

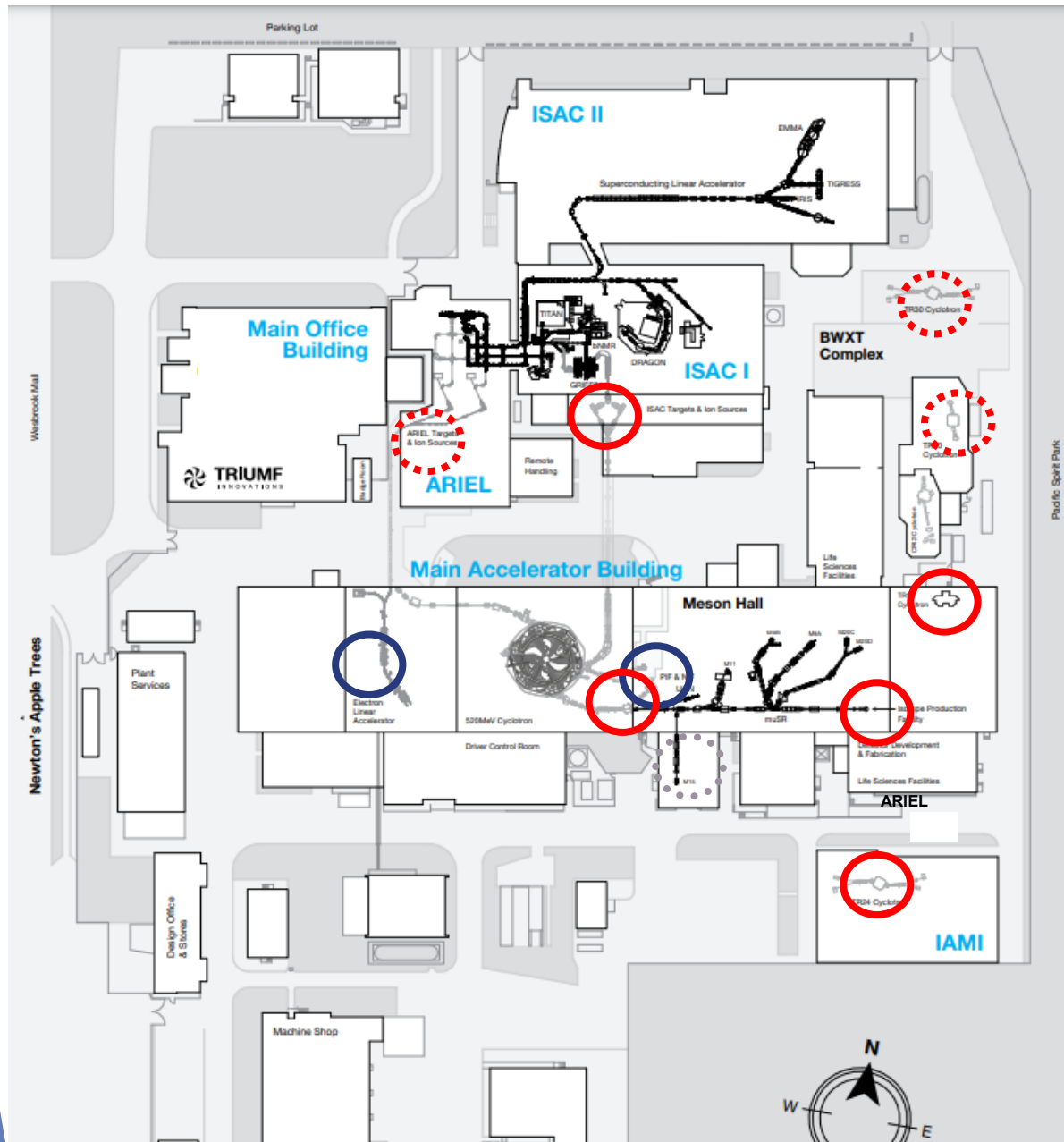
# Accelerator-based production of medical radioisotopes

Deputy Director | Life Sciences

Cornelia Hoehr



# Medical Application @ TRIUMF



TRIUMF - accelerator lab  
Expertise in

- Accelerator technology
- Accelerator operation
- Detectors
- Targets for isotope production
- Interaction of particles

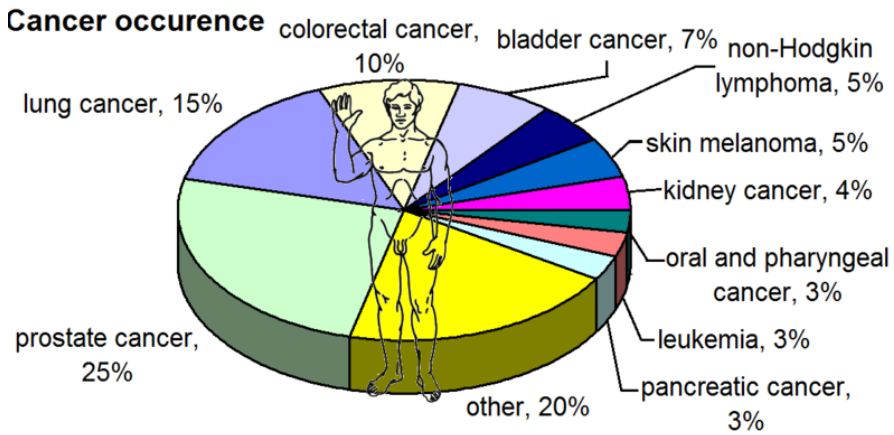
**Applicable to medical isotopes (and radiotherapy)**



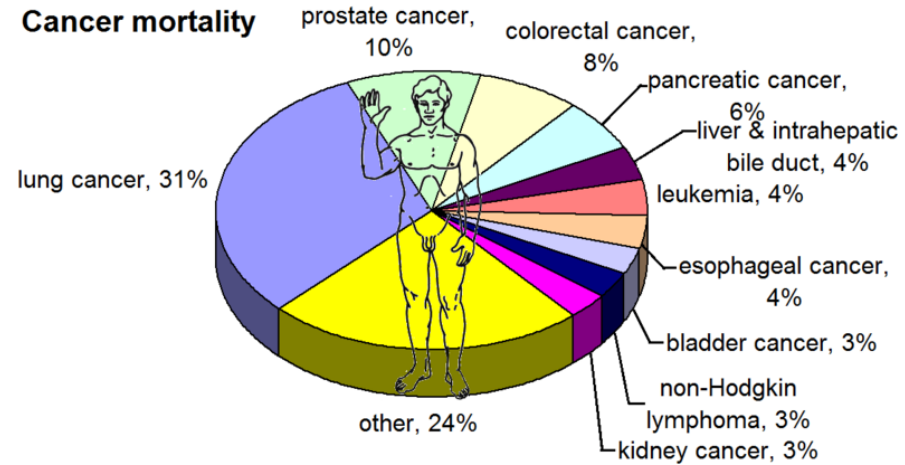


# Cancer

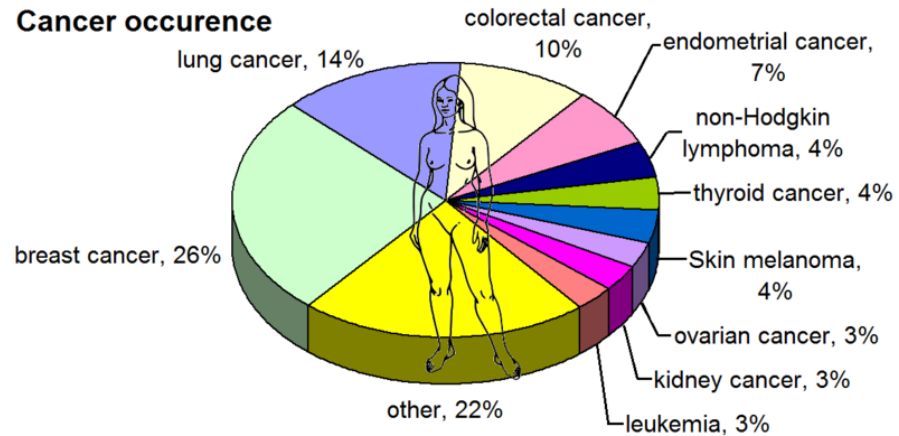
## Cancer occurrence



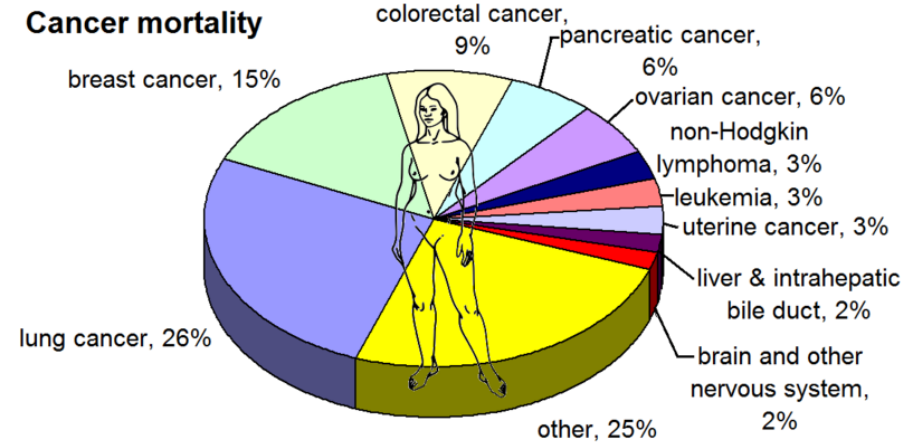
## Cancer mortality



## Cancer occurrence



## Cancer mortality



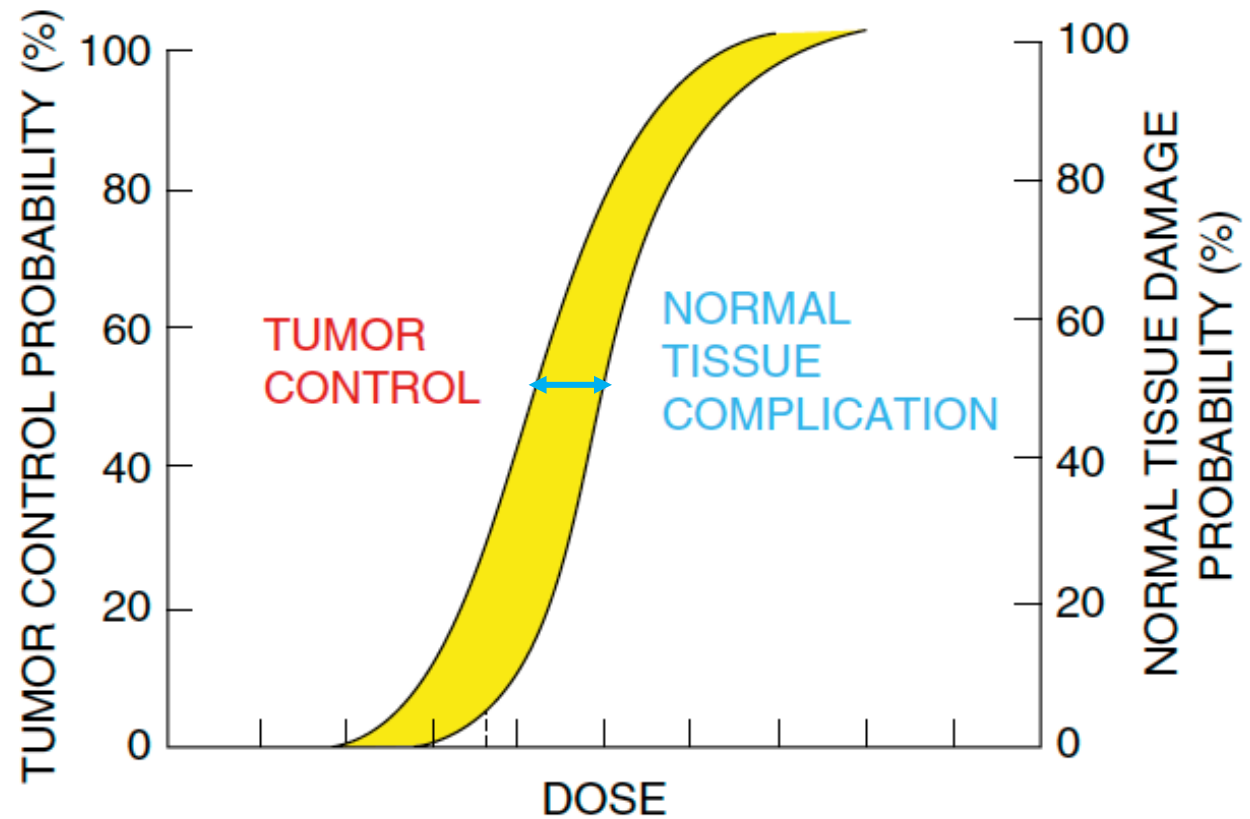
Norfolk, Virginia

AccelApp 24



# Cancer treatment

- Surgery
- Chemotherapy
- Ionizing radiation
  - External
  - Internal



- Holy grail of cancer research: **Increase gap (therapeutic index/window) as much as possible**



