

Summary: Radioisotopes in Diagnostics and Therapy

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'Star' Radionuclides for SPECT and PET

Centralized: 5_(+x) reactors

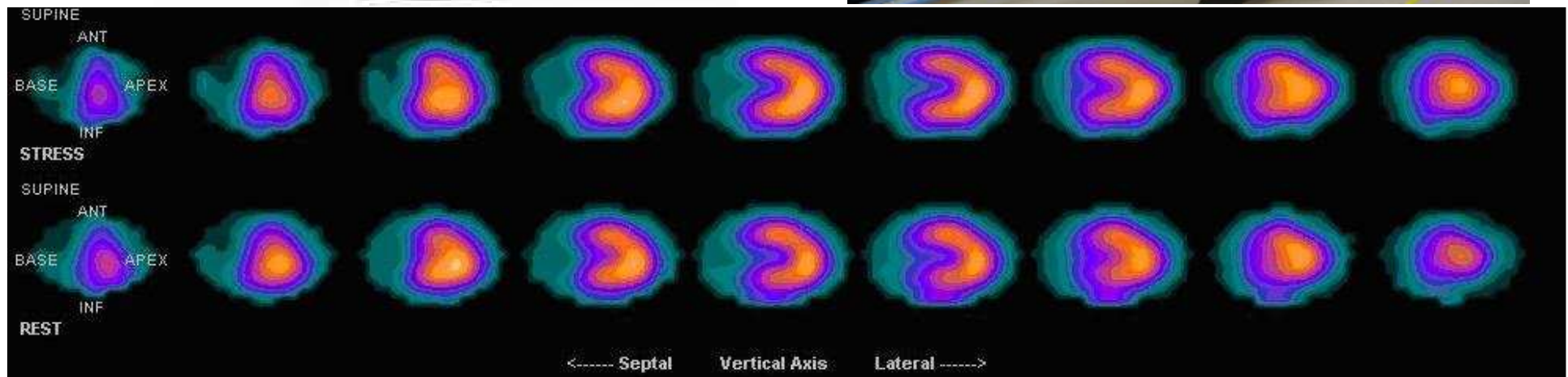
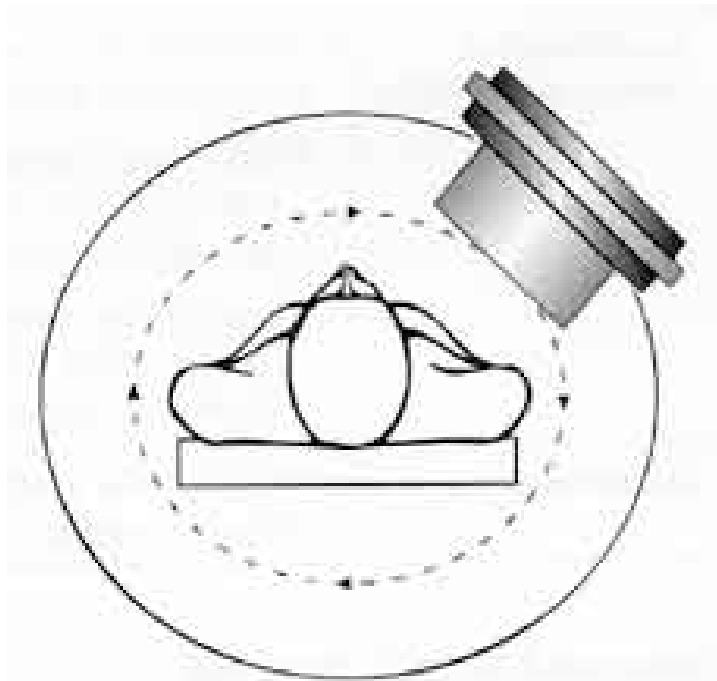
- **^{99m}Tc** 6 h E_γ 140 keV
- from ⁹⁹Mo-^{99m}Tc generator;
^{99m}Tc supplies from operations
in house/central radiopharmacy
- Ideal nuclear features for
imaging (gamma camera,
SPECT) and patient dose
- Versatile coordination chemistry
of technetium
- Multi-disciplinary synergy →
products for specific functional
imaging
- Easy, abundant, economic
availability (*? since 2008*)

