

Isotope Production at UAB: Expanding the toolbox for nuclear medicine

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Knowledge that will change your world

University of Alabama at Birmingham Cyclotron

TR 24

Advanced Cyclotron Systems, Inc. (ACSI)

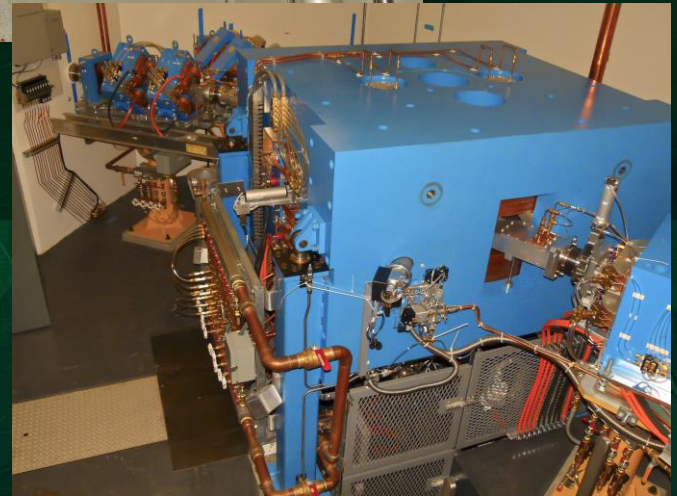
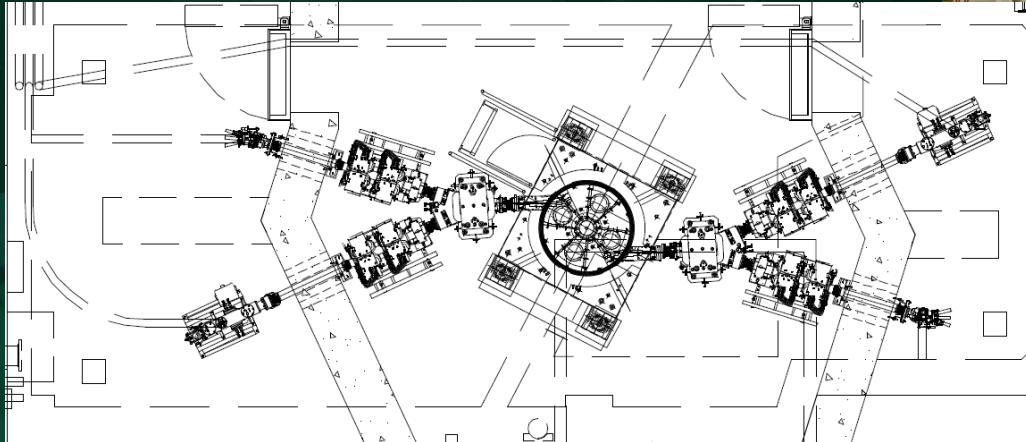
15-24 MeV protons;
variable energy

300 μ A (total)

2 extraction ports

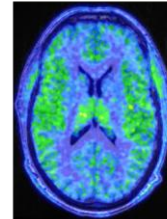
Solid, liquid, and gas targets

4 beamlines

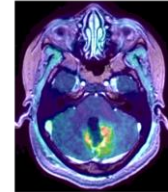


Status of Active Radiotracers for Human Use at UAB

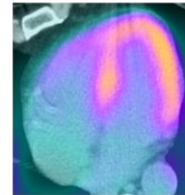
Radiopharmaceutical	Use
[¹⁸ F]FLT	Proliferation
[¹³ N]NH ₃	Cardiac blood flow
[⁶⁸ Ga]DOTATATE	SSTR status
[¹⁸ F]FMISO	Hypoxia
[⁸⁹ Zr]Trastuzumab	HER2 status (breast cancer)
[¹⁸ F]FET	Amino acid transport
[¹¹ C]PiB	Amyloid
[¹⁸ F]DPA-714	TSPO (neuroinflammation)
[⁶⁸ Ga]PSMA-11	PSMA status (prostate cancer)
[⁸⁹ Zr]Panitumumab	EGFR status (colon cancer)
[¹⁸ F]AV1451	Tau protein
[⁶⁸ Ga]GZP*	Granzyme B (Immune Activation)
[¹¹ C]Acetate	Cardiac Metabolism
[⁸⁹ Zr]Oxine/White Blood Cells*	WBC tracking
[⁶⁸ Ga]FAP-2286	Fibroblast Activation Protein