# Cancer treatment

- Surgery
- Chemotherapy
- Ionizing radiation
  - External
  - Internal

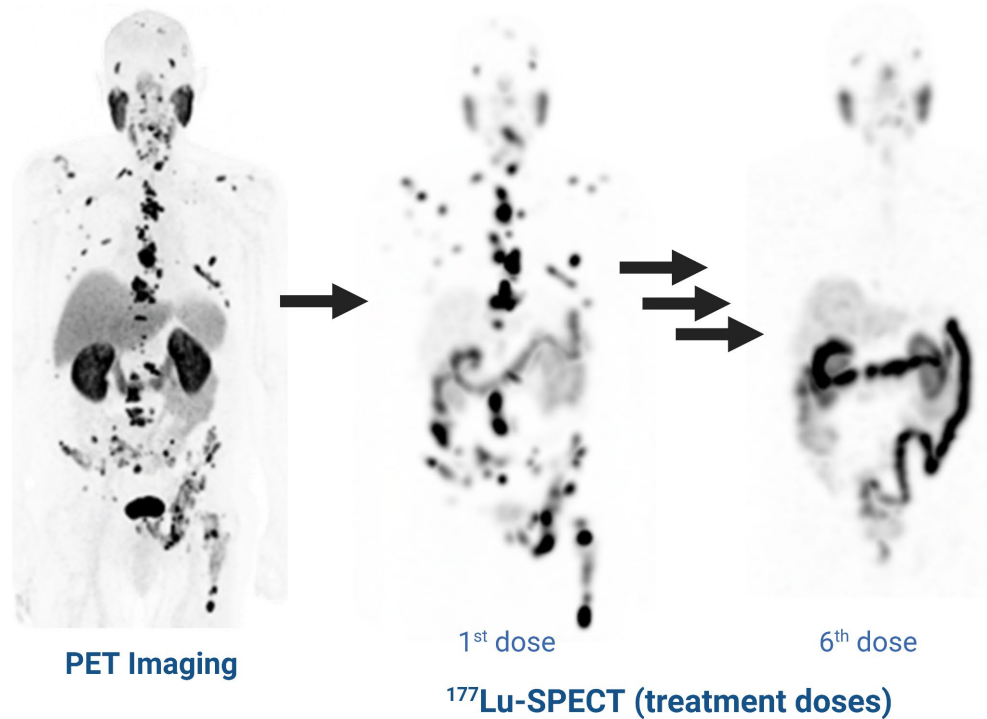


Image courtesy Dr. François Bénard (BC Cancer)

Targeted Radiation Therapy (TRT)

Theranostic - Therapy and Diagnostic





# Medical isotope selection

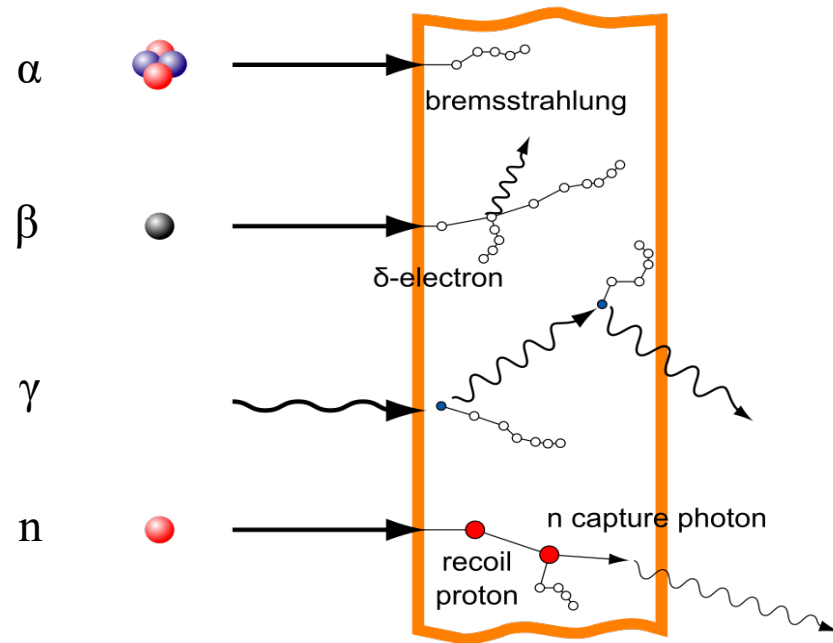
- Exercise in compromise and balance





# Medical isotope selection

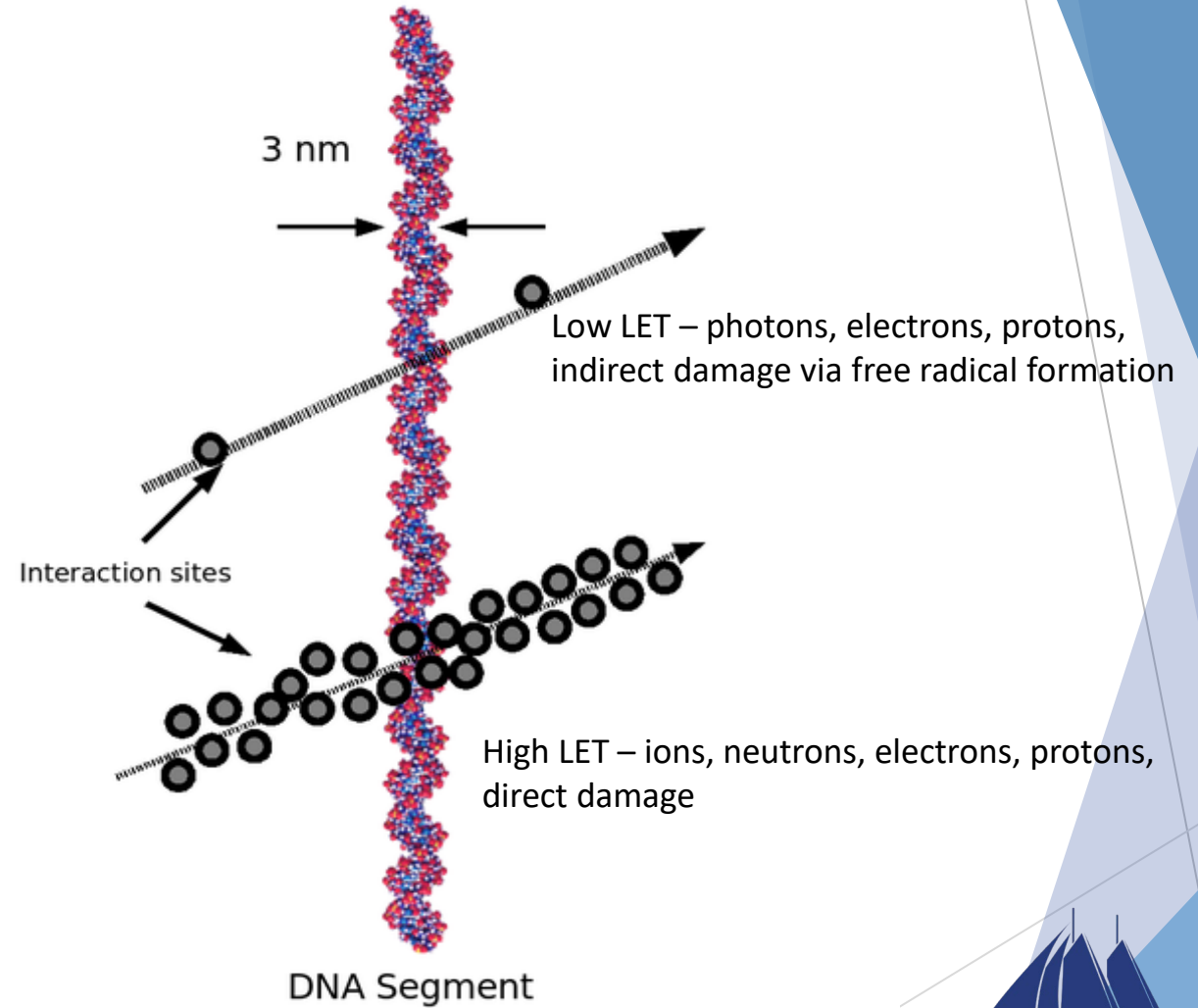
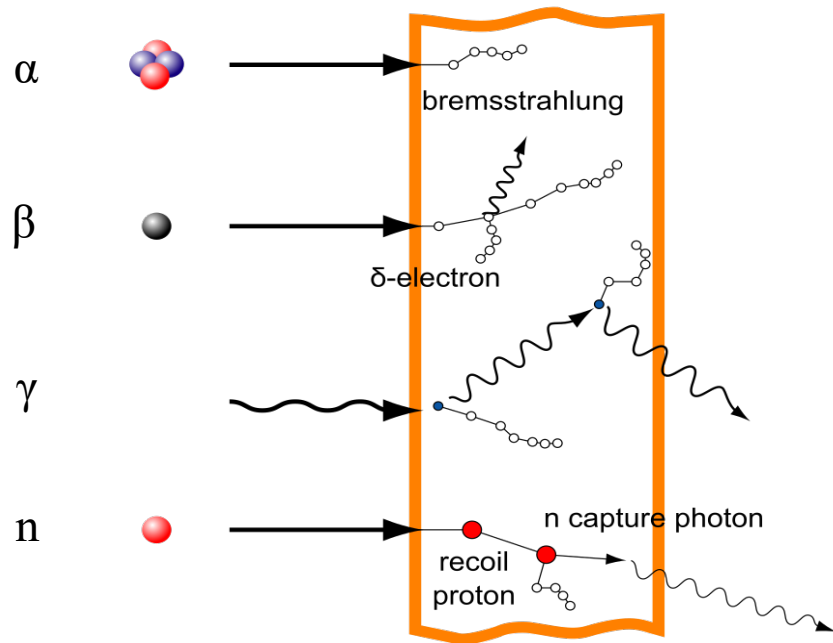
- Exercise in compromise and balance
- Selection
  - Different emitters





# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters - LET

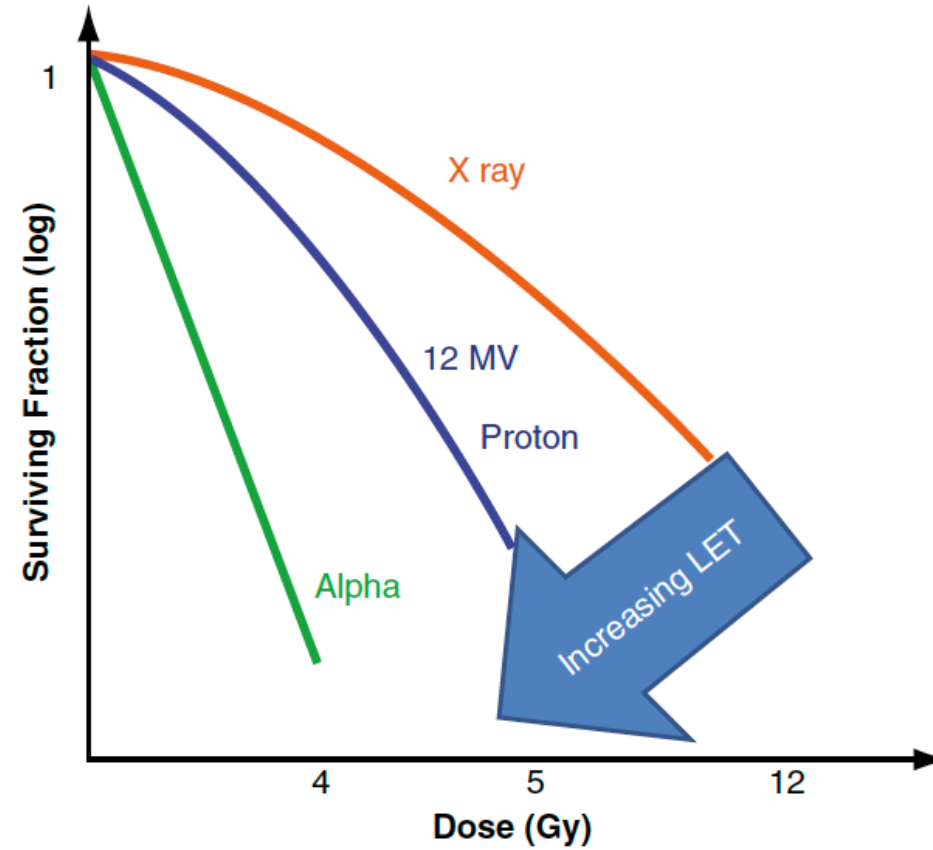
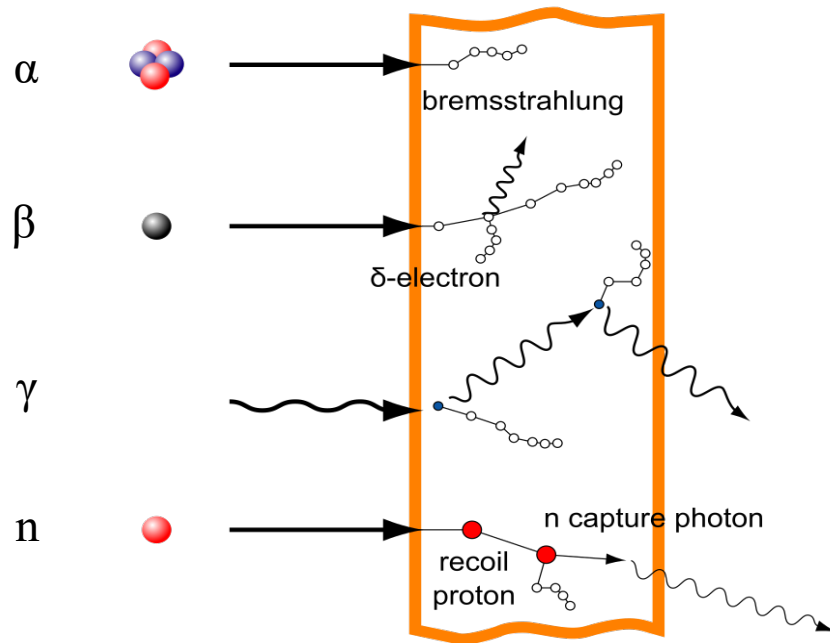