Decentralized: 671 cyclotrons

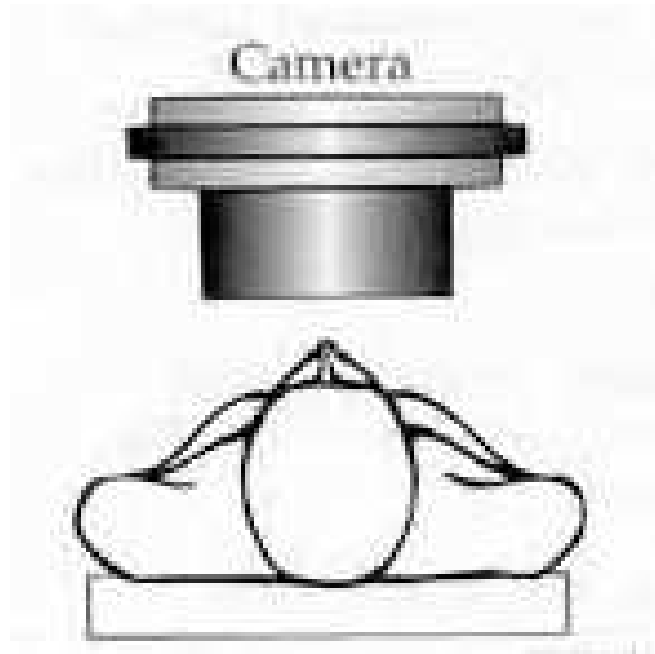
- **¹⁸F** 110 min β⁺ (0.635 MeV)
- ¹⁸O(p,n) Ep 10-18MeV; 20-40uA
- Decentralised facilities for
production and supplies
- Compatible to label organic and
biological molecules or analogs
- Suitable for PET, PET-CT
- T_{1/2} advantage over ¹¹C, ¹³N, ¹⁵O
- **Success of ¹⁸FDG**
- several pharmaceuticals containing
fluorine
- Relatively more expensive