Neuroinflammation through TSPO in microglia
[¹⁸F]DPA-714



Amino acid transport in neuro-oncology
[¹⁸F]FET



Myocardial perfusion
[¹³N]ammonia



HER2 as a target for therapy in breast cancer
[⁸⁹Zr]trastuzumab

*First in human compound

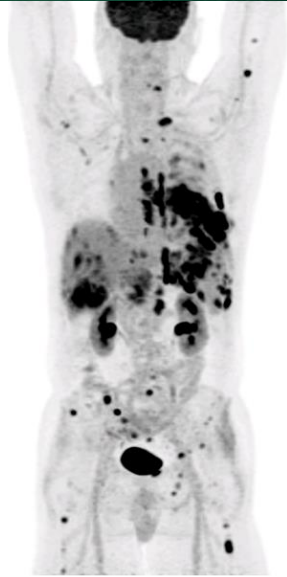
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Whole body PET tracers in use at UAB for oncology



Bone turnover
in skeletal metastases
[¹⁸F]fluoride



Glucose metabolism
in many cancers
[¹⁸F]FDG



Somatostatin receptors
in neuroendocrine cancers
[⁶⁸Ga]DOTATATE

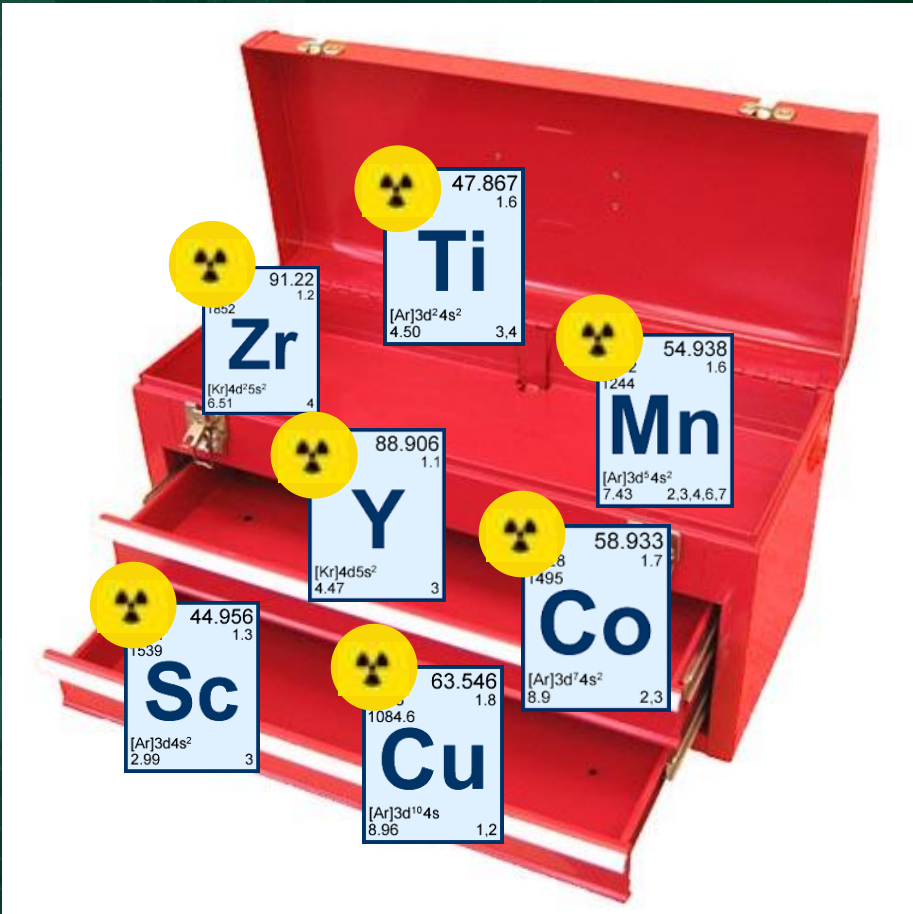


Amino acid transport
in prostate cancer
[¹⁸F]fluciclovine



HER2 as a target for
therapy in breast cancer
[⁸⁹Zr]trastuzumab

Expanding the Toolbox of Radioisotopes



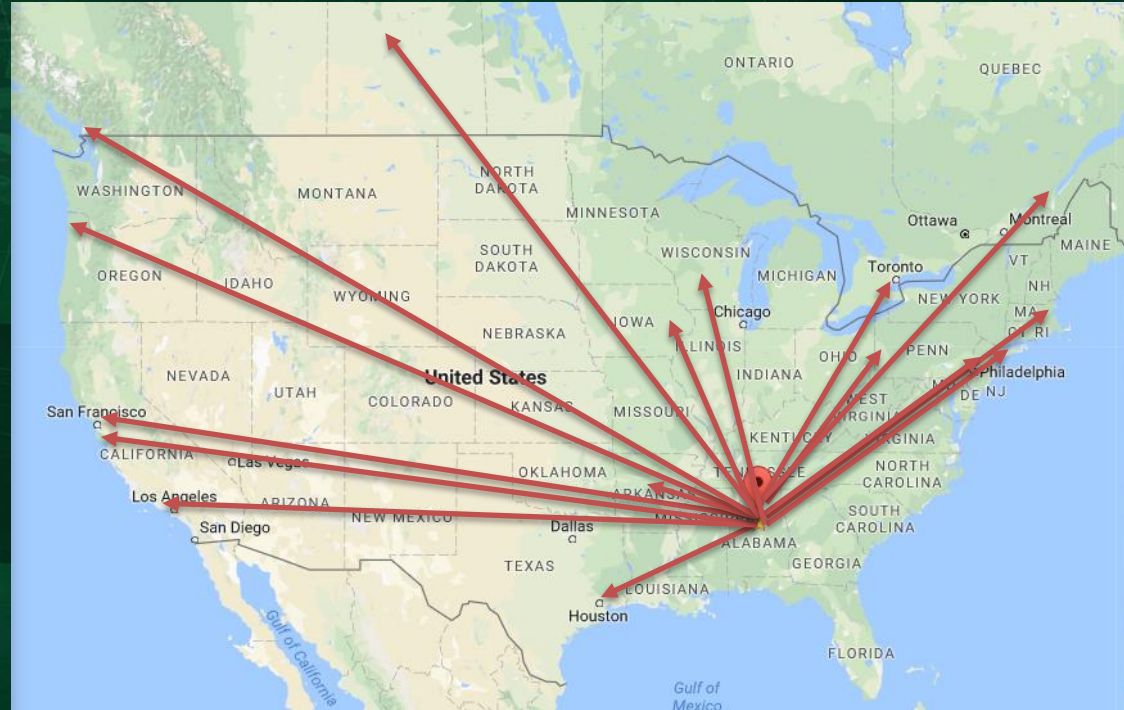