# Medical isotope selection

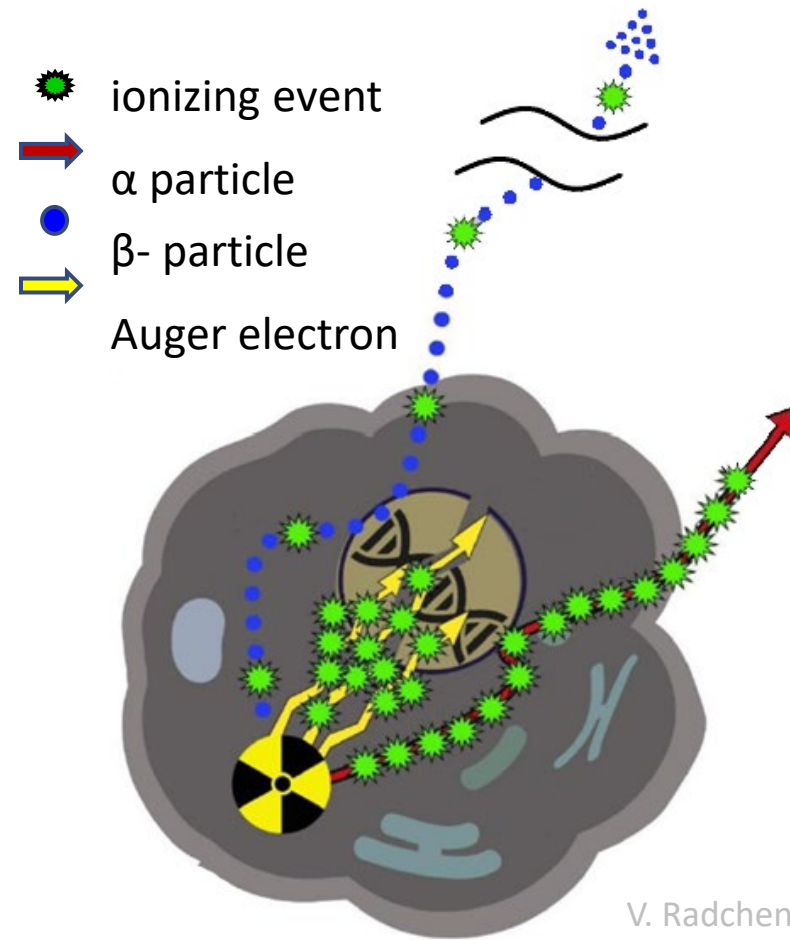
- Exercise in compromise and balance
- Selection
  - Different emitters - RBE





# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range



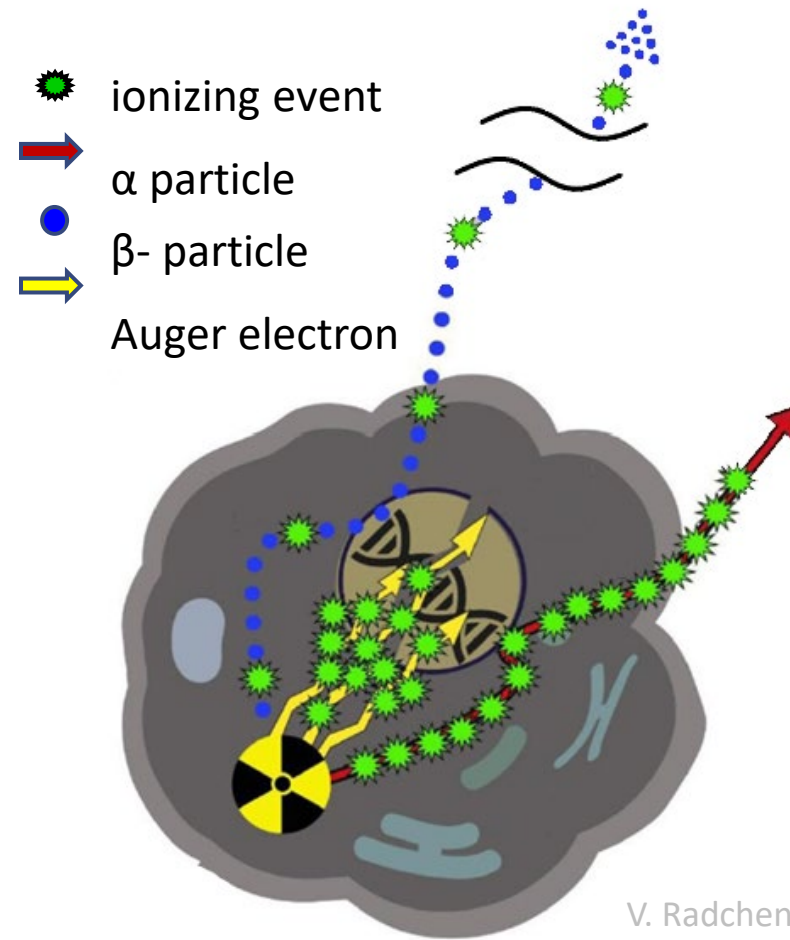
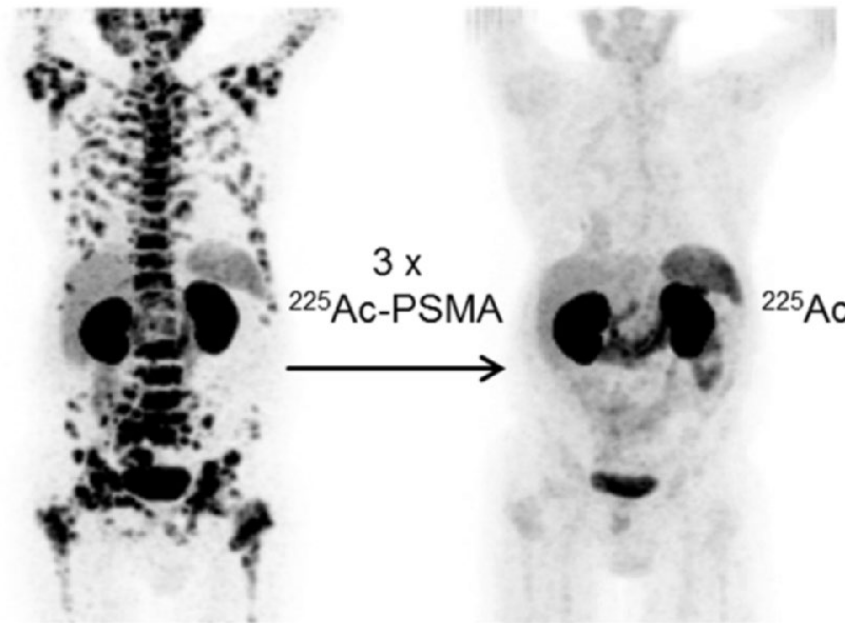
V. Radchenko





# Medical isotope selection

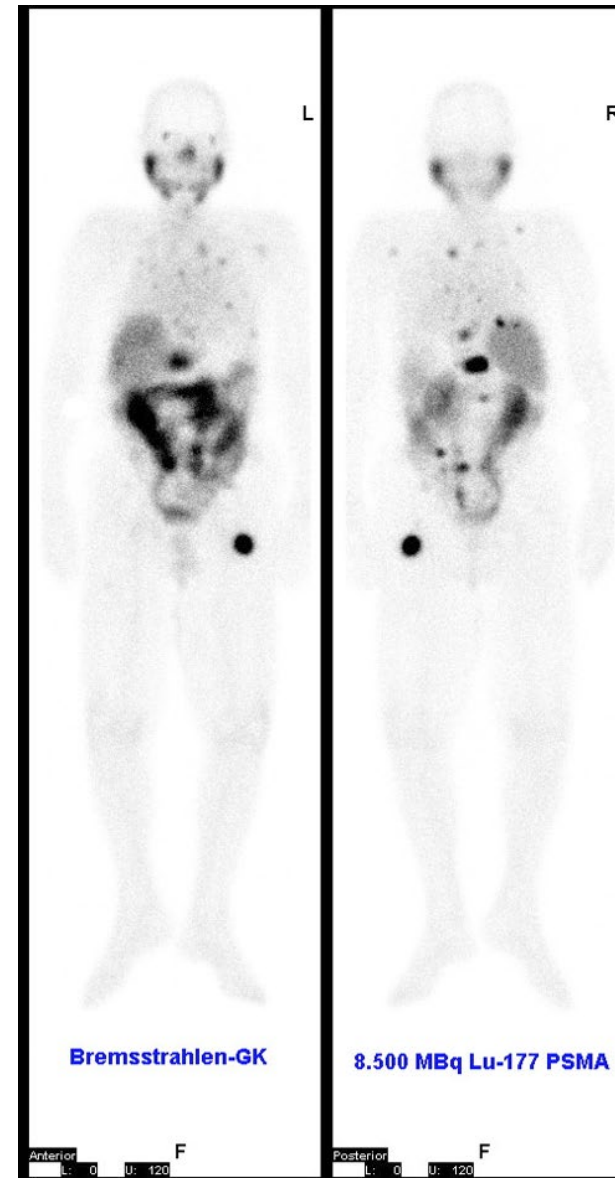
- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range





# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window





# Medical isotope selection

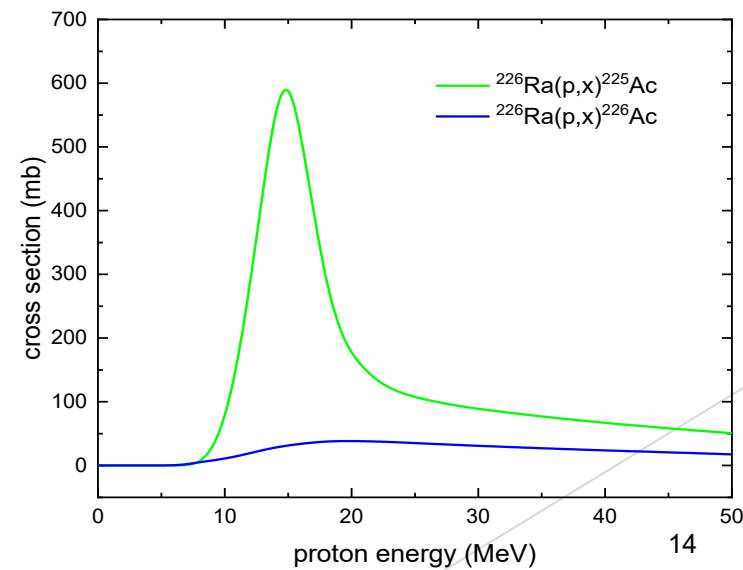
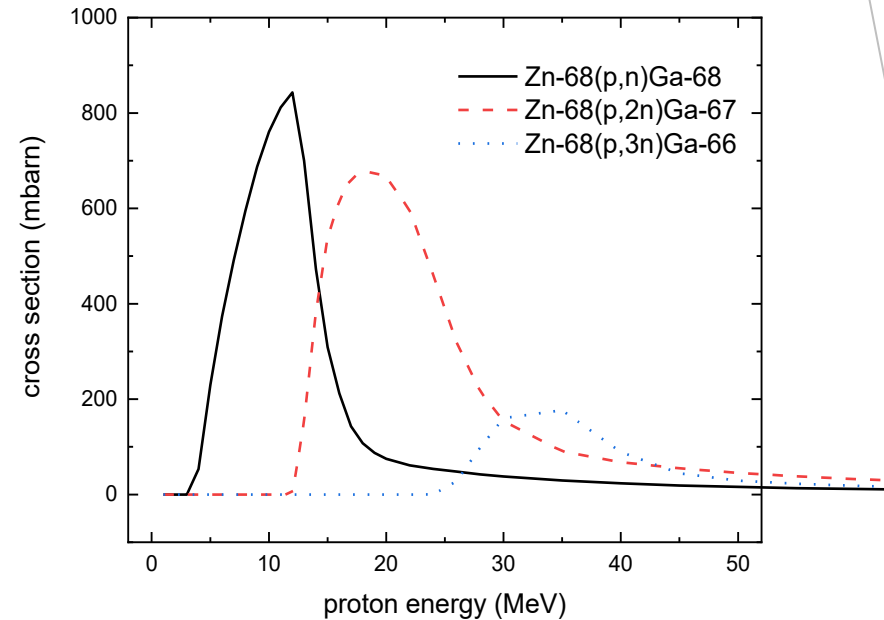
- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window
- Production
  - Sites and availability, delivery radius





# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window
- Production
  - Sites and availability, delivery radius
  - Cross sections, contamination



Norfolk, Virginia

AccelApp<sup>24</sup>



# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window
- Production
  - Sites and availability, delivery radius
  - Cross sections, contamination
  - Target availability and cost

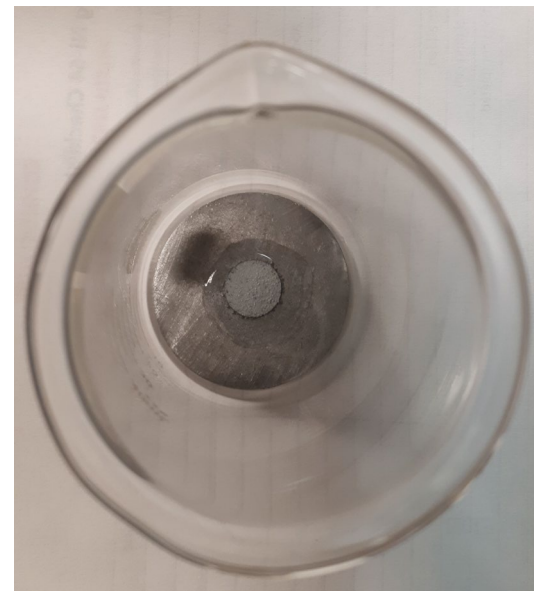
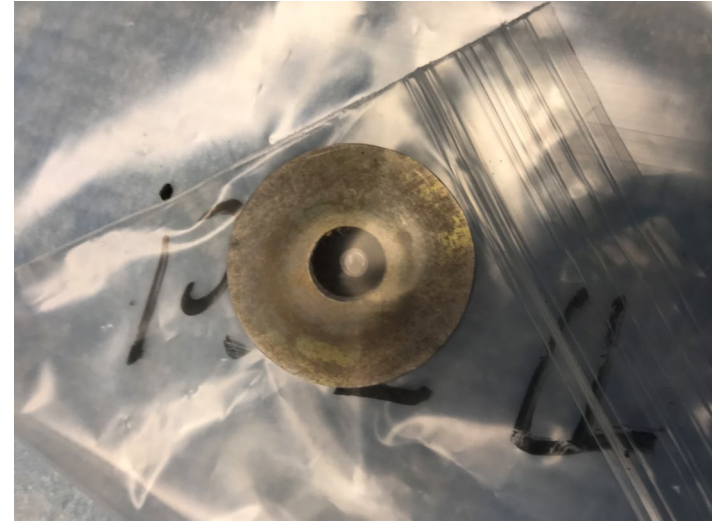
**OUT OF STOCK**





# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window
- Production
  - Sites and availability, delivery radius
  - Cross sections, contamination
  - Target availability and cost
  - Target physical and chemical properties







# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window
- Production
  - Sites and availability, delivery radius
  - Cross sections, contamination
  - Target availability and cost
  - Target physical and chemical properties
  - Labeling chemistry





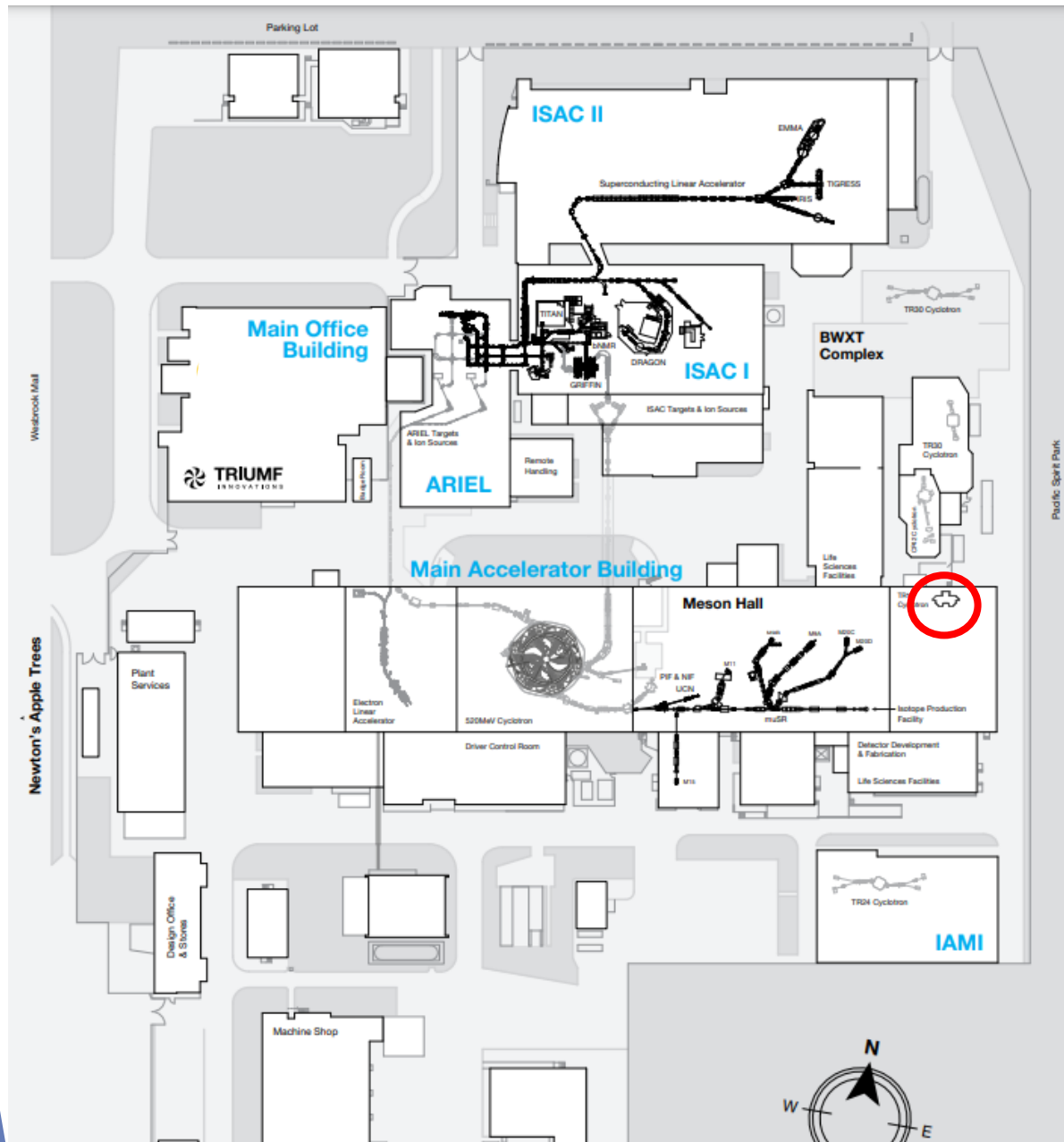
# Medical isotope selection

- Exercise in compromise and balance
- Selection
  - Different emitters – LET, RBE, range
  - Dosimetry – theranostic, therapeutic window
- Production
  - Sites and availability, delivery radius
  - Cross sections, contamination
  - Target availability and cost
  - Target physical and chemical properties
  - Labeling chemistry
  - Radioactive waste





# Low energy cyclotron

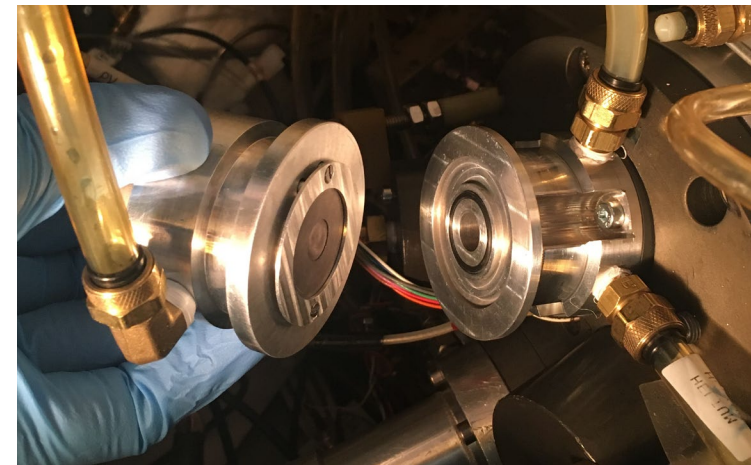
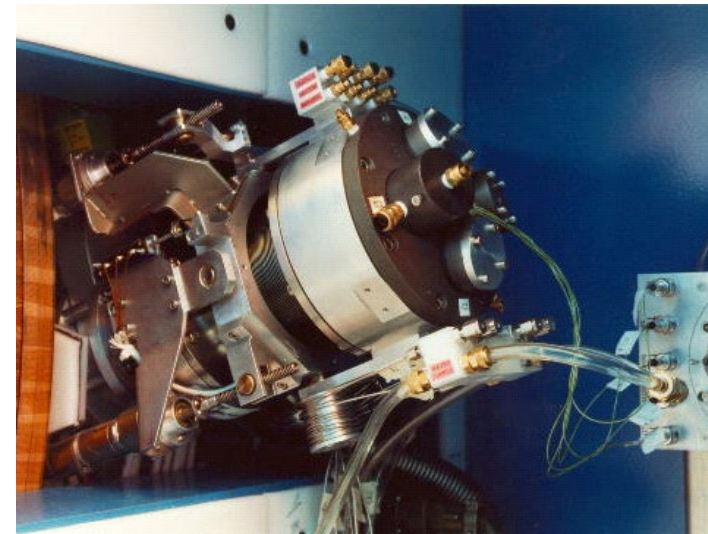
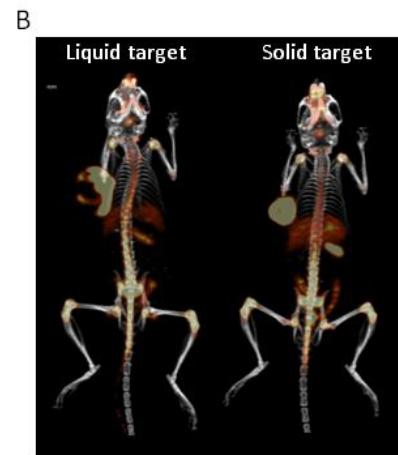
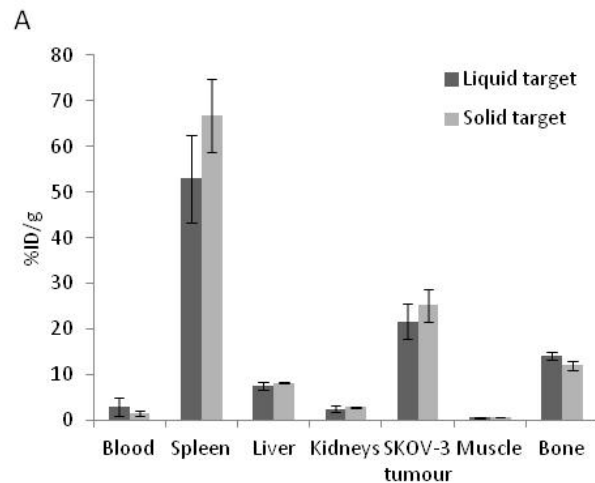


- Routine production of  $^{11}\text{C}$  and  $^{18}\text{F}$
- Radiometals



# Low energy cyclotron

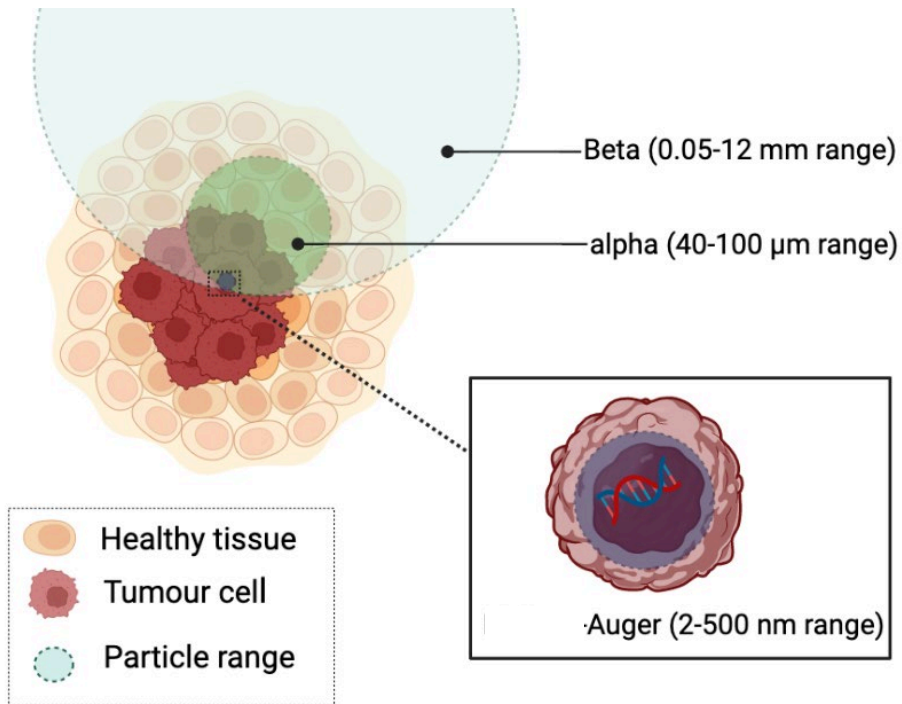
- Gaseous Target –  $^{11}\text{C}$ ,  $^{18}\text{F}$
- Liquid target –  $^{13}\text{N}$ ,  $^{18}\text{F}$ ,  $^{68}\text{Ga}$ ,  $^{44}\text{Sc}$ ,  $^{58}\text{Co}$ ,  $^{61/64}\text{Cu}$ ,  $^{86}\text{Y}$ ,  $^{89}\text{Zr}$ ,  $^{94\text{m}}\text{Tc}$ ,  $^{197}\text{Hg}$



- Solid target –  $^{44}\text{Sc}$ ,  $^{45}\text{Ti}$ ,  $^{52}\text{Mn}$ ,  $^{61/64/67}\text{Cu}$ ,  $^{68}\text{Ga}$ ,  $^{117/118/119}\text{Sb}$ ,  $^{132/135}\text{La}$ ,  $^{192}\text{Ir}$ ,  $^{197}\text{Hg}$ ,  $^{203}\text{Pb}$



# Low energy cyclotron – Therapeutic: Auger emitters



## Solid target:

- Au-197(p,n)Hg-197g/m  
Theranostic pair
- Sn-nat(p,n)Sb-119
- Ho-165(p,n)Er-165

## Liquid target:

- Au-197(p,n)Hg-197g/m  
Theranostic pair
- Rh-103(p,n)Pb-103



# Low energy cyclotron – Therapeutic: Alpha emitters

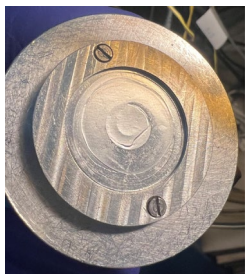
Target design with Ba salt



193.8 mg of  
 $\text{Ba}(\text{NO}_3)_2$



Encapsulated



Irradiated at TR13

## Ra-226(p,2n)Ac-225

### Future Plans

- Obtain external and internal safety approval for working with and irradiating  $^{226}\text{Ra}$
- Perform irradiation of  $\mu\text{g}$  quantities of  $^{226}\text{Ra}$  at TRIUMF
- Perform complementary measurements
- Develop a separation & purification with Ra/Ba/Ac, and  $^{226}\text{Ra}$  recycling scheme

