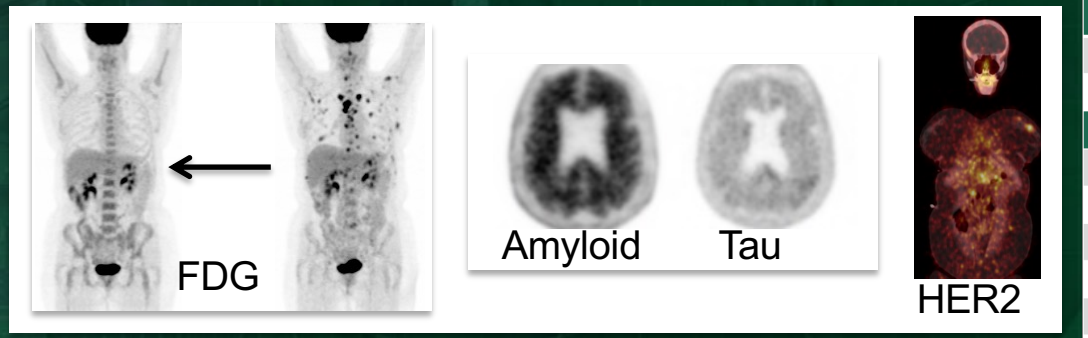
Production of high purity and high specific activity ^{203}Pb at UAB

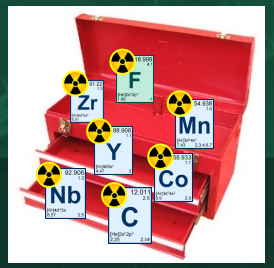
Jennifer Bartels, PhD
Cyclotron Facility Director, Suzanne Lapi, PhD
DOE IP Virtual Seminar Series, 10/05/23

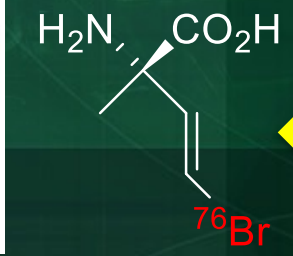
Translational Molecular Imaging Program at UAB



Clinical trials with molecular imaging and therapeuti

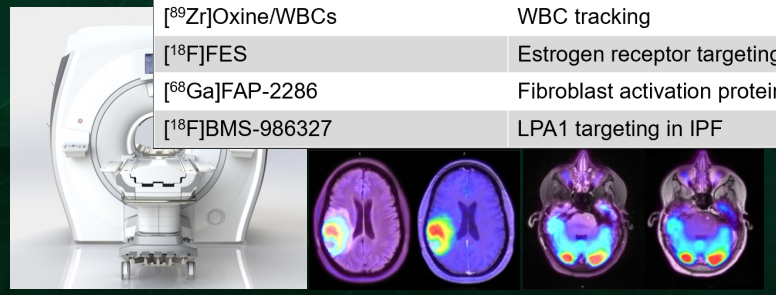
FDA Approved Drugs	Use
[^{68}Ga]DOTATATE (NETSPOT™)	Neuroendocrine tumors
[^{68}Ga]PSMA-11 (LOCAMETZ®)	Prostate cancer imaging
Active Radiotracers for INDs	**Use**
[^{18}F]FLT	Cell proliferation imaging
[^{13}N]Ammonia	Cardiac perfusion
[^{18}F]FMISO	Hypoxia imaging
[^{89}Zr]Trastuzumab	HER2 imaging
[^{18}F]DPA-714	TSPO-neuroinflammation
[^{18}F]FET	Amino acid transport
[^{11}C]PiB	Beta-amyloid plaque imaging
[^{18}F]AV1451	Tau aggregates
[^{89}Zr]Panitumumab	EGFR status (colon)
[^{11}C]Acetate	Cardiac metabolism
[^{68}Ga]GZP	Immune response
[^{89}Zr]Oxine/WBCs	WBC tracking
[^{18}F]FES	Estrogen receptor targeting
[^{68}Ga]FAP-2286	Fibroblast activation protein
[^{18}F]BMS-986327	LPA1 targeting in IPF





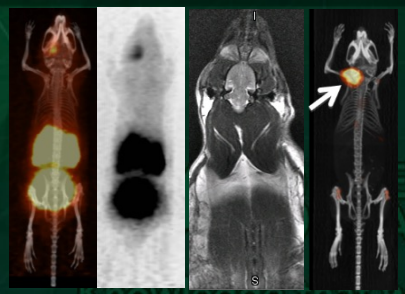
Isotope production and MI agent development

UAB Cyclotron Facility



PET/CT and PET/MRI in AIF

In vitro testing



Small animal imaging

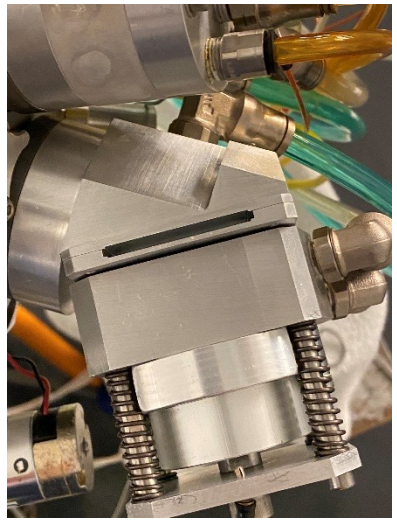
UAB Cyclotron and Advanced Imaging Facilities