Ischemic heart disease

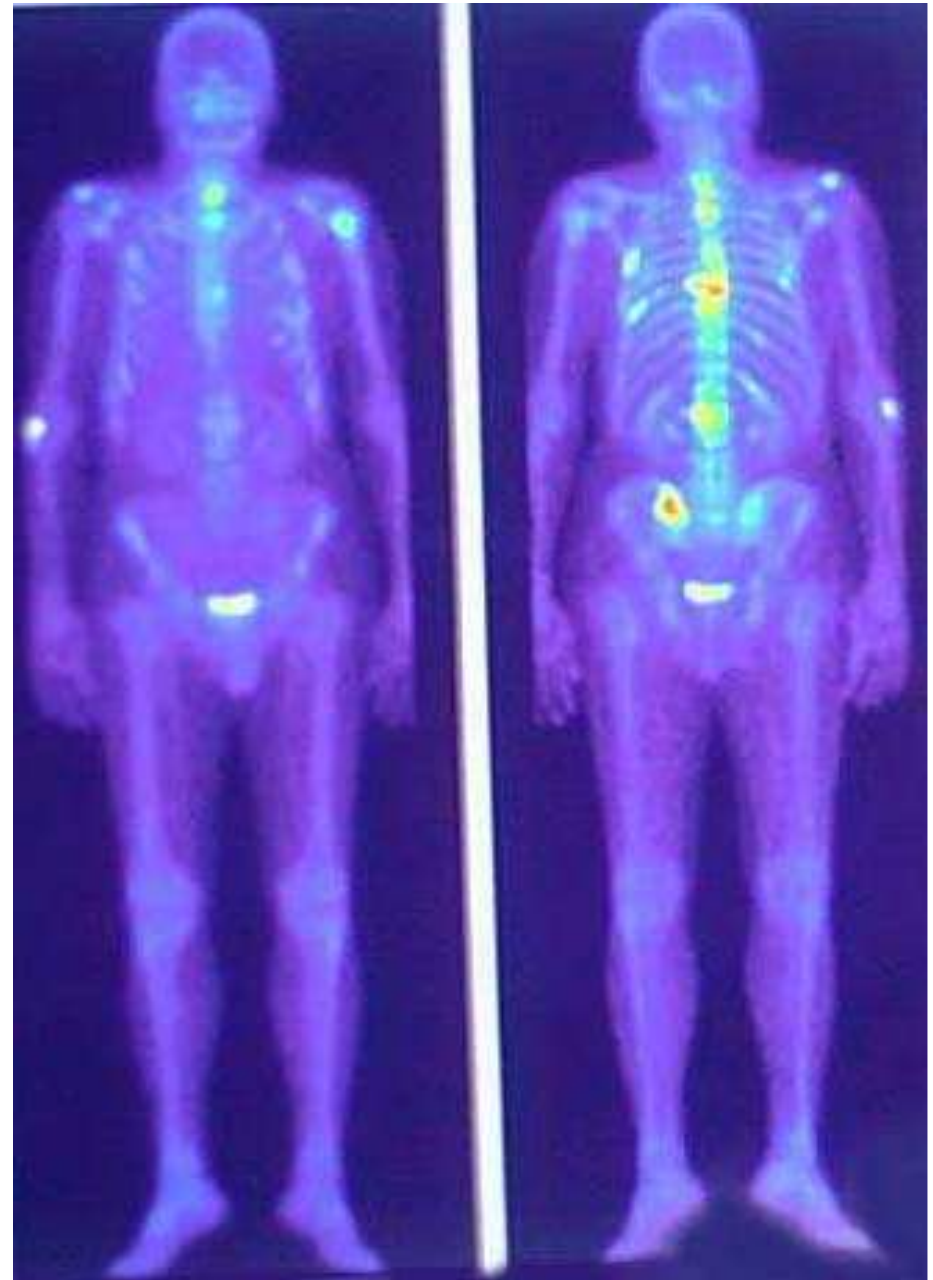
- diagnose by ECG and cardiac stress test with SPECT