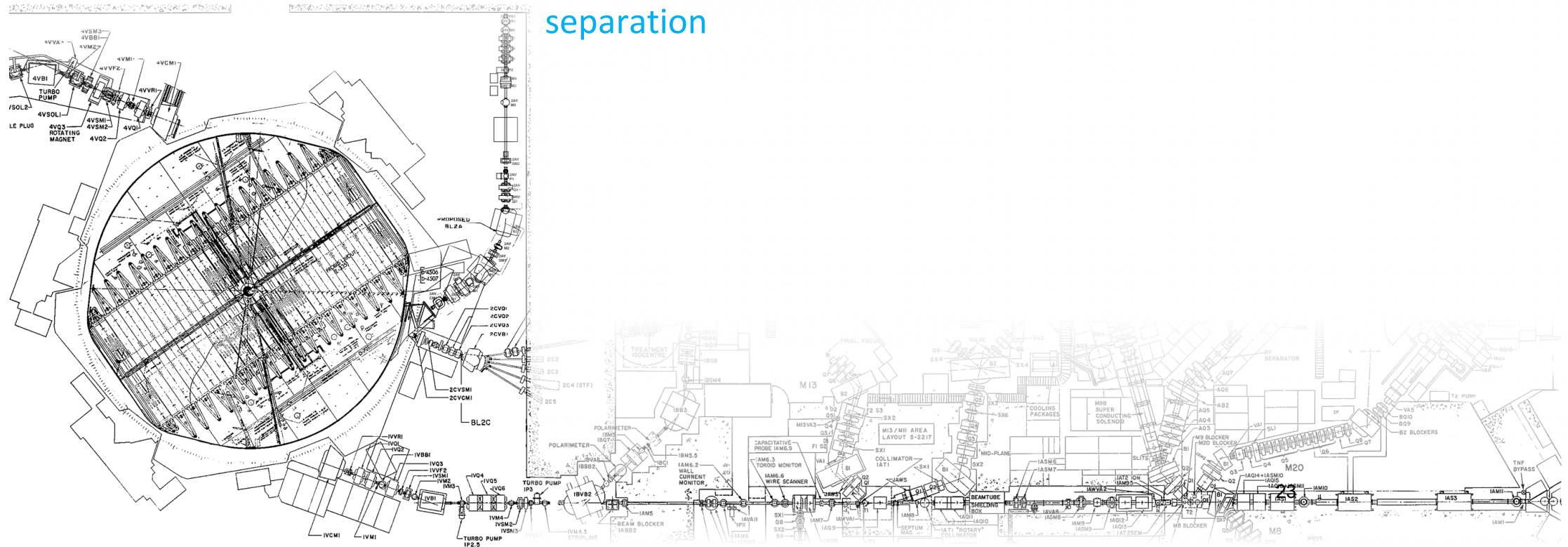


# Main Accelerator Program

## ISAC



- 480 MeV, 10  $\mu$ A, UCx targets
- Currently produces  $\sim 37$  MBq of  $^{225}\text{Ac}$  per year via mass separation



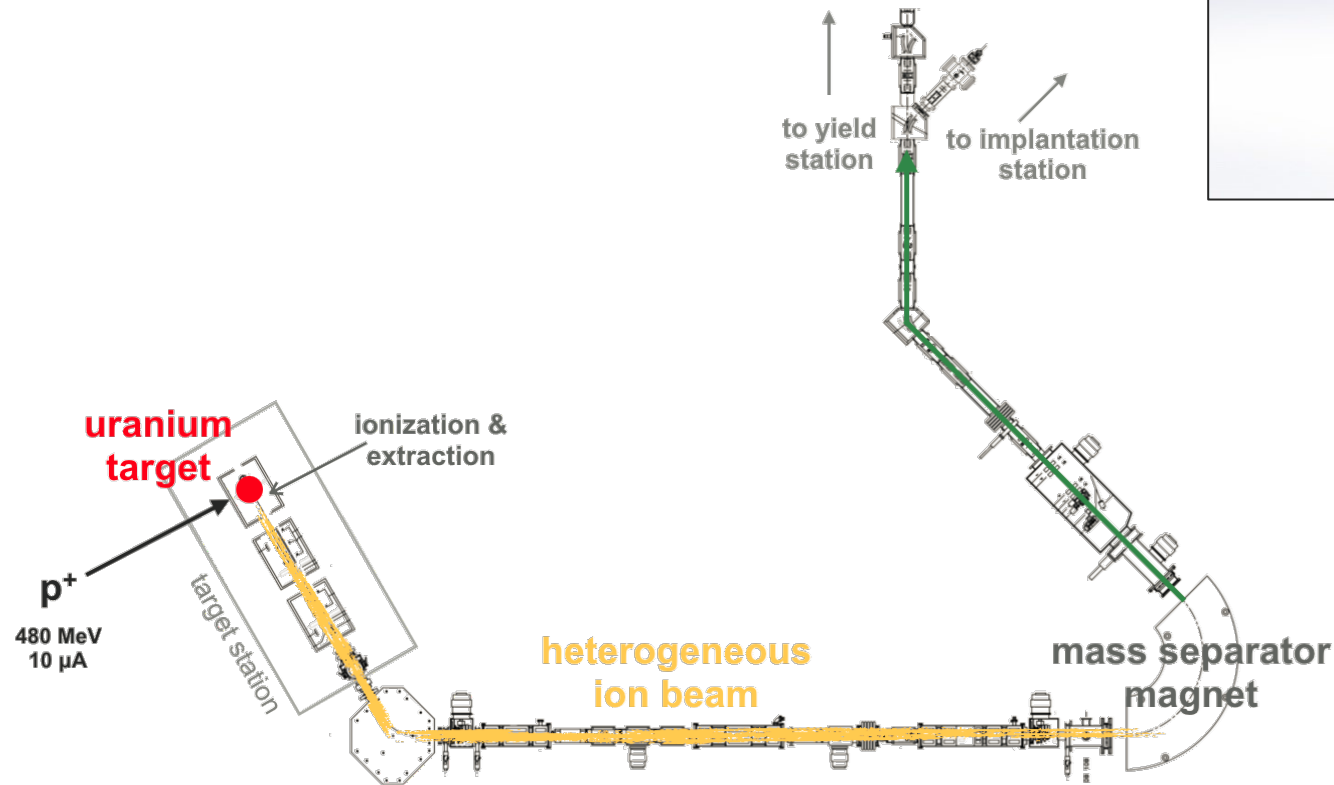
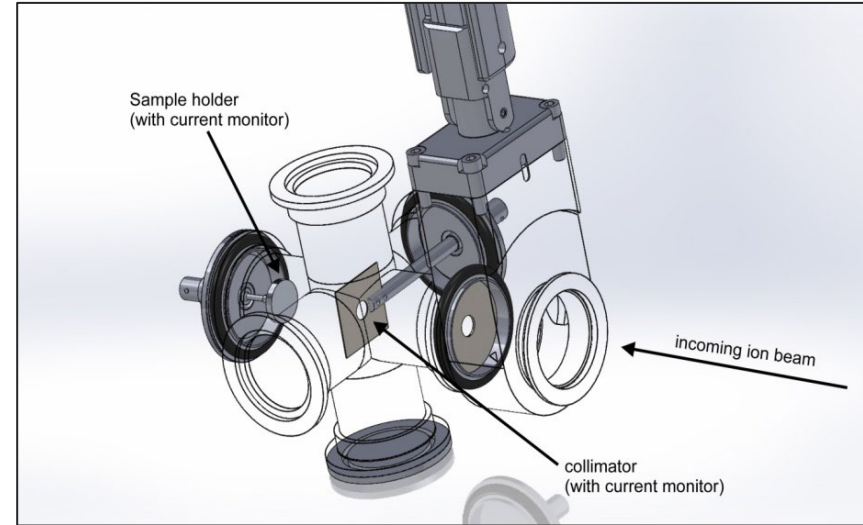


# Isotope Separation On-Line

ISAC - ISOL

Low activity (kBq to MBq), **high purity**

- Actinide targets
- Feasibility chemistry, radiolabeling



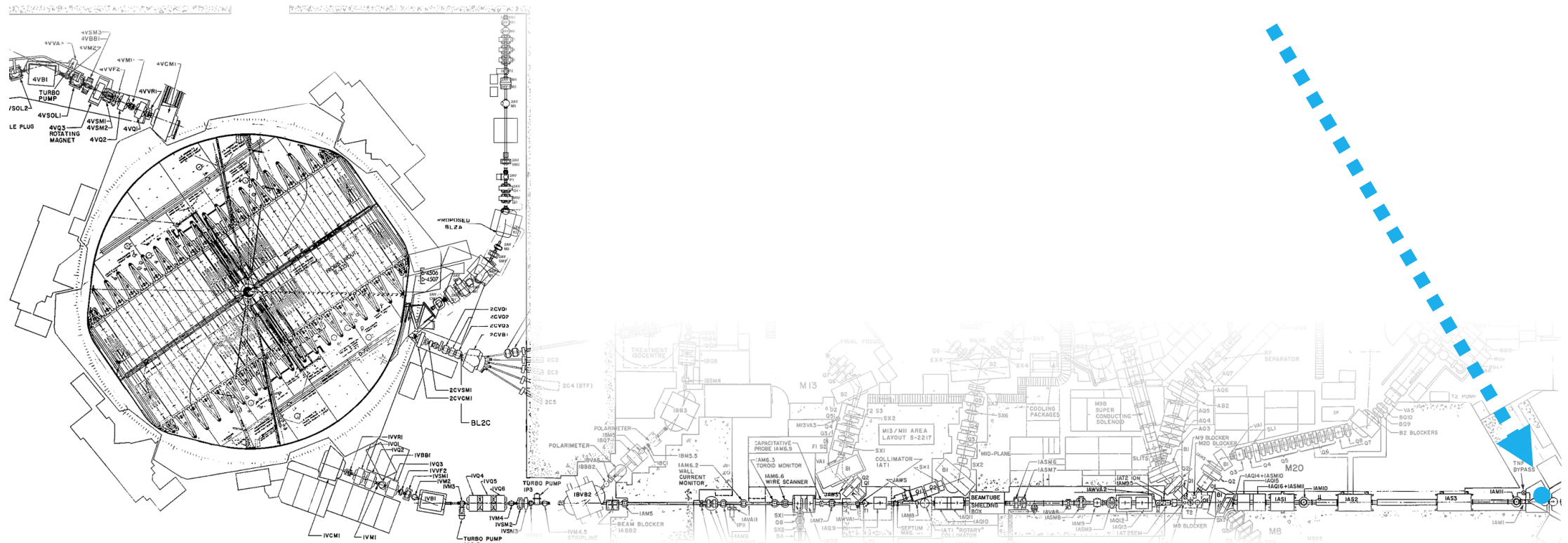
$^{211/209}\text{At}$ ,  
 $^{225}\text{Ra}/^{225}\text{Ac}$ ,  $^{224}\text{Ra}$ ,  
 $^{165}\text{Er}$ ,  $^{155}\text{Tb}$





# Main Accelerator Program

- 450-480 MeV, 60-150  $\mu$ A
- Continuously receives beam  $\sim$ 7 months/year



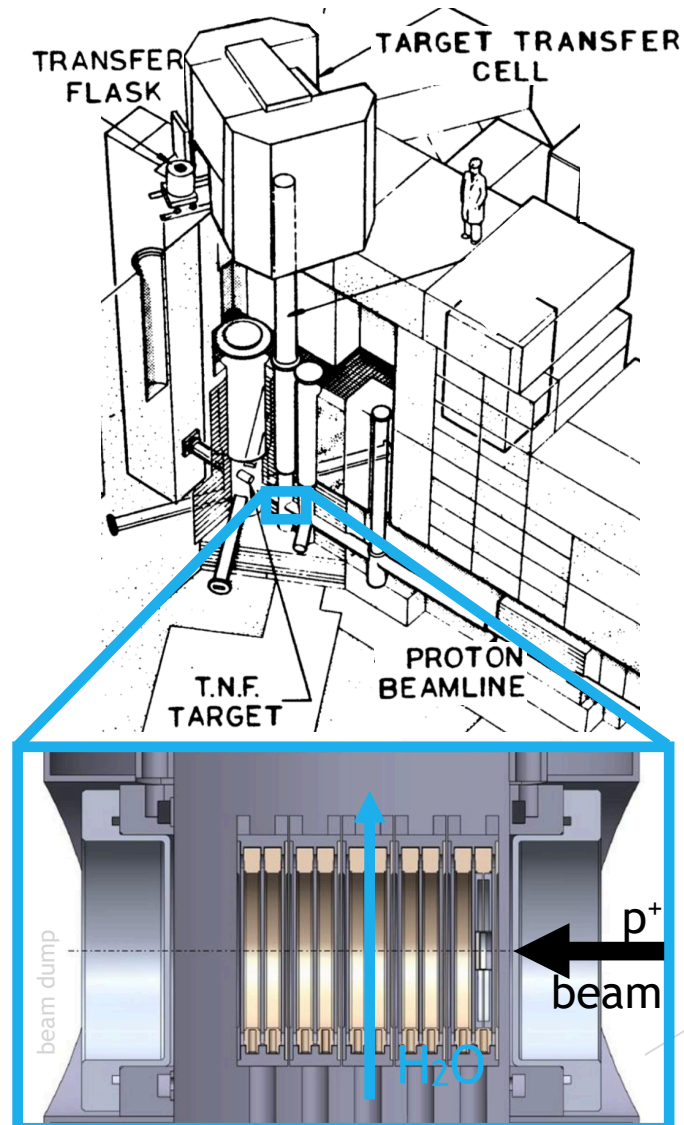


# Isotope Production Facility

500 MeV – IPF (BL1A)

Intermediate activity (MBq), spallation

- Routine, independent production



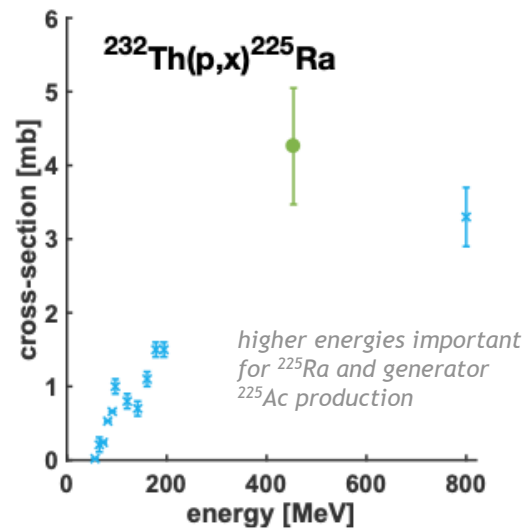
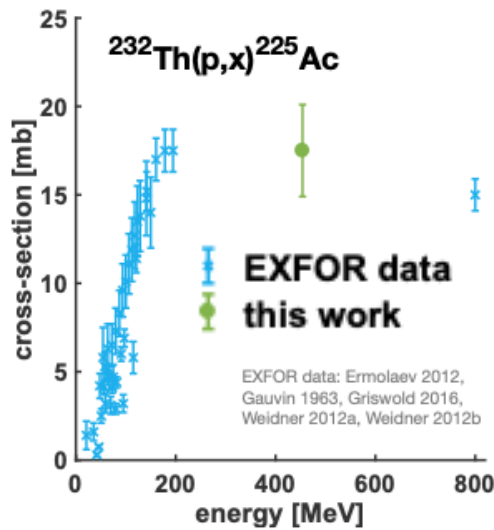