Expanding the toolbox: Radioisotopes (beyond ^{18}F , ^{11}C , ^{13}N , ^{15}O , ^{68}Ga)

Isotope	Half-Life	Target Material	Status
$^{43,47}\text{Sc}$	3.9 h	Nat/EnrTi	Chemistry development
^{45}Ti	3.1 h	NatSc	Chemistry development
^{48}V	16 d	NatTi	Chemistry development
^{52}Mn	5.6 d	Nat/ ^{52}Cr	Routine production for preclinical use
^{55}Co	17.5 h	^{58}Ni	Routine production for preclinical use
^{64}Cu	12.7 h	^{64}Ni	Routine production for preclinical and human use
^{89}Zr	3.27 d	^{89}Y	Routine production for preclinical and human use

UAB Cyclotron Facility : A Nationwide Resource

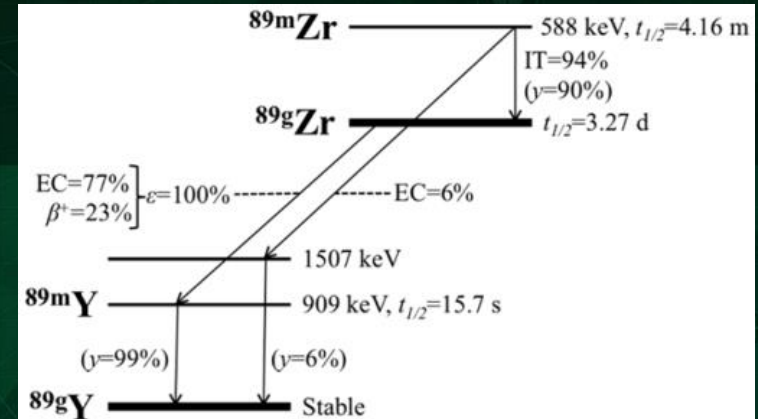
Multi-state pharmacist, pharmacy and manufacturing licenses to allow dispensing and distribution of radiopharmaceuticals into adjoining states.