Bone metastases from (prostate) cancer

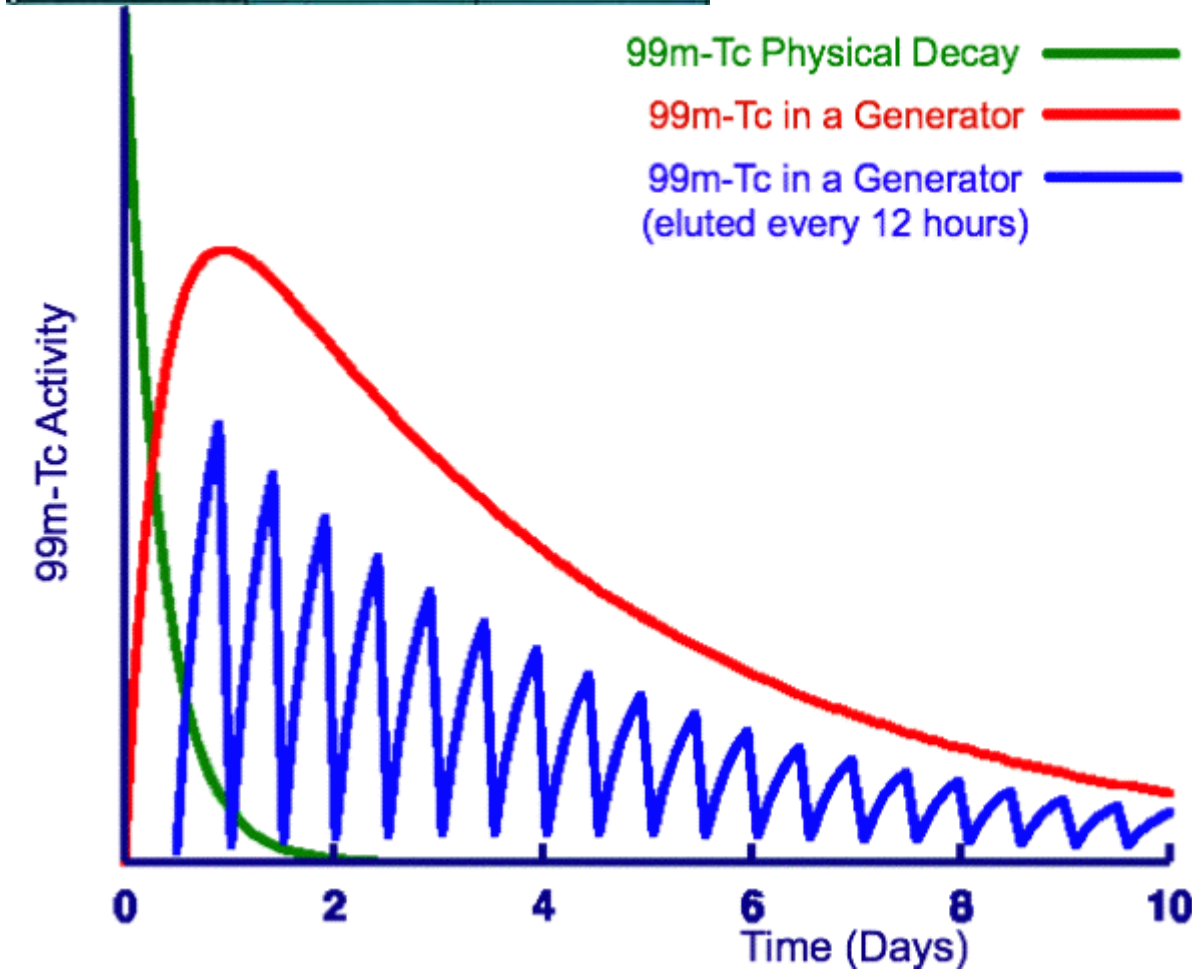


- **planar or SPECT scan for bone metastases**



⁹⁹Mo/^{99m}Tc generator

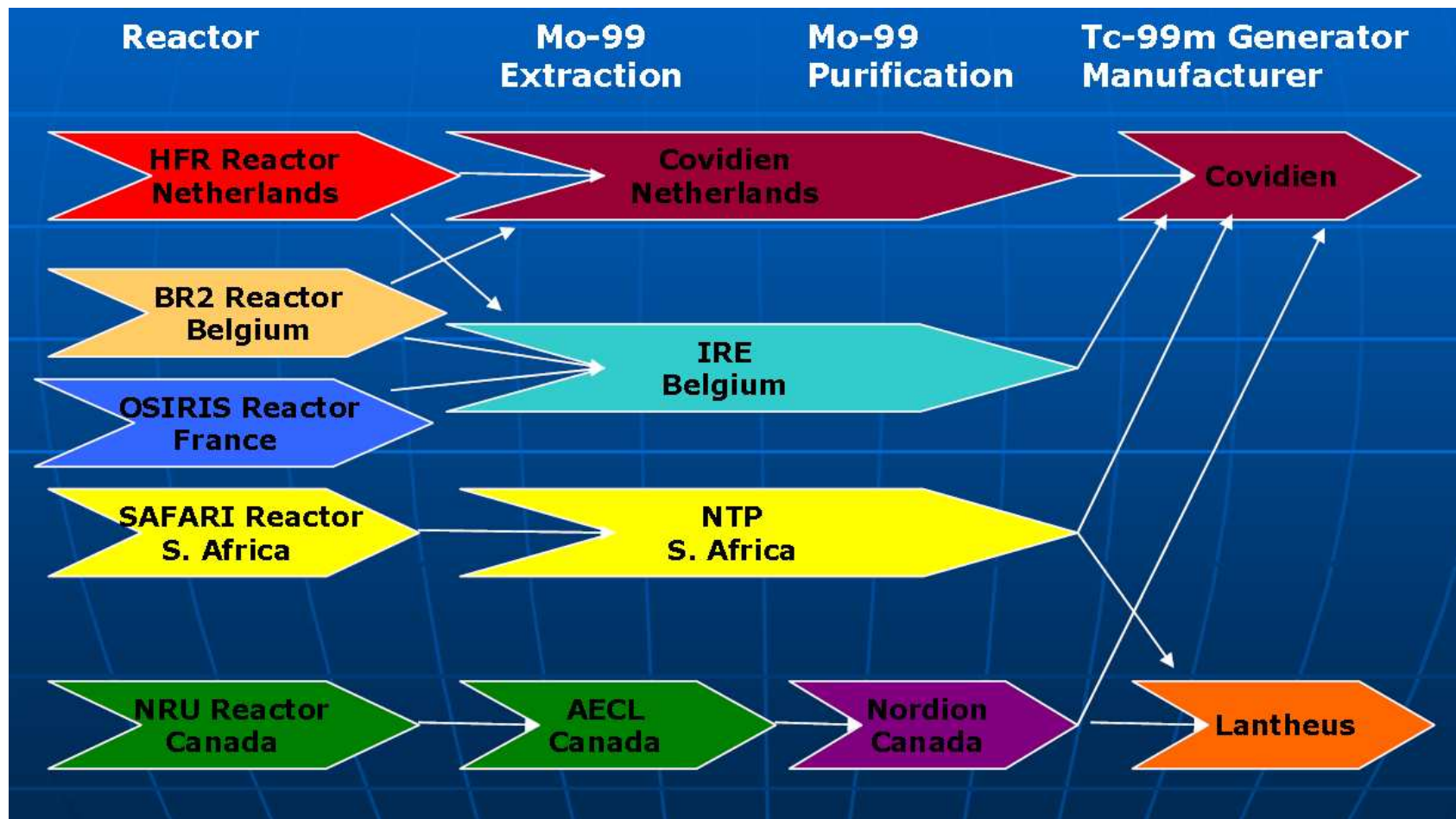
Tc 99 6.0 h $2.1 \cdot 10^5$ a β^- 0.3... γ (90) γ (322)	Tc 100 15.8 s β^- 3.4... ϵ γ 540; 591...	Tc 101 14.2 m β^- 1.3... γ 307; 545...
Mo 98 24.19 α 0.14	Mo 99 66.0 h β^- 1.2... γ 740; 182; 778... m; g	Mo 100 9.67 $1.15 \cdot 10^{19}$ a $2\beta^-$ α 0.19



- simple
- reliable
- portable
- cheap

World market for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$

- $^{99\text{m}}\text{Tc}$ is the most important radionuclide in nuclear medicine (80% of all nuclear medicine applications)
- 28 million applications per year
- 80 000 Ci (3000 TBq) of ^{99}Mo needed per week



NRU Reactor, Canada

- 15 May 2009: D₂O leak
- stopped till spring 2010+
- license till October 2011



HFR Petten, NL

- extended maintenance stop from 19 February 2010



Reactors presently used for ^{99}Mo production with HEU targets

Reactor	Location	Country	Power (MW)	Fuel	Operation (days per year)	Operation since	Typical ^{99}Mo world market share
NRU	Chalk River	Canada	135	LEU	315	1957	40%
HFR	Petten	Netherlands	45	LEU	290	1961	30%
BR2	Mol	Belgium	100	HEU	115	1961	10%
OSIRIS	Saclay	France	70	LEU	220	1966	3%
SAFARI	Pelindaba	South Africa	20	HEU	315	1965	10%

MAPLE reactors MMIR-1, MMIR-2



MAPLE 1 and 2 reactors, and New Processing Facility, at AECL Chalk River Laboratories (NRU and NRX reactors are behind, on the left and right, respectively).

Project officially stopped!