# Isotope Production Facility

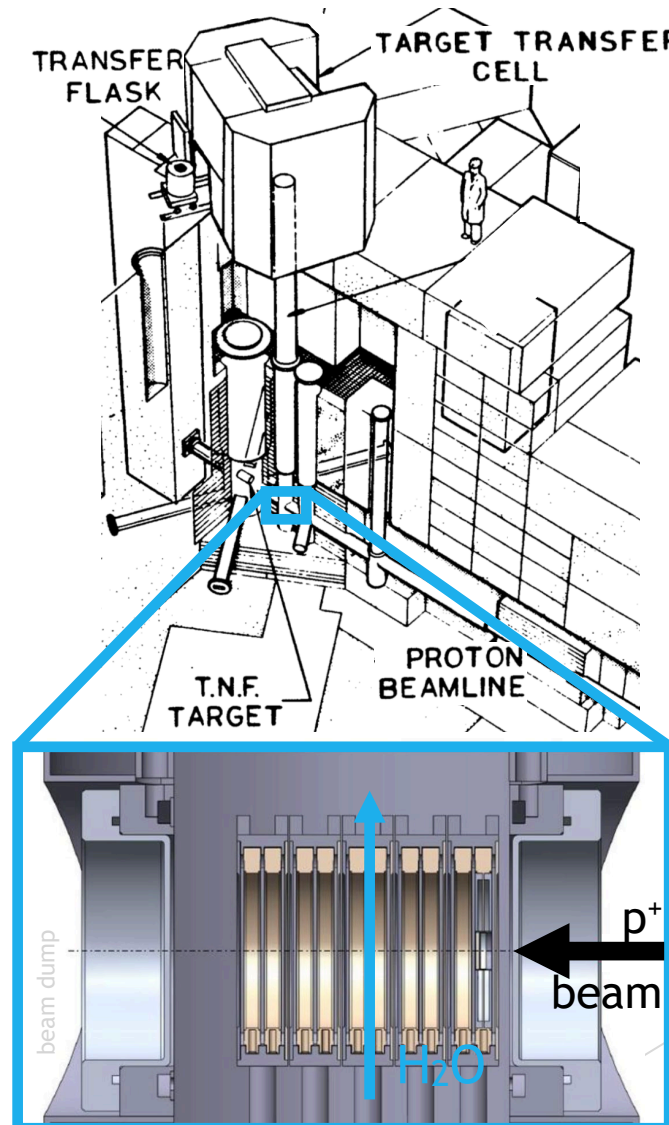
500 MeV – IPF (BL1A)

Intermediate activity (MBq), spallation

- Routine, independent production



Typical beam: 65-85  $\mu\text{A}$ , 454 MeV



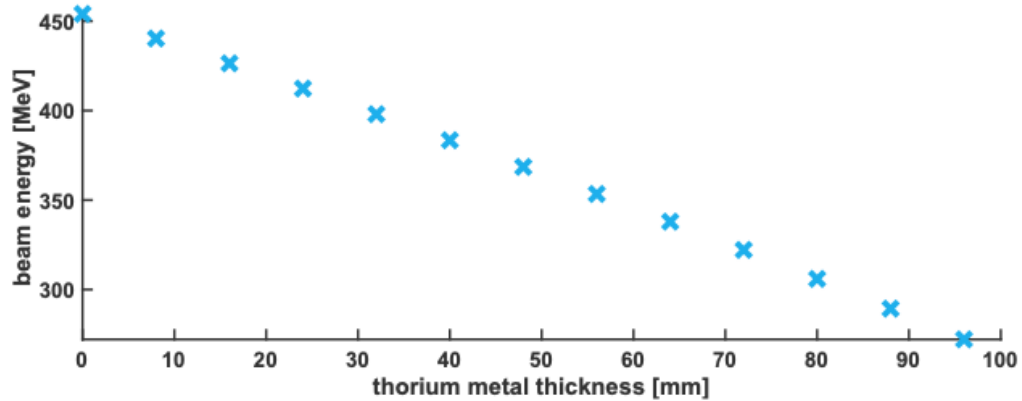


# Isotope Production Facility

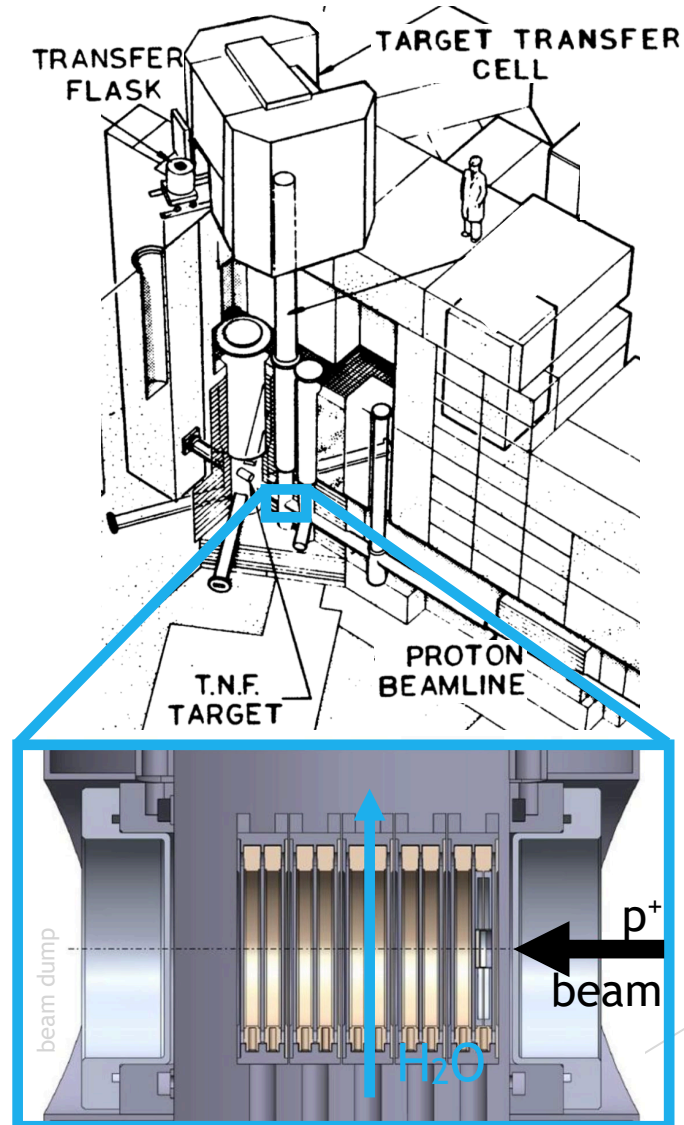
500 MeV – IPF (BL1A)

Intermediate activity (MBq), spallation

- Routine, independent production

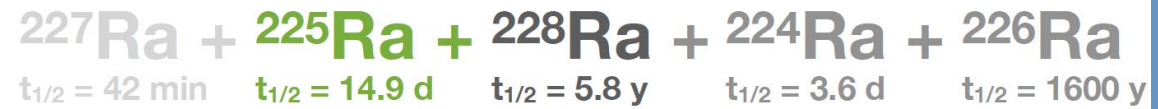
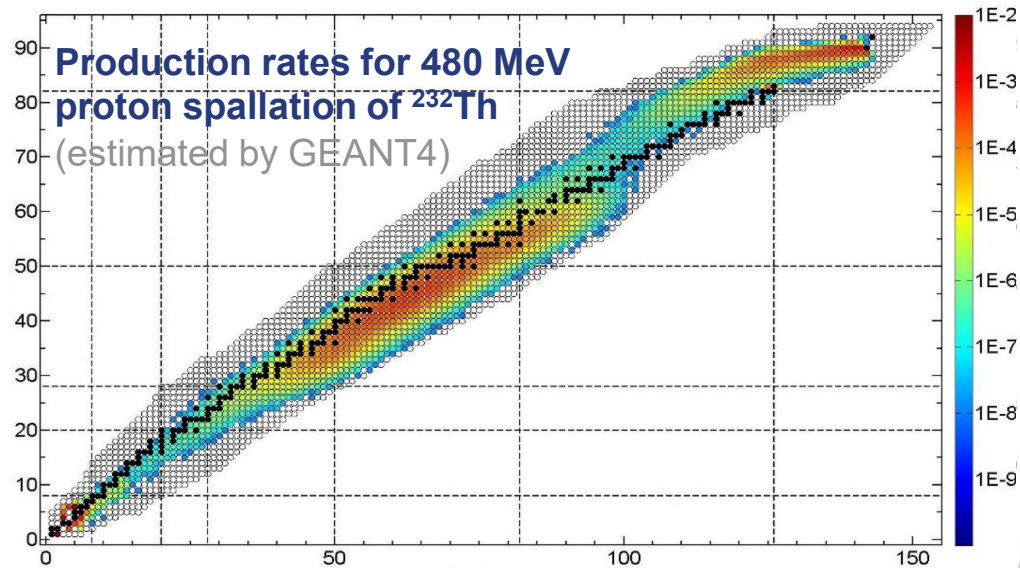


Simultaneous irradiation of 12 targets (max 8 mm each)





# Isotope Production Facility



rapid decay



concerns (from some) about  $^{227}\text{Ac}$  content and impact on waste management

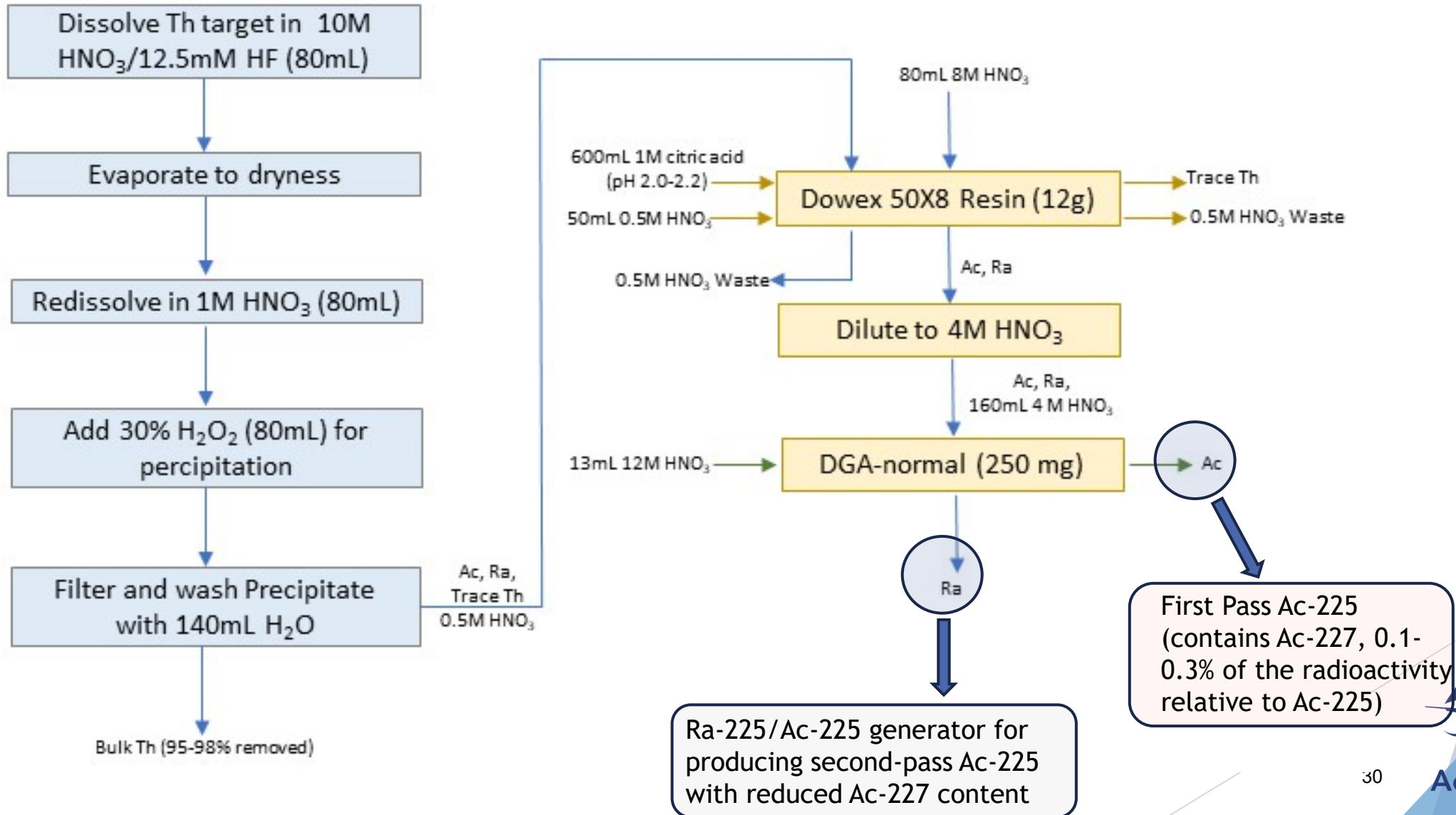
“directly-produced  $^{227,225}\text{Ac}^{\dagger}$ ”