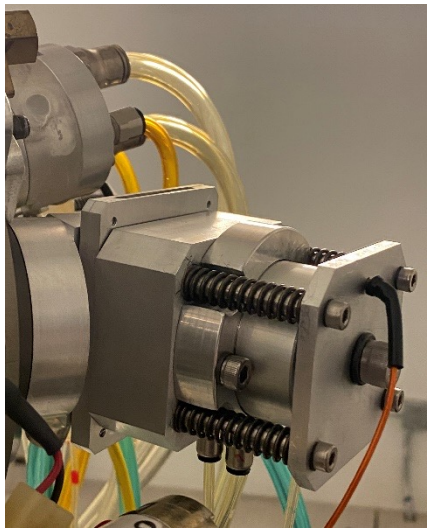
- GE Signa 3-T PET/MRI
- Two GE 710 TOF PET/CTs
- Metabolite Analysis

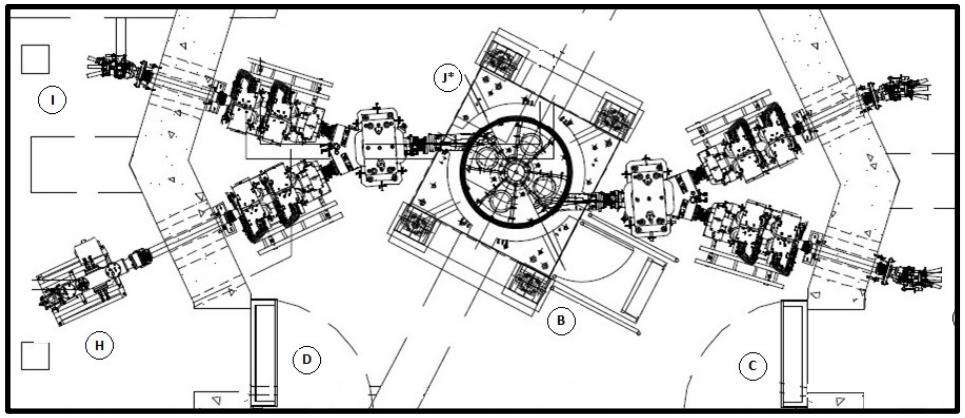
- Cyclotron control room
- TR-24 cyclotron/equipment room
- Preclinical radiochemistry/Radiometal purification
- Human use QC
- cGMP production
- Radiopharmacy

UAB Cyclotron Facility

- TR-24 (Advanced Cyclotron Systems, Inc) Cyclotron
  - → Variable energy protons, 17-24 MeV
  - → Current up to 300 μA
  - → Dual extraction ports, 4 beamlines
  - → Solid, liquid and gas targets