**Correction should be possible.
Costs? Delays?**

**30 MW MAPLE-type reactor HANARO
operates nicely in Korea**

Power coefficient:

Designed as: -0.12 mk/MW

Found as: $+0.28$ mk/MW



Blue "Cerenkov radiation" from MAPLE 1 reactor core during commissioning tests at high power (8 MW). The Cerenkov glow is caused by high-speed electrons (beta particles or secondary electrons due to the core's operation) slowing down in the surrounding water.

Reactors foreseen for future ⁹⁹Mo production with HEU targets

Reactor	Location	Country	Power (MW)	Fuel	Operation (days per year)	Operation	Potential ⁹⁹ Mo world market share
MARIA	Warsaw	Poland	20-30	LEU	138	1974 Mo: 2010+	
FRM2	Garching	Bavaria	20	HEU	240	2004 Mo: 2014+	(13%)
RJH	Cadarache	France	100	LEU		2014+	(12-25%)
PALLAS	Petten?	Netherlands	(45)	LEU	>300	2016+	
MAPLE	Chalk River	Canada	2x10	LEU	→ 365	?	(100%)

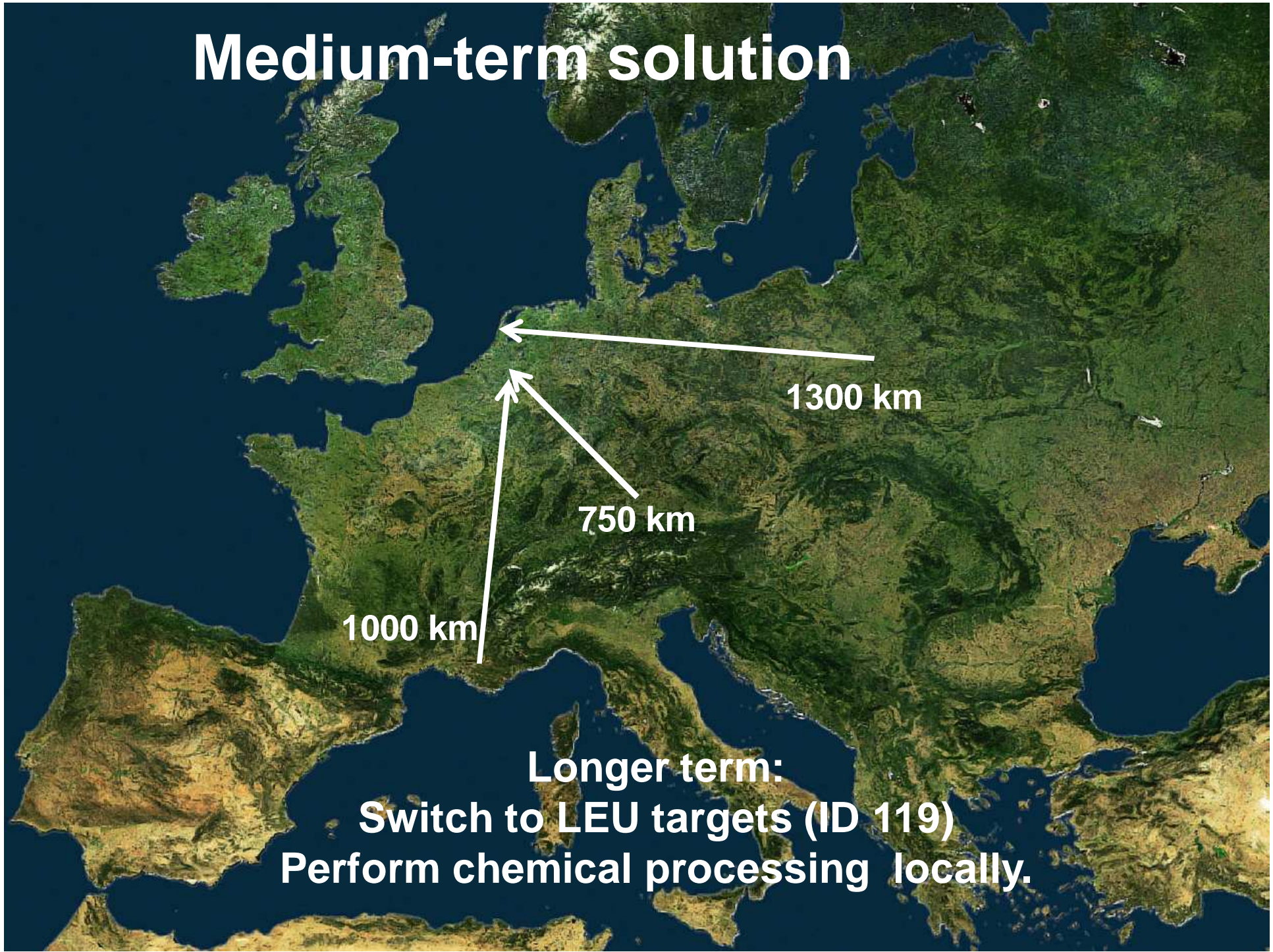
Medium-term solution

1300 km

750 km

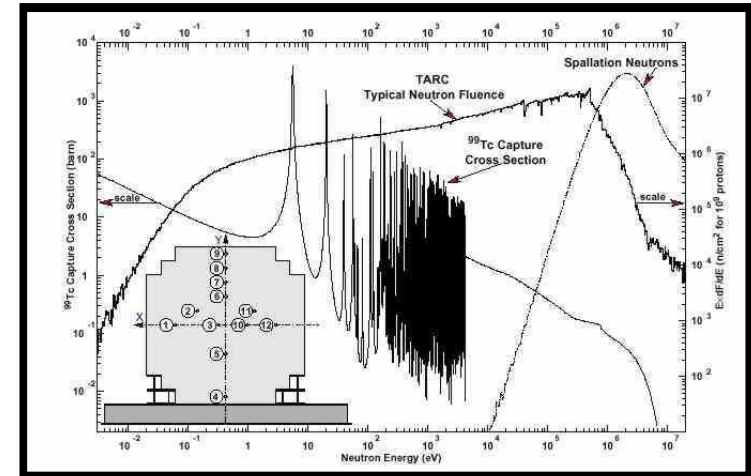
1000 km

Longer term:
Switch to LEU targets (ID 119)
Perform chemical processing locally.