DOT certified shipping containers and internal training to distribute ^{89}Zr and other isotopes to other research facilities throughout the country and internationally.



Zirconium-89

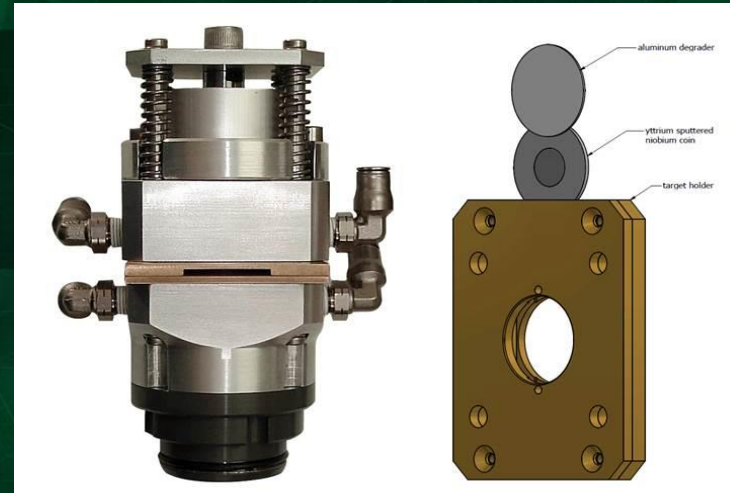
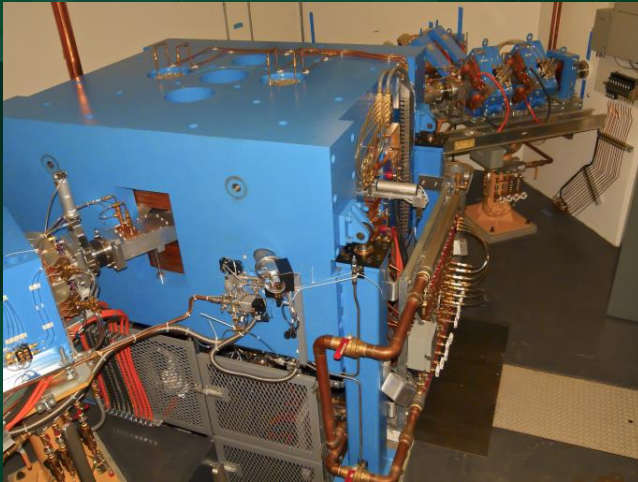
- Half-life of 3.27 d – well suited for study of pharmacokinetics of antibodies (achieve optimal biodistribution ~4-5 d)
- Scouting in preparation for antibody therapy, confirming tumor targeting, and estimating dosimetry
- Generally inert to biological systems
- Decay properties
 - EC = 76.6%
 - β^+ = 22.3%
 - $R_{\text{ave.}}(\beta^+) = 1.18 \text{ mm}$