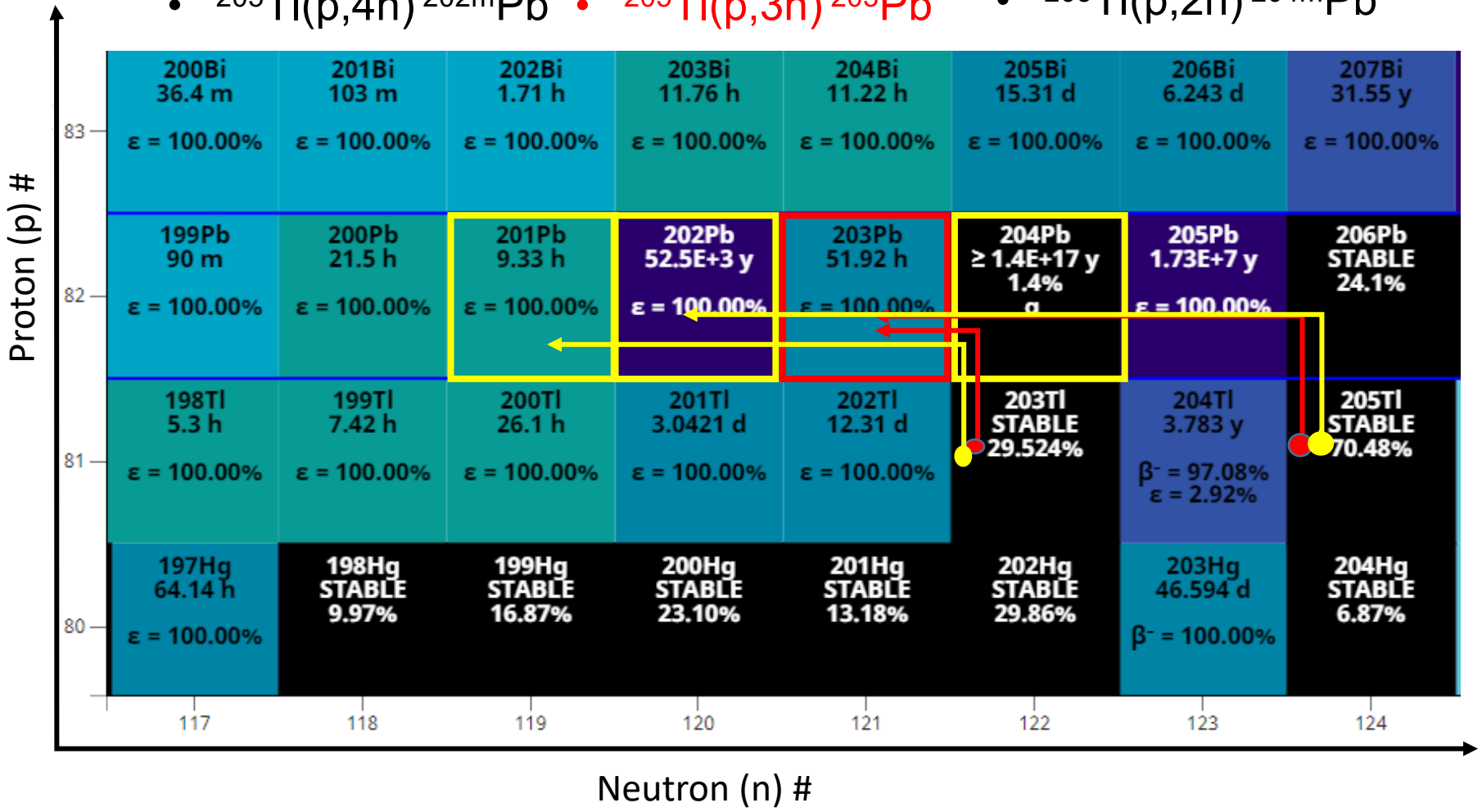
Current list of Isotopes

UAB Radioisotope Toolbox			
Isotope	**Half-life**	**Target material**	**Status**
^{43}Sc	3.89 h	^{46}Ti	Routine production for preclinical use
$^{44m/44g}$Sc	58.6 h/3.97 h	^{47}Ti	Routine production for preclinical use
^{45}Ti	185 min	^{Nat}Sc	Routine production for preclinical use
^{47}Sc	3.35 d	$^{48/50}$Ti	Chemistry development, preclinical use
^{64}Cu	12.7 h	^{64}Ni	Routine production for preclinical and human use
^{89}Zr	78.4 h	^{89}Y	Routine production for preclinical and human use

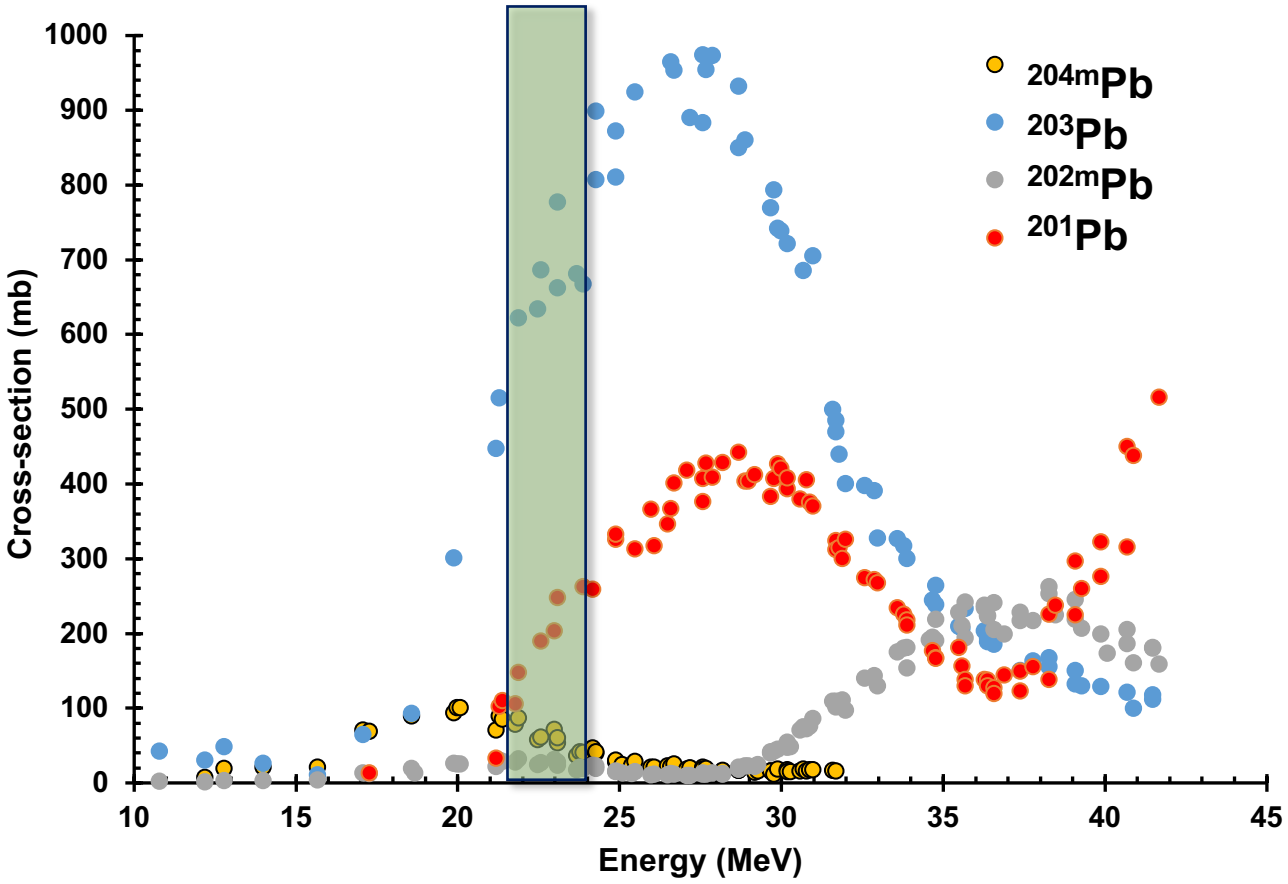
Department of Energy University Isotope Network Radioisotopes			
Isotope	**Half-life**	**Target material**	**Status**
^{48}V	16.0 d	^{Nat}Ti	Chemistry development, preclinical use
^{52}Mn	5.59 d	^{Nat}Cr	Routine production for preclinical use
^{55}Co	17.5 h	^{58}Ni	Routine production for preclinical use
^{203}Pb	2.1 d	^{205}Tl	Routine production for preclinical and human use

