4: Elution profile for ^{47}Sc

	^{43}Sc(mCi)			^{48}V(µCi)		
Starting	3.03	1.37	2.29	832.2	339.8	414.6
FT	.023	.038	.163	0	249.6	213.4
E1	0	.007	.001	538.6	54.4	1.4
E2	0	.013	.0004	114.1	61.7	93.1
E3	.013	.002	.013	69.6	1.8	0
E4	3.04	1.19	1.75	0.2	0	0
E5	.037	.025	.102	0	0	0
E6	.006	.003	.003	0	0	0

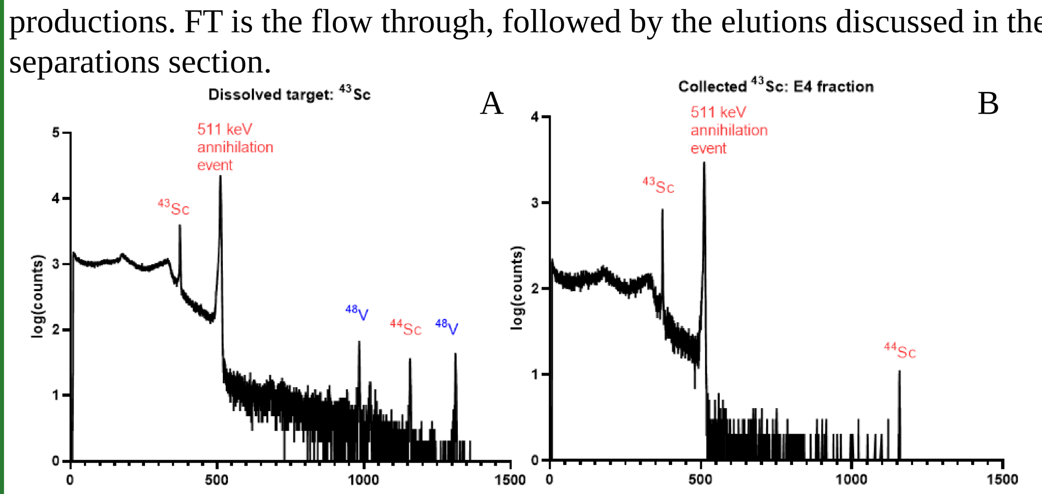


Figure 8: HPGe spectra of the dissolved target and collected ^{43}Sc from enriched [^{46}Ti]TiO_2

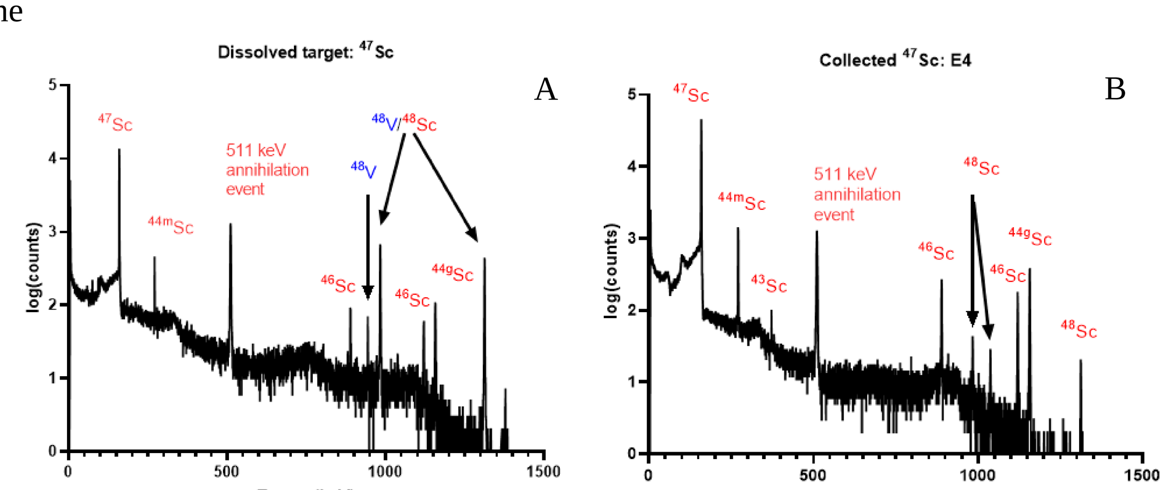


Figure 9: HPGe spectra of the dissolved target and collected ^{47}Sc from enriched [^{46}Ti]TiO_2

Table 4: Activity corrected to end of bombardment for the collected ^{43}Sc: E4

Radionuclide	^{43}Sc	^{44m}Sc	^{44g}Sc	^{46}Sc	^{47}Sc	^{48}Sc	Total radioscandium
Activity (mCi) [^{46}Ti]	12.9	0.031	0.141	0.38	0.11	0.07	13.1
Percentage	98.8	0.02	1.08	0	0.08	0	100
Activity (µCi) [^{50}Ti]	Decayed	65.8	65.8	39	1786.9	8.8	1966.1
Percentage	Decayed	3.3	3.3	1.9	91	0	100