Zr-89 production

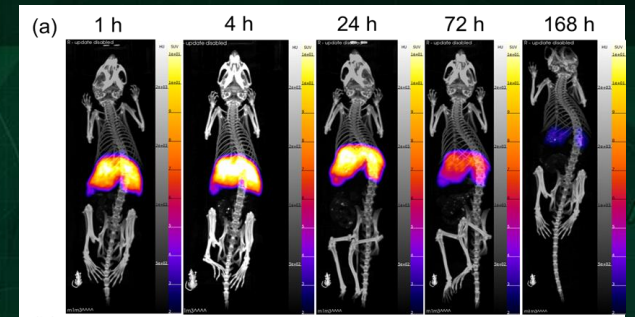
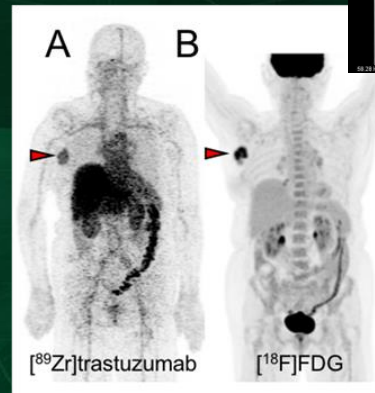
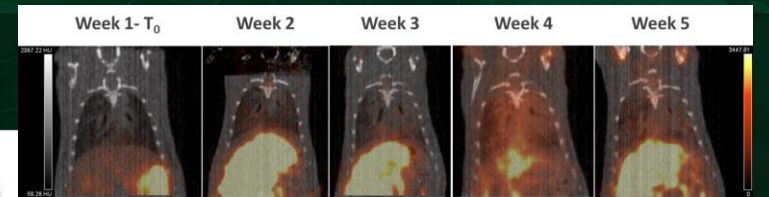
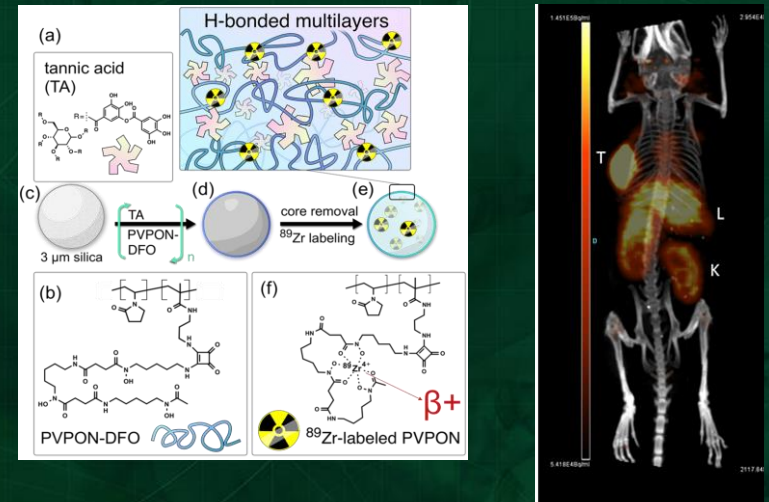
- $^{89}\text{Y}(p,n)^{89}\text{Zr}$

^{87}Zr 1.68 H ε: 100.00%	^{88}Zr 83.4 D ε: 100.00%	^{89}Zr 78.41 H ε: 100.00%	^{90}Zr STABLE 51.45%	^{91}Zr STABLE 11.22%	^{92}Zr STABLE 17.15%	^{93}Zr 1.53E+6 Y β-: 100.00%
^{86}Y 14.74 H ε: 100.00%	^{87}Y 79.8 H ε: 100.00%	^{88}Y 106.626 D ε: 100.00%	^{89}Y STABLE 100%	^{90}Y 64.053 H β-: 100.00%	^{91}Y 58.51 D β-: 100.00%	^{92}Y 3.54 H β-: 100.00%



Ongoing work related to ^{89}Zr

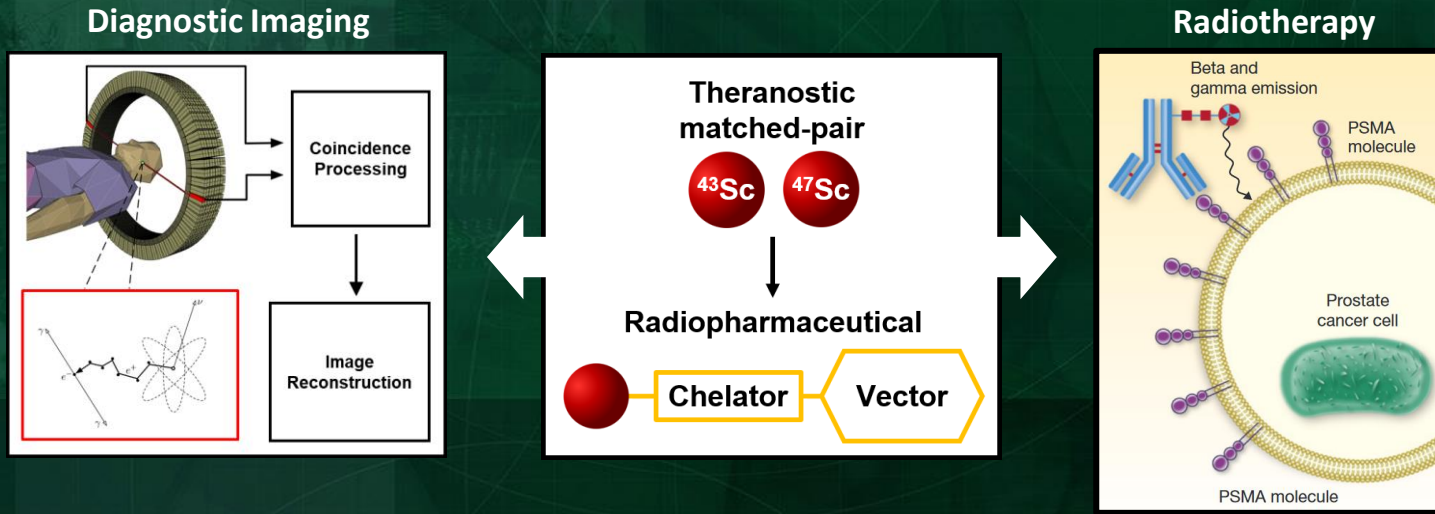
- Routine production via sputtered targets
- Internal use and shipping to external sites – nationally and internationally
- Preclinical radiochemistry – mAbs, nanoparticle and cell labeling
- Small animal imaging studies
- Preparation of GMP ^{89}Zr radiopharmaceuticals
- Early phase clinical trials:
 - [^{89}Zr]Trastuzumab
 - [^{89}Zr]Panitumumab