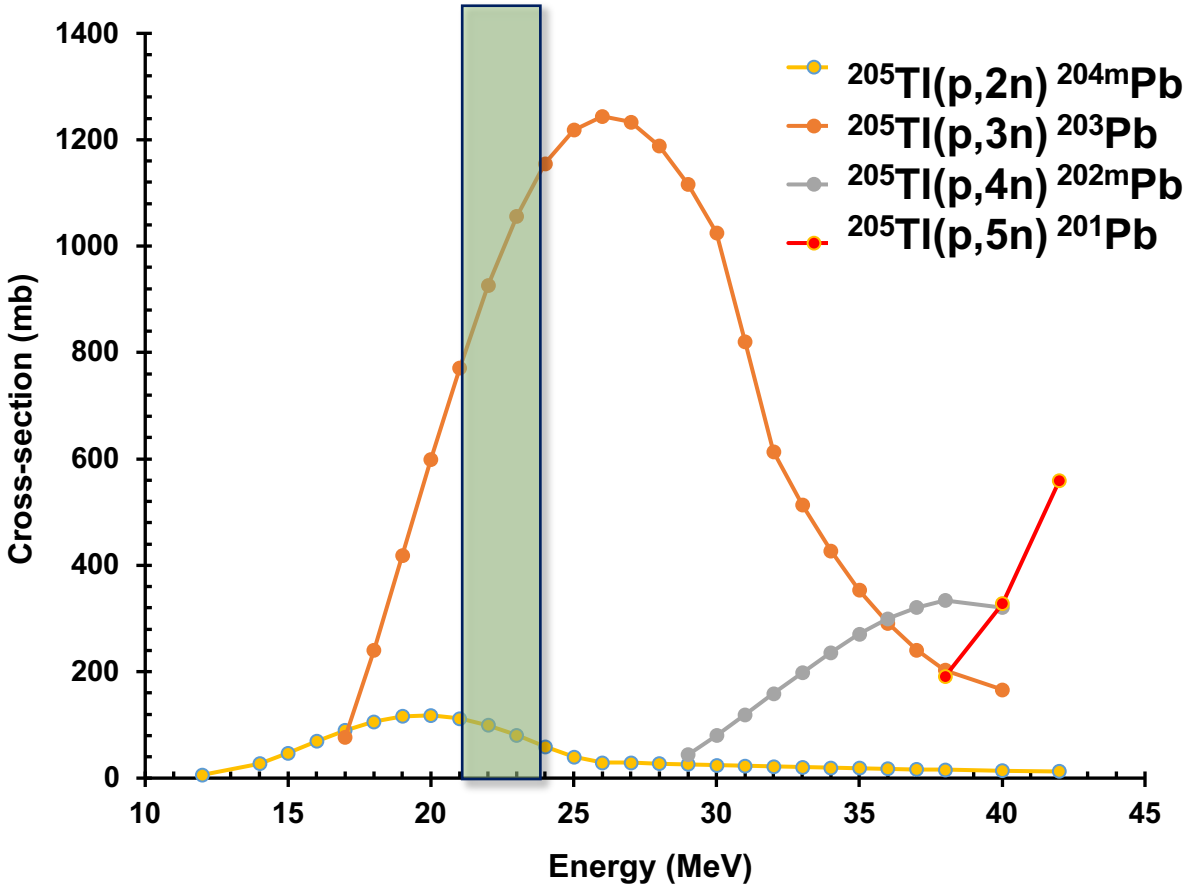
Nuclear Reactions

- $^{203}Tl(p,3n)^{201}Pb$
- $^{203}Tl(p,2n)^{202m}Pb$
- $^{203}Tl(p,n)^{203}Pb$
- $^{205}Tl(p,4n)^{202m}Pb$
- $^{205}Tl(p,3n)^{203}Pb$
- $^{205}Tl(p,2n)^{204m}Pb$



Nuclear Reactions of Proton Irradiation for ^{203}Pb from ^{nat}Tl vs enriched ^{205}Tl materical