“generator-produced  $^{225}\text{Ac}^*$ ”



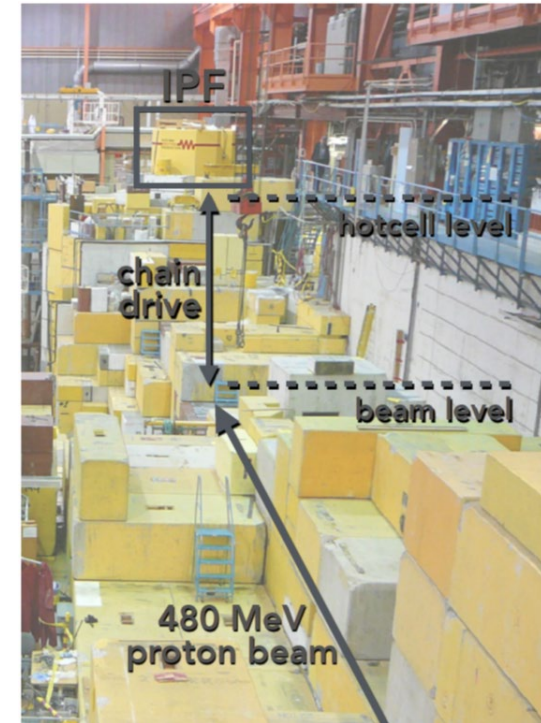
# Isotope Production Facility





# Isotope Production Facility

Target Irradiation				Actinium Production	
Year	In Beam	Out of Beam	Dose( $\mu$ Ah)	1 <sup>st</sup> Pass Ac225 Activity (MBq)	2 <sup>nd</sup> Pass Ac225 Activity (MBq)
2020	2020-10-19	2020-10-20	1,191		
	2020-11-13	2020-11-16	2,639		
	2020-11-18	2020-11-21	2,490		
2021	2021-07-29	2021-07-30	1,381		
	2021-09-09	2021-09-10	1,840		3.8
	2021-11-29	2021-11-29	760		
	2021-12-13	2021-12-20	12,461	715	74.85*
	2021-12-13	2021-12-20	12,461	273	63.15*
2022	2022-07-07	2022-07-12	7,456	293	84.5*
	2022-08-22	2022-08-30	11,493	351	83.68*
	2022-09-16	2022-09-24	12,484	503.5	146.45*
	2022-09-26	2022-10-03	11,110	26.3	15.54
2023	2023-11-17	2023-11-24	10,145		3.90
	2023-12-11	2023-12-20	12,222		8.88
	BWXT generator			n/a	44.92*



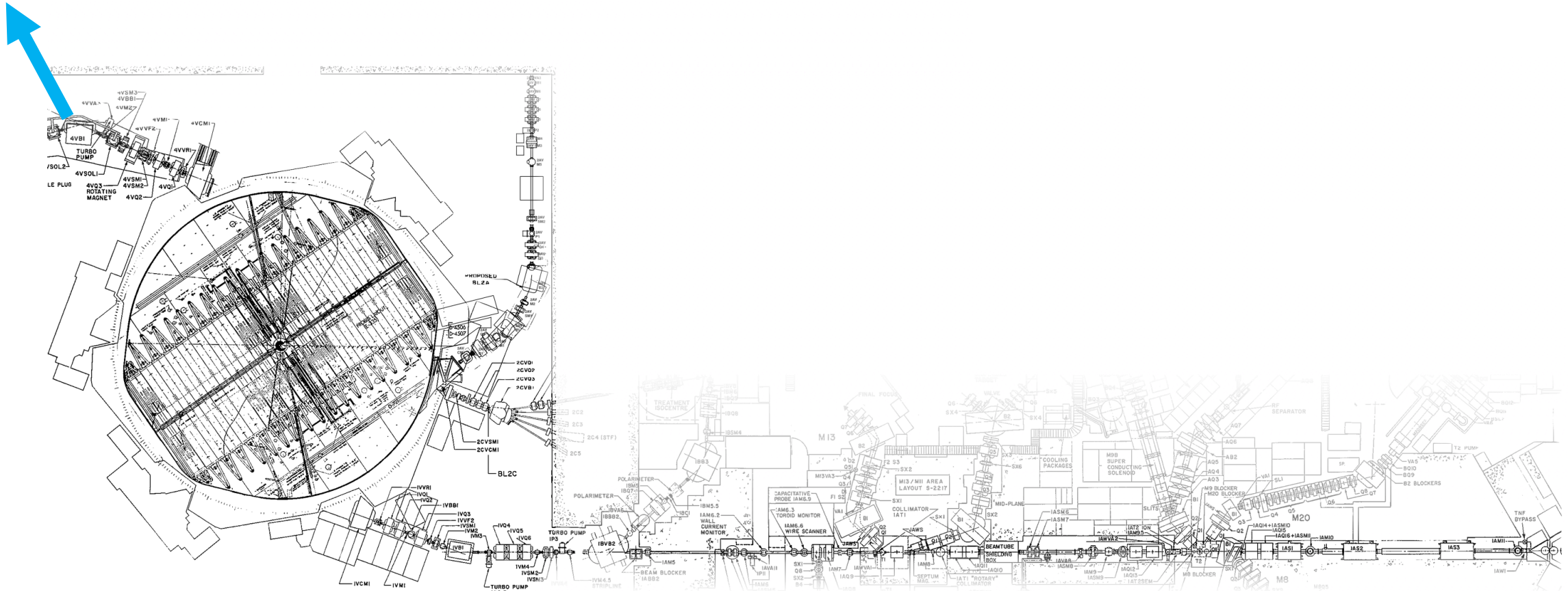
\*These figures represent the cumulative result of multiple generator elutions



# Main Accelerator Program

## ARIEL

- 480 MeV, 10  $\mu$ A, Th targets
- Planned for 2027

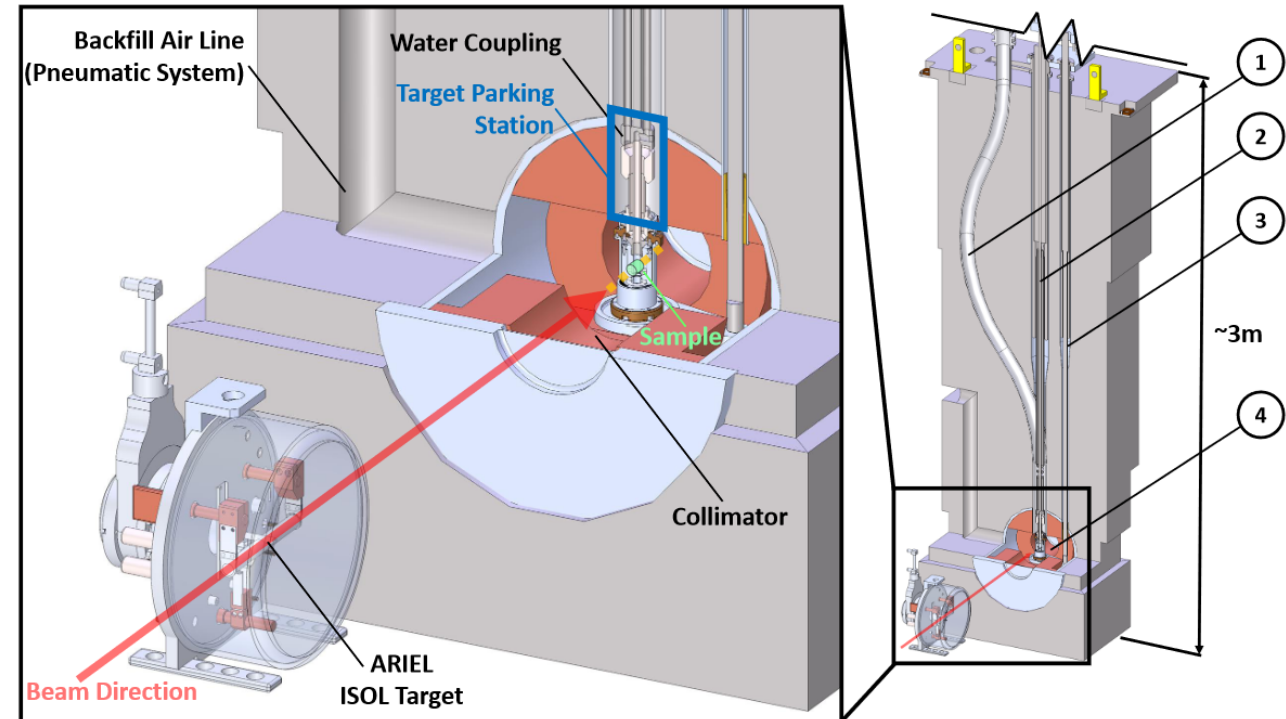
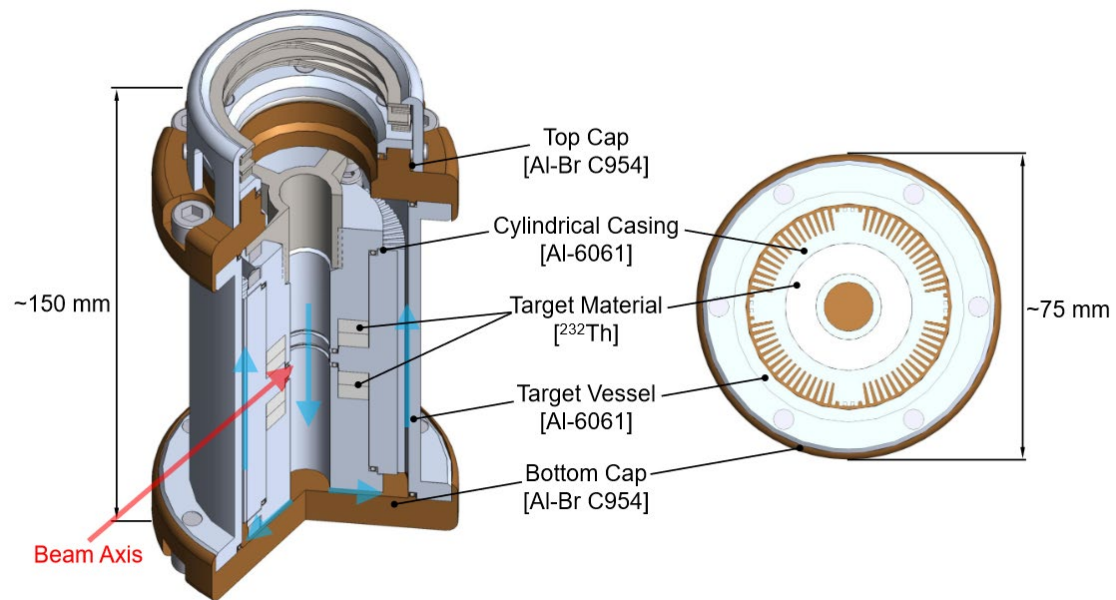




ARIEL/H<sup>+</sup>

High activity (GBq), spallation

- Enable radiopharmaceutical development and clinical trials - 400 mCi (15 GBq) <sup>225</sup>Ac per target