Wooten et al Appl. Sci 2013
 Queern et al Nuc Med Bio 2017
 Ikotun et al PloS ONE 2013
 Zheleznyak et al Mol. Imaging 2013
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Laforest et al Mol Imaging Bio 2016
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 Massicano et al J. Lab. Comp. and Rad. 2020
 Tekin et al Nuc Med Bio 2021

Matched Pair Radionuclides: ^{43}Sc and ^{47}Sc



- Disease diagnosis, dosimetry evaluation, therapy, and assessment of response with identical pharmacokinetic profiles
- Potential production and separation using the same cyclotron, targets and separation chemistry

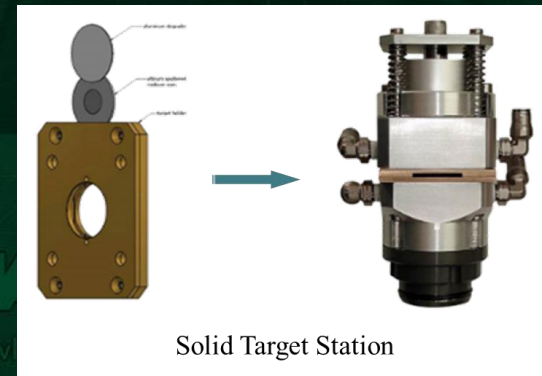
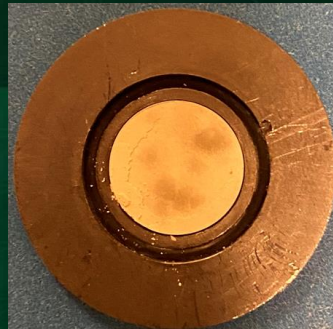
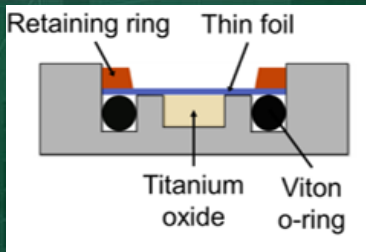
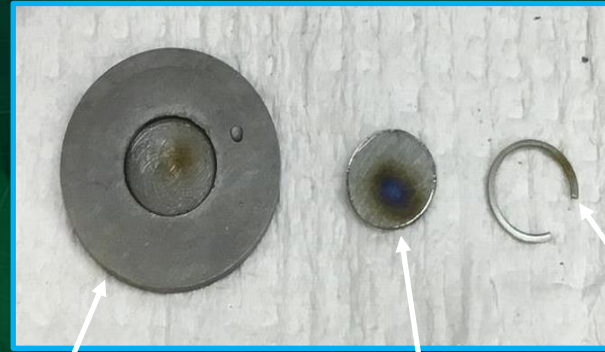
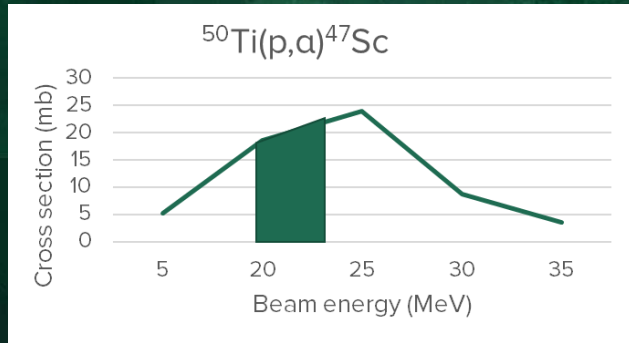
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 Langner, Jens.. MCS Thesis, University of Applied Sciences, Dresden, DE 2003
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 Simone II, C.B.; Hahn, S.M. *Clin Cancer Res*; 19(18), 2013