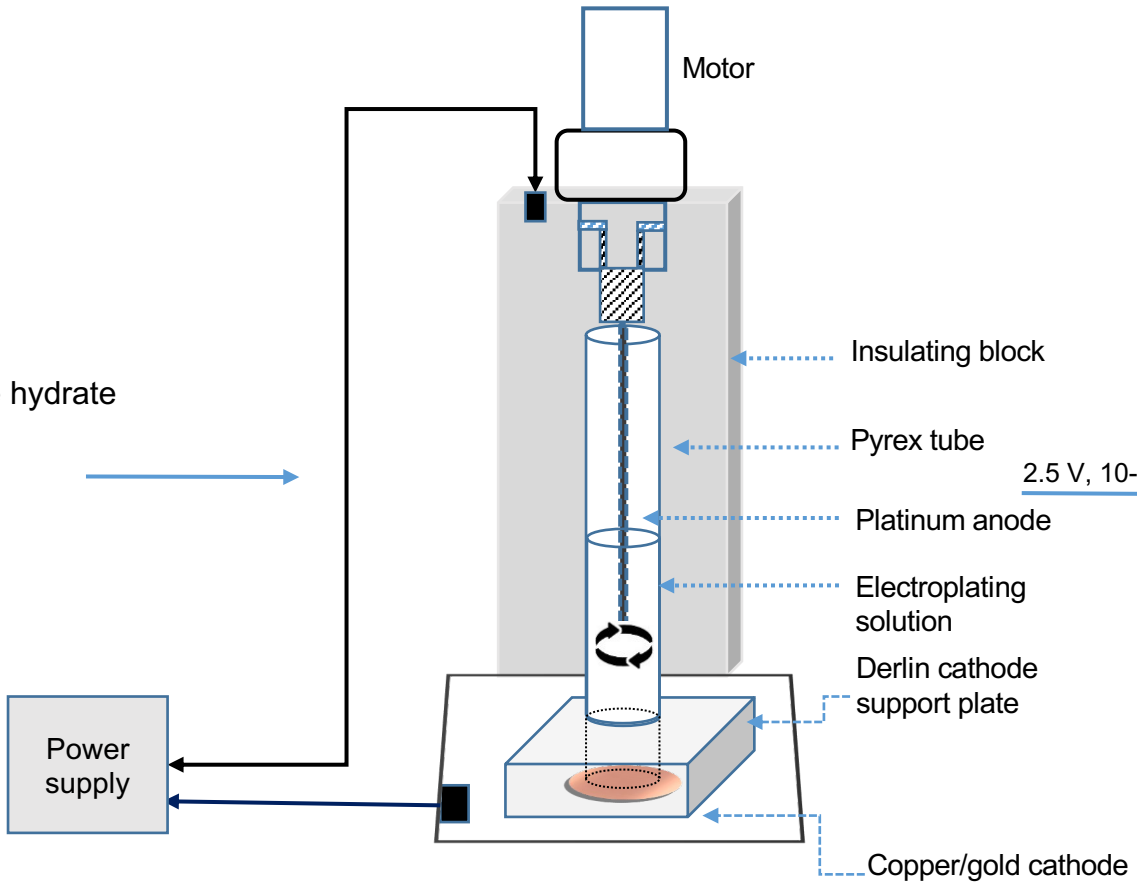


Azzam A. et al." *Applied Radiation and Isotopes* 91 (2014): 109-113
Hermanne, Alex et al." *Nuclear Data for Science and Technology*. Springer, Berlin, Heidelberg, 1992.

Electroplating set-up for target preparation

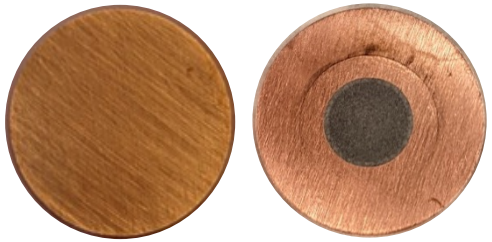
Shefali Saini

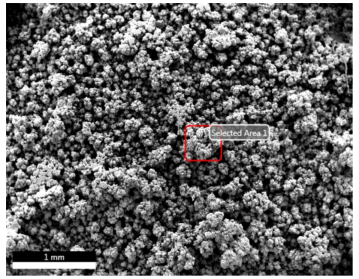
Hydrazine hydrate
NaOH
BRIJ
Tl_2O_3
MQ water