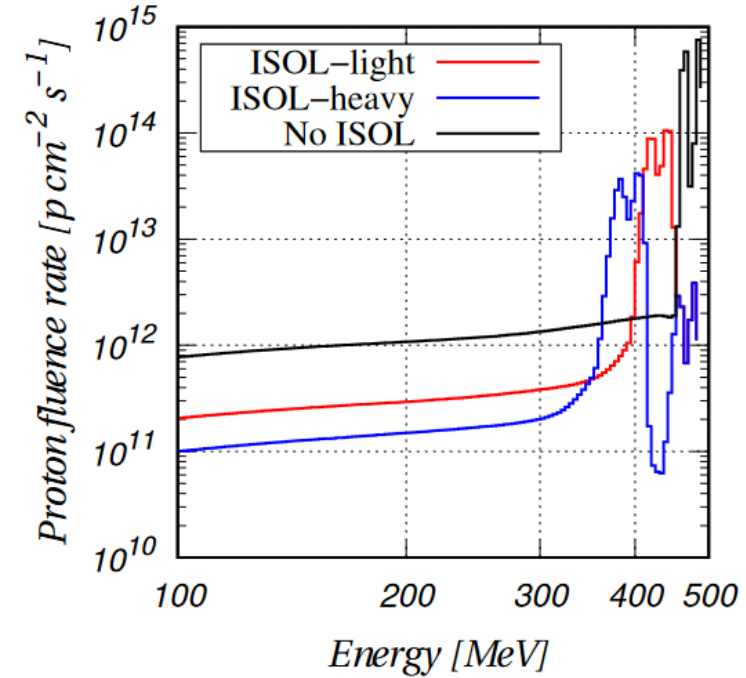
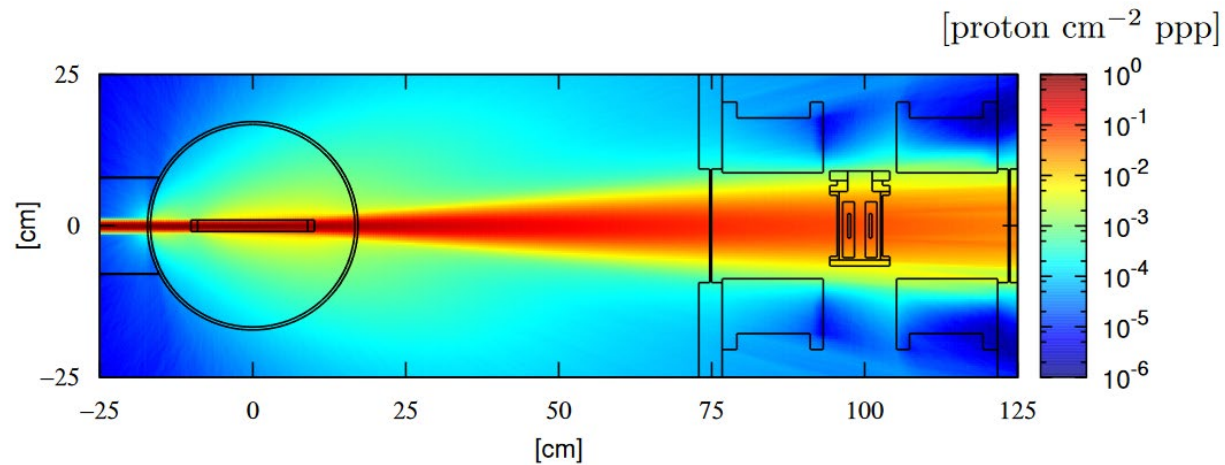
Norfolk, Virginia

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## ARIEL/H<sup>+</sup>

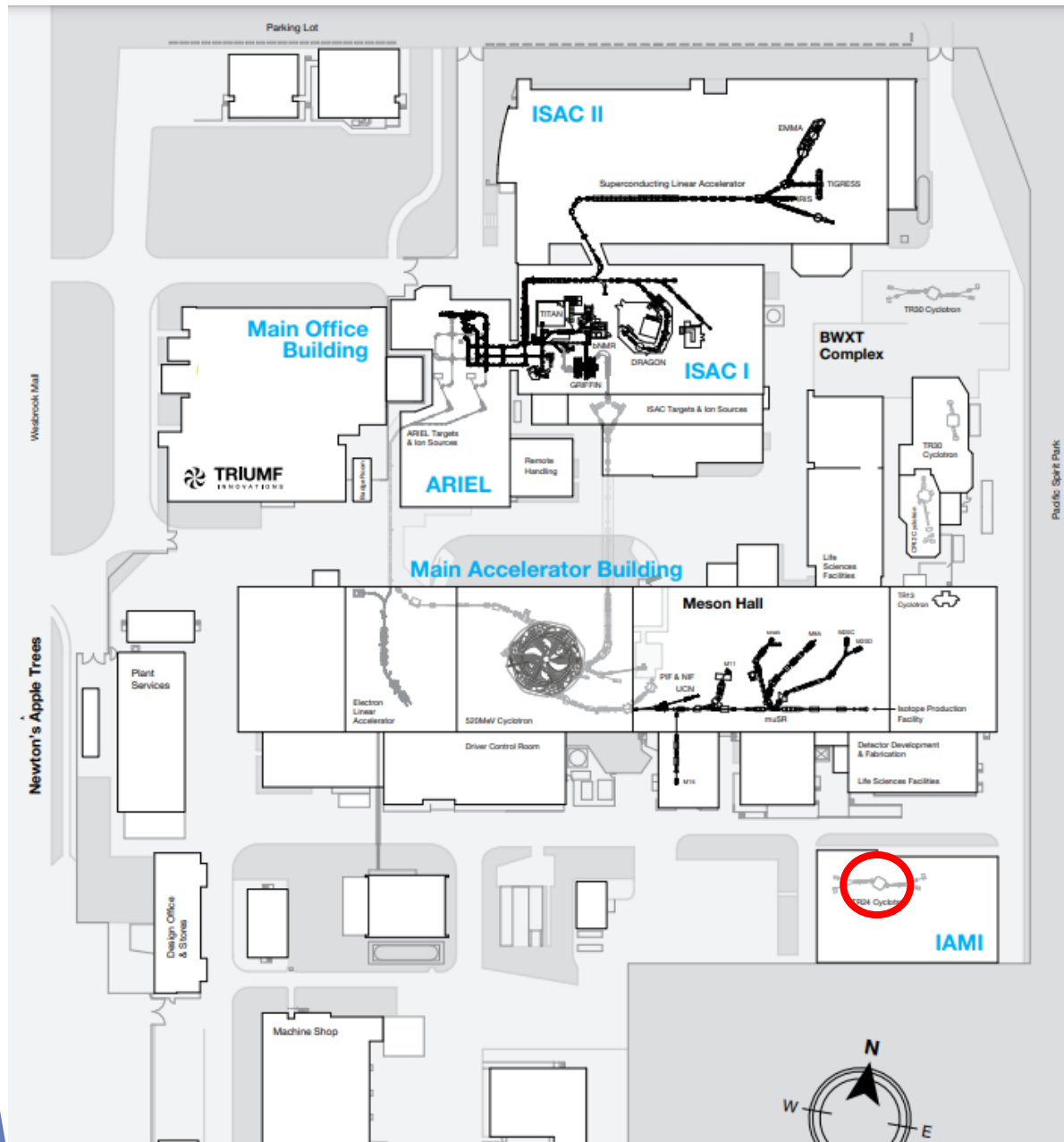
High activity (GBq), spallation

- Enable radiopharmaceutical development and clinical trials - 400 mCi (15 GBq) <sup>225</sup>Ac per target





# IAMI - Institute for Advanced Medical Isotopes





# IAMI - Institute for Advanced Medical Isotopes



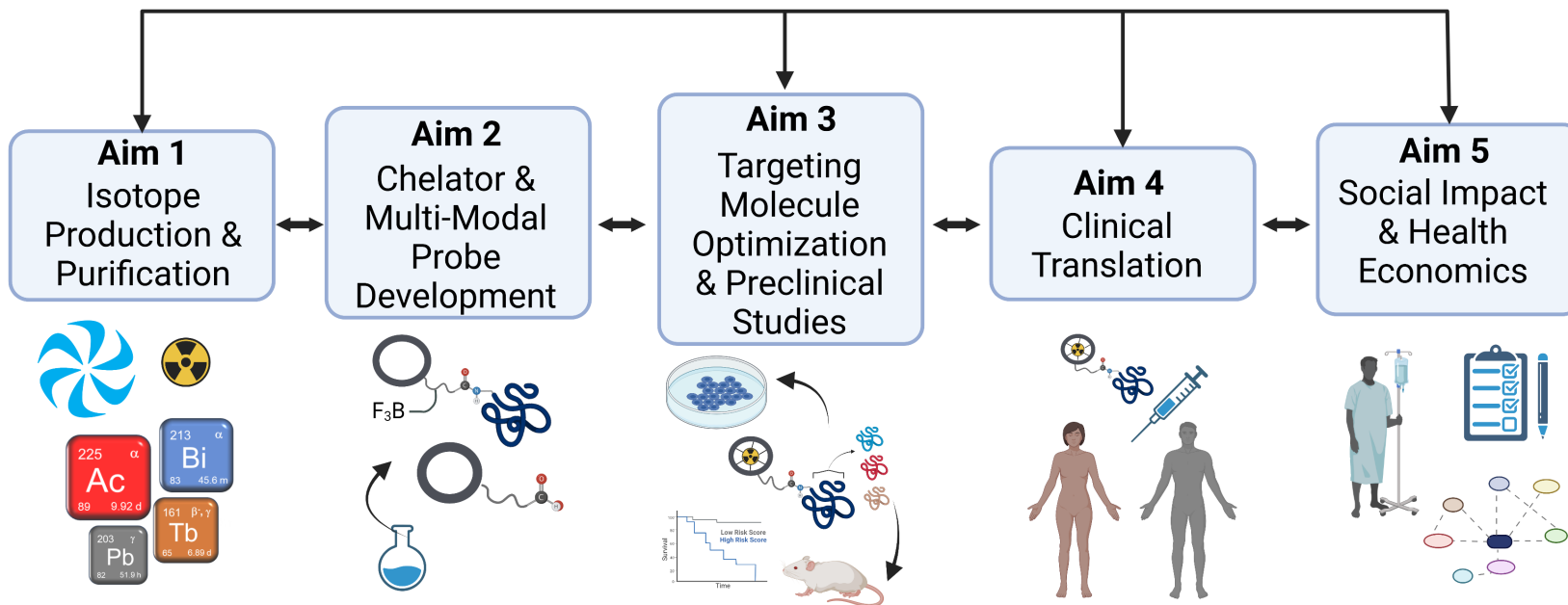


# NFRF-Transformation: Rare Isotopes to Transform Cancer Therapy



New Frontiers in Research Fund  
Fonds Nouvelles frontières en recherche

- \$23.7 mil over 6 years
- NPI: Bénard (UBC/BC Cancer)
- Co-PI: Ramogida (SFU/TRIUMF)
- TRIUMF Team: Hoehr, Radchenko, Schaffer, Yang





# TRIUMF's 'hot kitchen'

- $^{11}\text{C}$  PET
- $^{18}\text{F}$  PET
- $^{44}\text{Sc}$  PET
- $^{45}\text{Ti}$  PET
- $^{52,54}\text{Mn}$  PET
- $^{58}\text{Co}$  Auger therapy
- $^{64}\text{Cu}$  PET /  $^{67}\text{Cu}$   $\beta^-$  therapy
- $^{68}\text{Ga}$  PET
- $^{86}\text{Y}$  PET
- $^{89}\text{Zr}$  PET
- $^{99\text{m}}\text{Tc}$  SPECT /  $^{94\text{m}}\text{Tc}$  PET
- $^{103}\text{Pd}$  Auger therapy
- $^{119}\text{Sb}$  Auger /  $^{118}\text{Sb}$  PET /  $^{117}\text{Sb}$  SPECT
- $^{132/135}\text{La}$  PET / Auger
- $^{149,155,161}\text{Tb}$  / alpha / SPECT /  $\beta^-$  therapy
- $^{165}\text{Er}$  Auger therapy
- $^{197}\text{Hg}$  Auger therapy
- $^{203}\text{Pb}$  /  $^{212}\text{Pb}$  SPECT / alpha therapy
- $^{223,224}\text{Ra}$  alpha therapy
- $^{225}\text{Ac}$  /  $^{213}\text{Bi}$  alpha therapy
- $^{230}\text{U}$  /  $^{226}\text{Th}$  alpha therapy

hydrogen 1 H 1.0079																	helium 2 He 4.0026						
lithium 3 Li 6.941	beryllium 4 Be 9.0122																	boron 5 B 10.811	6 C 12.011	7 N 14.007	8 O 15.999	9 F 18.998	10 Ne 20.180
sodium 11 Na 22.990	magnesium 12 Mg 24.305																	aluminum 13 Al 26.982	14 Si 28.086	15 P 30.974	16 S 32.065	17 Cl 35.453	18 Ar 39.948
potassium 19 K 39.098	calcium 20 Ca 40.078	21 Sc 44.956	22 Ti 47.88	vanadium 23 V 50.942	24 Cr 51.996	25 Mn 54.938	26 Fe 55.845	27 Co 58.933	28 Ni 58.693	29 Cu 63.546	30 Zn 65.38	31 Ga 69.723	32 Ge 72.61	33 As 74.922	34 Se 78.96	35 Br 79.904	36 Kr 83.80						
rubidium 37 Rb 85.468	strontium 38 Sr 87.62	39 Y 88.906	40 Zr 91.224	niobium 41 Nb 92.906	42 Mo 95.96	43 Tc 98.906	44 Ru 101.07	45 Rh 102.91	46 Pd 106.90	47 Ag 107.87	48 Cd 112.41	49 In 114.82	50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29						
caesium 55 Cs 132.91	barium 56 Ba 137.33	57-70 * Lu 174.97	71 Hf 178.49	72 Ta 180.95	73 W 183.84	74 Re 186.21	75 Os 190.23	76 Ir 192.22	77 Pt 195.08	78 Au 196.97	79 Hg 200.59	80 Tl 204.38	81 Pb 207.2	82 Bi 208.98	83 Po [209]	84 At [210]	85 Rn [222]	86 Rn [222]					
francium 87 Fr [223]	88 Ra [226]	89-102 **	103 Lr [262]	104 Rf [267]	105 Db [268]	106 Sg [271]	107 Bh [272]	108 Hs [270]	109 Mt [276]	110 Ds [281]	111 Rg [280]	112 Uub [285]	113 Uut [284]	114 Uuq [289]	115 Uup [288]	116 Uuh [293]	117 Uus —	118 Uuo [294]					
		*lanthanoids																					
		57 La 138.905	58 Ce 140.12	59 Pr 140.91	60 Nd 144.24	61 Pm [145]	62 Sm 150.36	63 Eu 151.96	64 Gd 157.25	65 Tb 158.93	66 Dy 162.50	67 Ho 164.93	68 Er 167.26	69 Tm 168.93	70 Yb 173.06								
		**actinoids																					
		89 Ac [227]	90 Th [232]	91 Pa 231.04	92 U 238.03	93 Np [237]	94 Pu [244]	95 Am [243]	96 Cm [247]	97 Bk [247]	98 Cf [251]	99 Es [252]	100 Fm [257]	101 Md [258]	102 No [259]								

Thank you!  
Merci!