Nuclear Reactions on Titanium

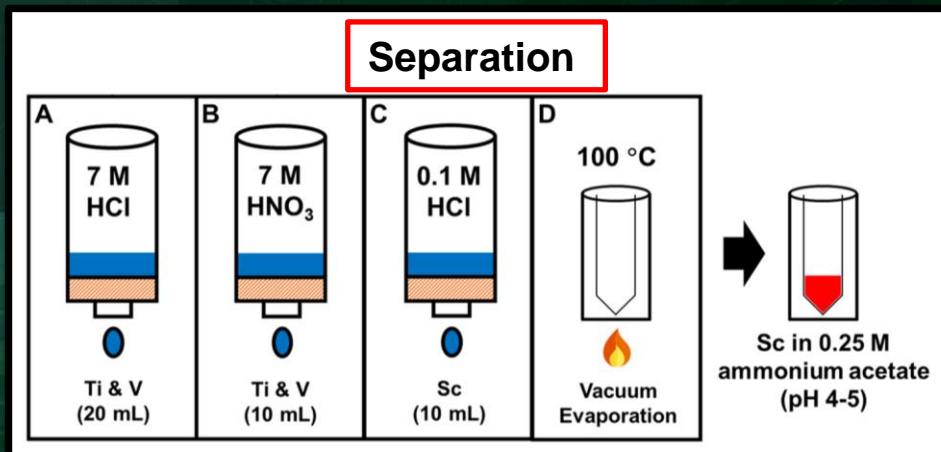
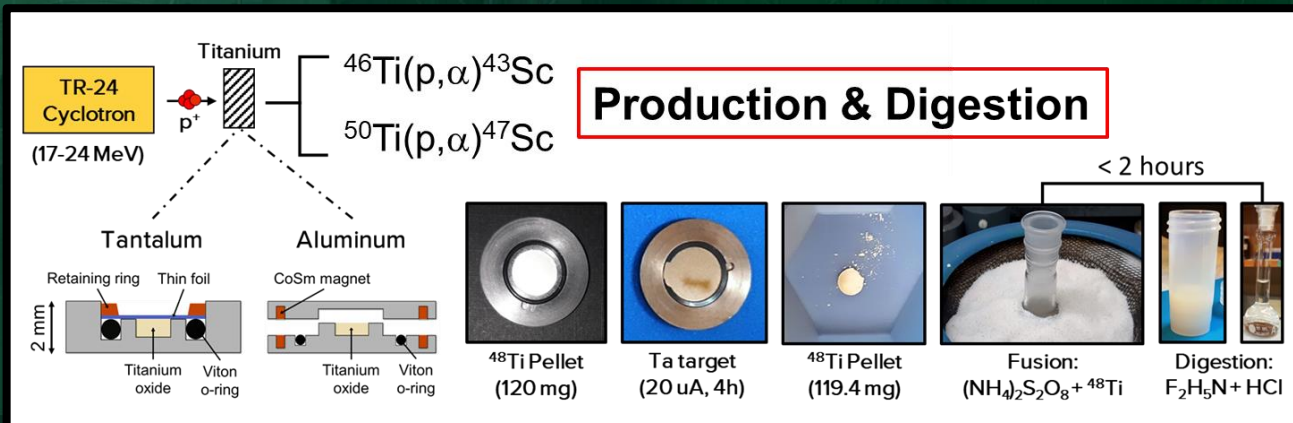
V45 7/- 0.55 s β+ γ 40.1	V46 0+ 422.3 ms β+ 6.03 ε ω	V47 3/- 32.6 m β+ 1.89, ... ε γ 1794.0	V48 4+ 15.98 d β+ 1.04, ... ε γ 719.6 ω, 1408.1, ...	V49 7/- 331 d ε no γ	V50 6+ 0.250 1.4E17 a β+ 1.04, ... ε γ 719.6 ω, 1408.1, ...	V51 7/- 99.75
Ti44 59.9 a ε γ 78.3D, 67.8D, ...	Ti45 7/- 3.078 h β+ 1.04, ... ε γ 719.6 ω, 1408.1, ...	Ti46 8.25	Ti47 5/- 7.44	Ti48 73.72	Ti49 7/- 5.41	Ti50 5.18
Sc43 7/- 3.90 h β+ 1.20, .82, ... ε γ 372.8 $^{46}\text{Ti}(p,\alpha)$	Sc44 2+ 2.442 d IT 271.2 ε γ 1001.8 1126.1 1157.0 $^{47}\text{Ti}(p,\alpha)$	Sc45 7/- 100.0	Sc46 4+ 83.81 d β- .357, ... γ 1120.5, 889.3	Sc47 7/- 3.349 d β- 439, 600, ... γ 159.4 $^{48}\text{Ti}(p,2p)$	Sc48 6+ 43.7 h β- 66, 1.990, ... γ 983.5, 1312.1, 1037.5, ...	Sc49 7/- 57.3 m β- 2.01, ... γ 1762 (ω), 1623