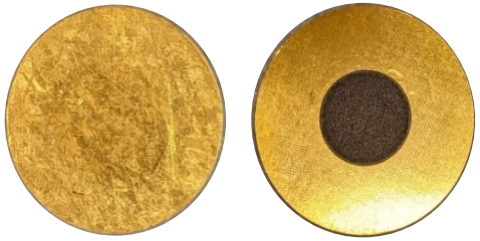
2.5 V, 10-30 mA

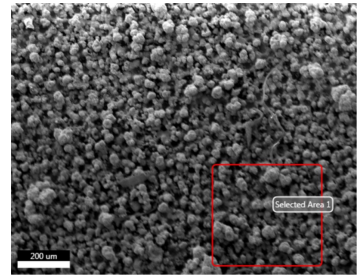
Copper backing





Gold backing

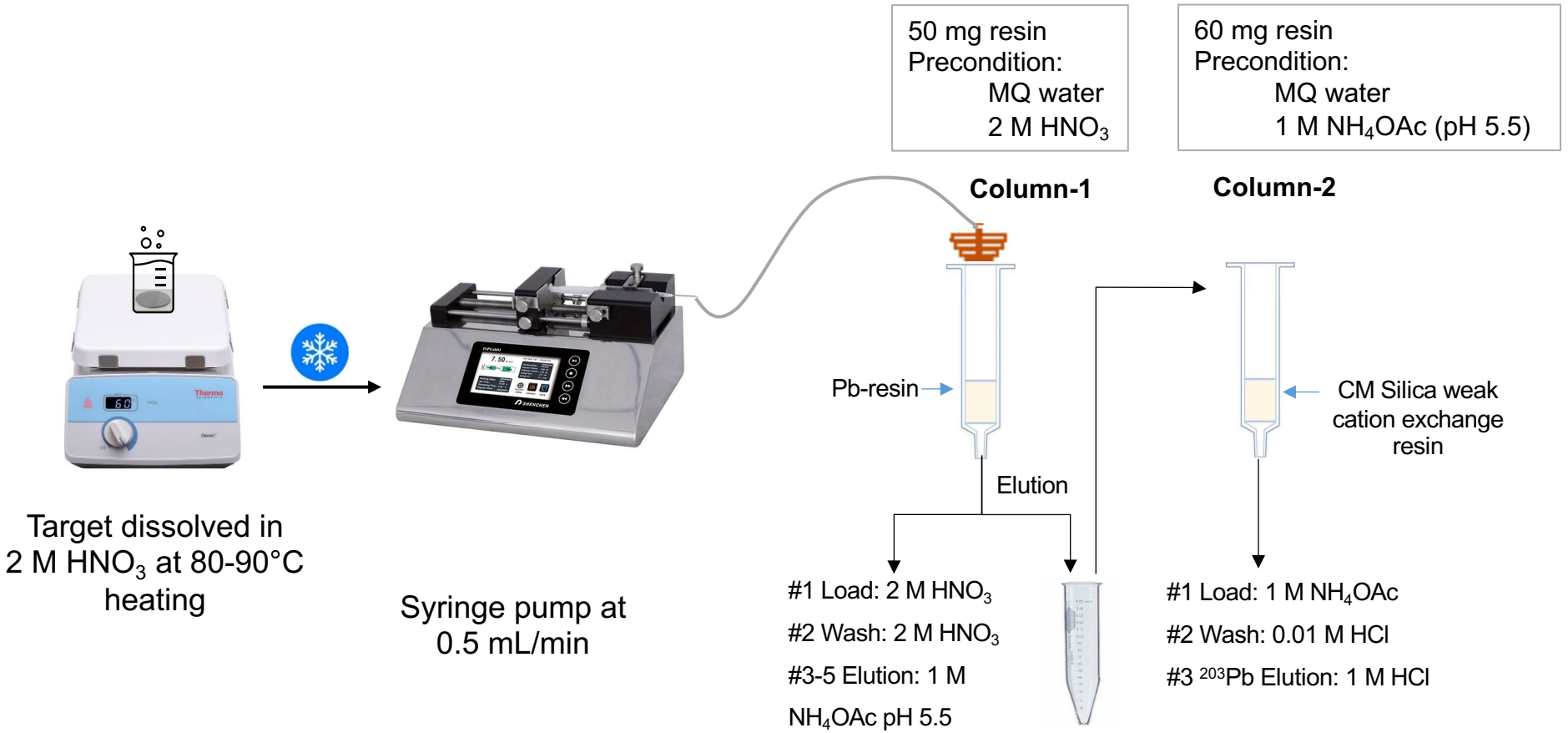




76-114 mg/cm^2 (n = 16)

Electroplating method adapted from Suparman, Ibon. e*t al.* No. INIS-XA--397. 2000.
Electroplating setup adapted from McCarthy, Deborah W., *et al. Nuc Med Biol,* 24,*1* (1997): 35-43.
Saini, S. *et al.* (2023), *J Nucl Med,* online publication: https://doi.org/10.2967/jnumed.123.265976