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Recycling

Step 1
- Combine the eluents with Ti ions and dilute to 500 mL of MQ water

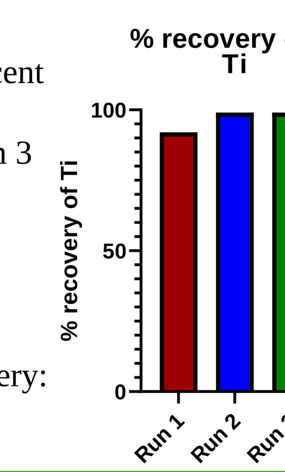
Step 2
- Heat for 1 hour at 160°C

Step 3
- pH adjust with 25% ammonium hydroxide to precipitate out

Step 4
- Filter using mixed cellulose .22 µm

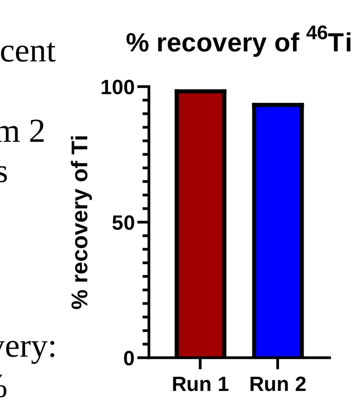
Step 5
- Remove and add into beaker and heat at 250°C for at least 24 hours

Figure 10: Percent recovery for [^{50}Ti]TiO_2 from 3 bombardments



Average recovery: 96.6±4%

Figure 11: Percent recovery for [^{46}Ti]TiO_2 from 2 bombardments



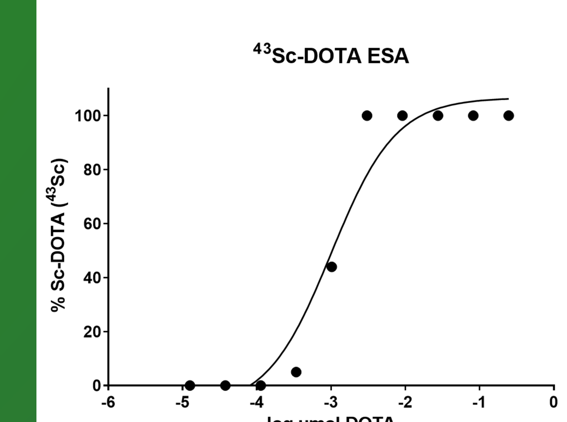
Average recovery: 96.5±3.5%

Table 6: Trace metal analysis of collected ^{47}Sc from recycled ^{50}Ti targets

	Cycle: 1 (ppb)	Cycle: 4 (ppb)	Cycle: 6 (ppb)
Zn	430.8	47.6	29.7
Cr	311.3	<15	<15
Mn	340.1	<15	<15
Fe	1,433.1	129.1	<15
Ni	189.5	<15	<15
Cu	263.9	11.6	<15
Pb	2,172.3	<15	<15
W	10,170.7	53.1	32.7

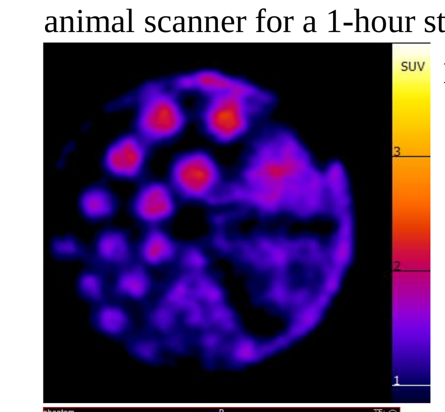
Radiolabeling and phantom

A serial dilution of DOTA was performed in 0.25M ammonium acetate pH 4. Equal amounts of ^{43,47}Sc were added and complexed at 95°C at 800 rpm for 30 minutes. SG-iTLC in 1M citrate buffer was used to determine percent complexation.

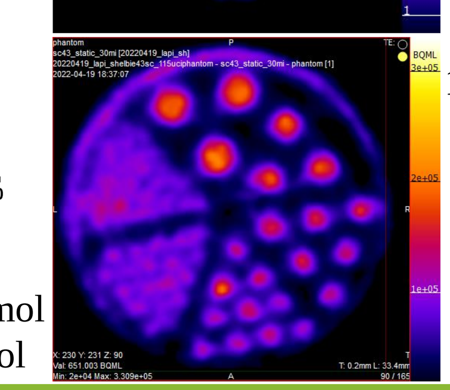


^{43}Sc-DOTA ESA: 160.29 mCi/µmol
^{47}Sc-DOTA ESA: 91.73 mCi/µmol

Derenzo phantoms were prepared with a solution MQ water with 100 µCi of either [^{68}Ga] or [^{43}Sc]. The phantoms were imaged on a SOFIE PET/CT small animal scanner for a 1-hour static scan.



100 µCi of ^{68}Ga



100 µCi of ^{43}Sc

Conclusions

- Production of high purity ^{43,47}Sc from proton bombardment of enriched [^{46,50}Ti]TiO_2 has been shown to be feasible with high recovery from recycling
- Effective radiolabeling of ^{43,47}Sc produced from [^{46,50}Ti]TiO_2 has shown promising application for high purity ^{43,47}Sc

Acknowledgements

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