Targetry – natural and enriched Ti

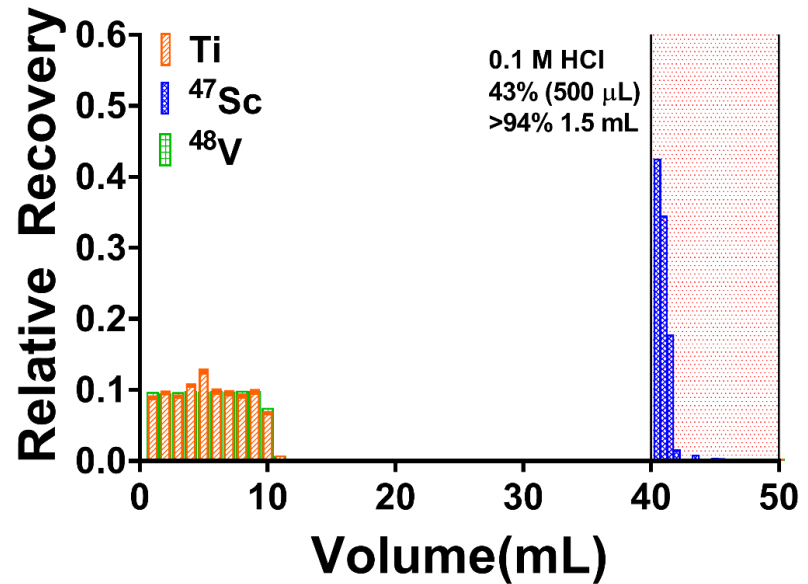
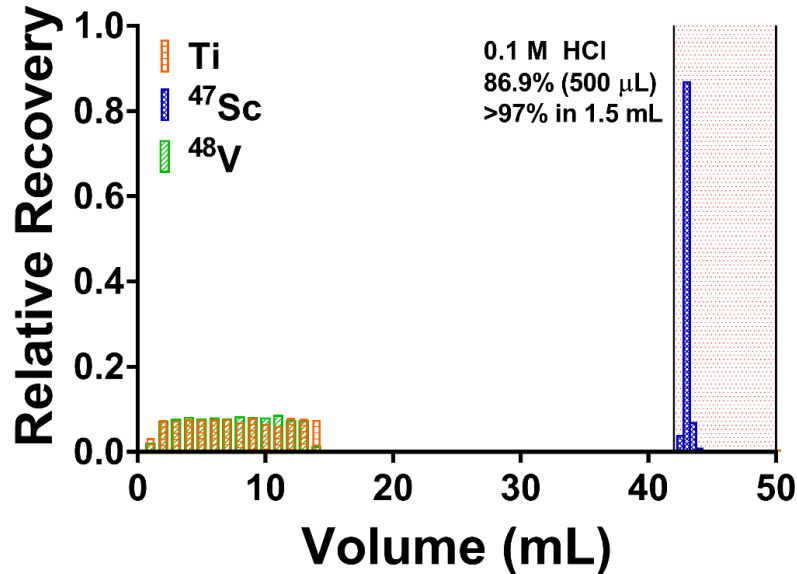
- Irradiation: 24.0 MeV protons
- Ti foils or pressed TiO_2 powder



^{43}Sc and ^{47}Sc targets and chemistry



Separation profile – Ti(0) vs. TiO₂



» Details: 200 mg BDGA resin, 1.5 x 20 cm column, 1.0 mL/min flow rate, 1 mL fractions (1-40 mL), 0.5 mL fractions (40-50 mL)

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