Purification



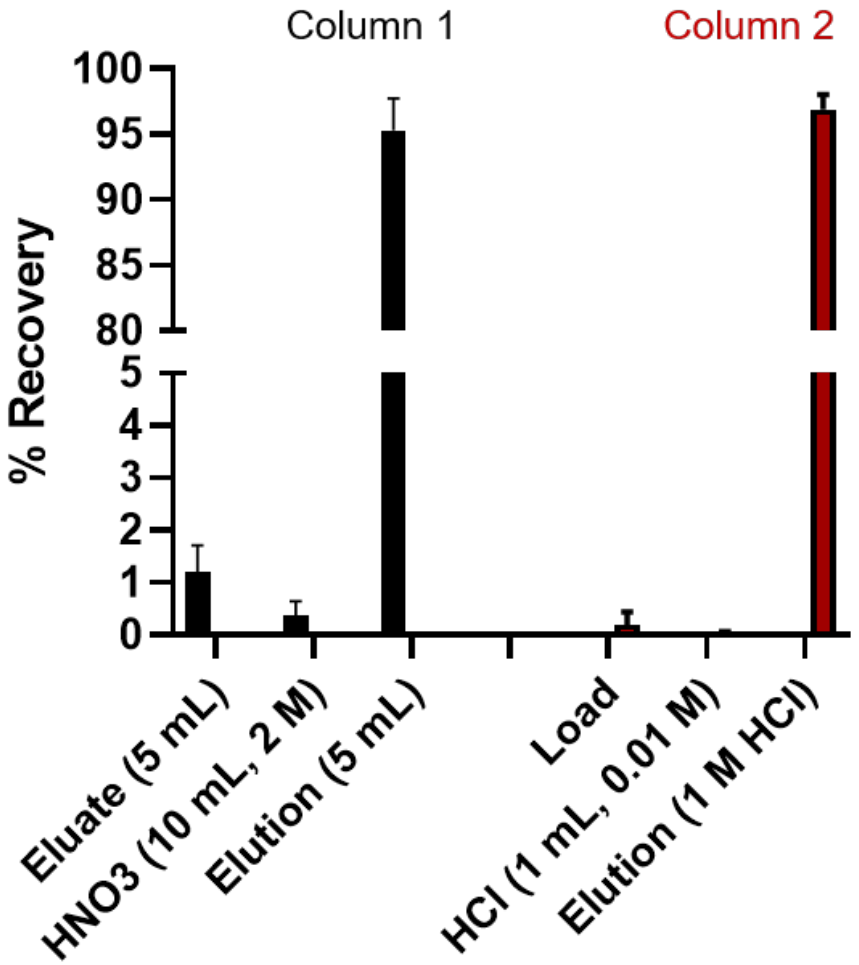
Adapted from: McNeil, Brooke L., *et al. EJNMMI radiopharmacy and chemistry,* 6,1 (2021): 1-18.
Saini, S. *et al.* (2023), *J Nucl Med,* online publication: https://doi.org/10.2967/jnumed.123.265976

Purification – ^{203}Pb Elution Profile

- Elution from first column

  → Ammonium acetate (pH 5): 5 mL
- Elution from second column

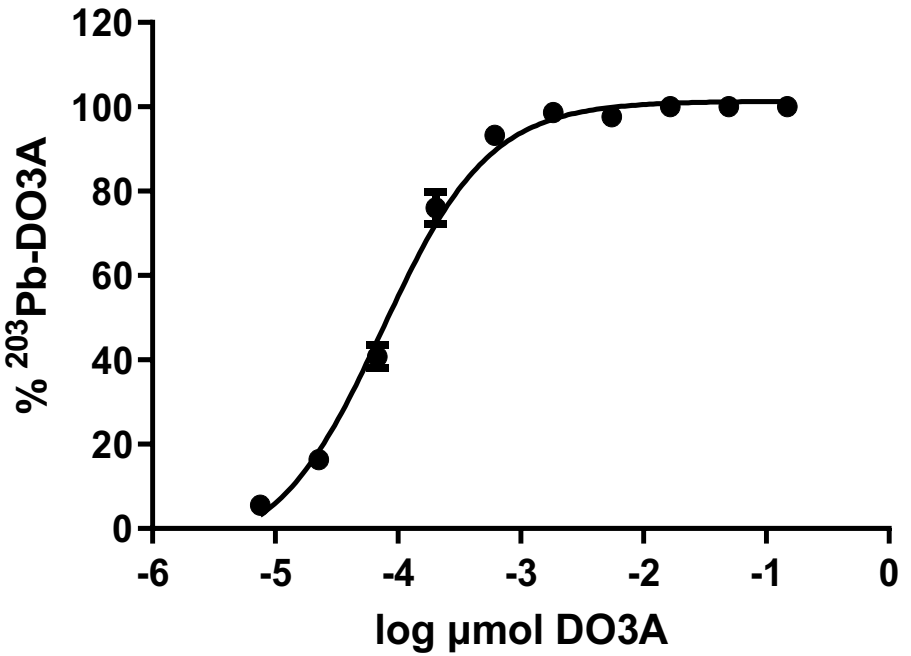
  → 1 M HCl: 0.4 mL
- Average recovery yields: 93 ± 3 %



Saini, S. *et al.* (2023), *J Nucl Med,* online publication: https://doi.org/10.2967/jnumed.123.265976

Molar activity measurements

- DO3A chelator
- Starting 10 mg/mL stock
- Concentration range between 1-200 nmol
- 3.7 MBq [^{203}Pb]$PbCl_2$
- Incubation at 37°C for 30 min
- iTLC-SG using 50 mM EDTA as mobile phase



Average apparent molar activity:
~37.68 ± 5.36 GBq/µmol

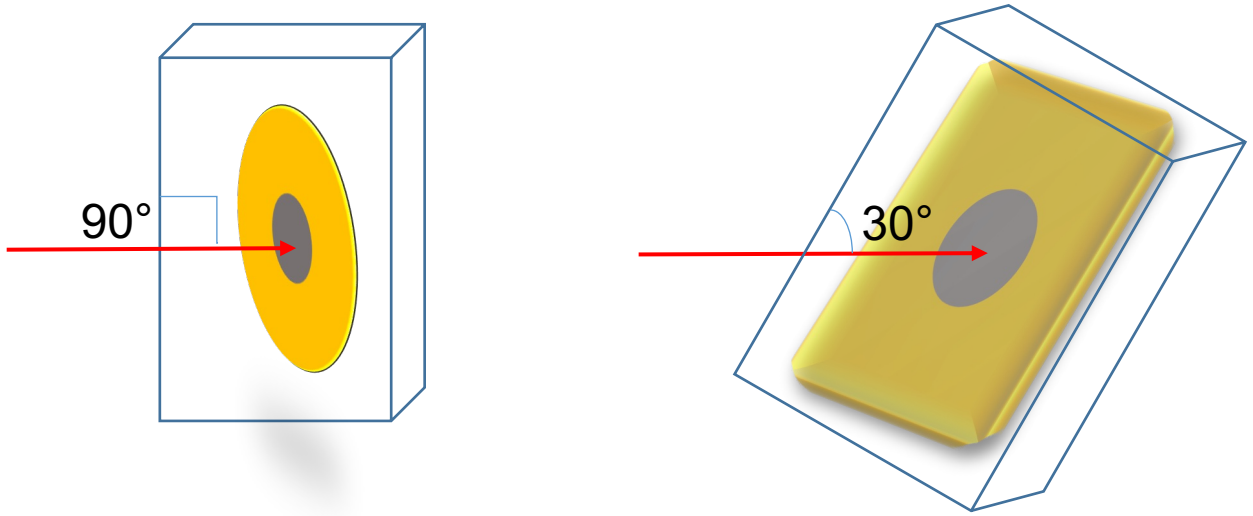
Saini, S. *et al.* (2023), *J Nucl Med,* online publication: https://doi.org/10.2967/jnumed.123.265976

ICP-MS Analysis of Final ^{203}Pb Product

#	Backing	Target	µg				
			Fe	Cu	Zn	Tl	Pb
1.	Copper	**^{205}Tl**	0.01 ± 0.01	0.40 ± 0.48	0.09 ± 0.05	0.22 ± 0.38	0.16 ± 0.06
2.	Gold	**^{205}Tl**	0.01 ± 0.00	0.01 ± 0.01	0.19 ± 0.08	below LOD	0.20 ± 0.08

Saini, S. *et al.* (2023), *J Nucl Med,* online publication: https://doi.org/10.2967/jnumed.123.265976

Preliminary results for 30° slant target design

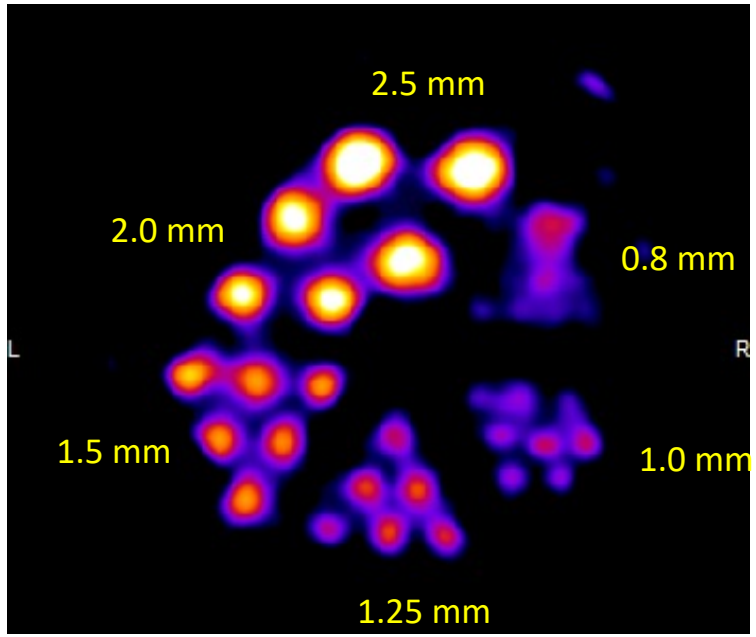


	Target type-1	Target type-2
24 MeV and 3-hour irradiation for 100 mg target		
• Beam current	~40 µA	~80 µA
• Production yields	3.7 GBq	7.4 GBq
• Batch size	9.25 GBq/mL	18 GBq/mL
• AMA (using DO3A)	~37 GBq/µmol	~66 GBq/µmol

***Decay corrected to EOB**

Summary and future directions

- Targetry
  - → Electroplating method yields promising results
  - → Successful target irradiation at 24 MeV and up to 80 μA on the 30° target design without any damage to the target
- Separation method
  - → Separation of ^{203}Pb from ^{205}Tl target material was successfully achieved with robust recovery
- Successfully transitioned the production to the Cyclotron Facility team
  - → Semi-automated separation method in progress
- Ongoing work for recycling ^{205}Tl



Current production status

- Shipping around US and Internationally
- Batch sizes up to 7.4 GBq (200 mCi) in < 500 µL 1 M HCl
- Shipments available nearly every week on Tuesday for Wednesday arrival (US)

Oct-23	Nov-23	Dec-23
10, 17, 24, 31	14, 28	12, 19

Jan-24	Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24
16, 23, 30	13, 20, 27	12, 19, 26	2, 16, 23, 30	14, 21, 28	18, 25	9, 16, 23, 30	13, 20, 27	10, 17, 24

To purchase ^{203}Pb or any other DOE isotope we provide - ^{48}V, ^{52}Mn, ^{55}Co - place orders through www.isotopes.gov.

Acknowledgements

UAB

- Suzanne Lapi, PhD
- Shefali Saini
- Jean-Pierre Appiah
- Jason Rider

Collaborators

- Viewpoint Molecular Targeting (now Perspective therapeutics): Michael Schultz and Nicholas Baumhover

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THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Thank you!