Alternative methods of producing ^{99}Mo

1. Neutron irradiation (n,γ)
2. Liquid core reactor (n,f)
3. Cyclotron bombardment ($p,2n$)
4. Photo-nuclear reaction (γ,n)
5. Photo-fission reaction (γ,f)
6. Spallation source (neutrons) ID94
7. Spallation source (resonance crossing) ID47
8. Neutron generator fission



Cost of new projects has to compete against depreciated subsidized reactors.

“Parasitic” operation interesting to generate backup capacity.

“Value” of ^{99m}Tc

Typical SPECT exam in Switzerland:

Medical service	167.42 CHF	114 €	18%
Technical service	729.73 CHF	495 €	78%
700 MBq ^{99m}Tc activity`	32.30 CHF	22 €	3%
Kit DPD	9.45 CHF	6 €	1%
Total	938.90 CHF	637 €	100%

Compare:

“AeroChamber” 50.10 CHF
 34 €

plastic tube with two
rubber end caps

**Milk, fossile fuel and
 ^{99m}Tc are too cheap
⇒ not sustainable!**



From diagnostics

The death and the radiologist.

Bad news: you are going to die soon.

Oh my God! Where did you find all these nude photos of me?

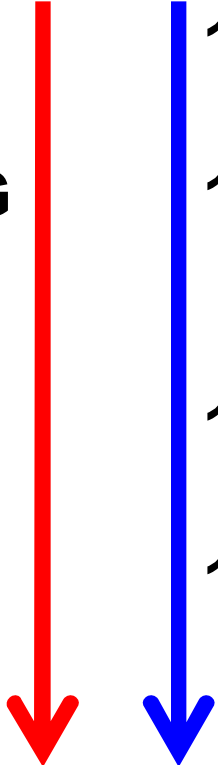


WWW.NICHTLUSTIG.DE

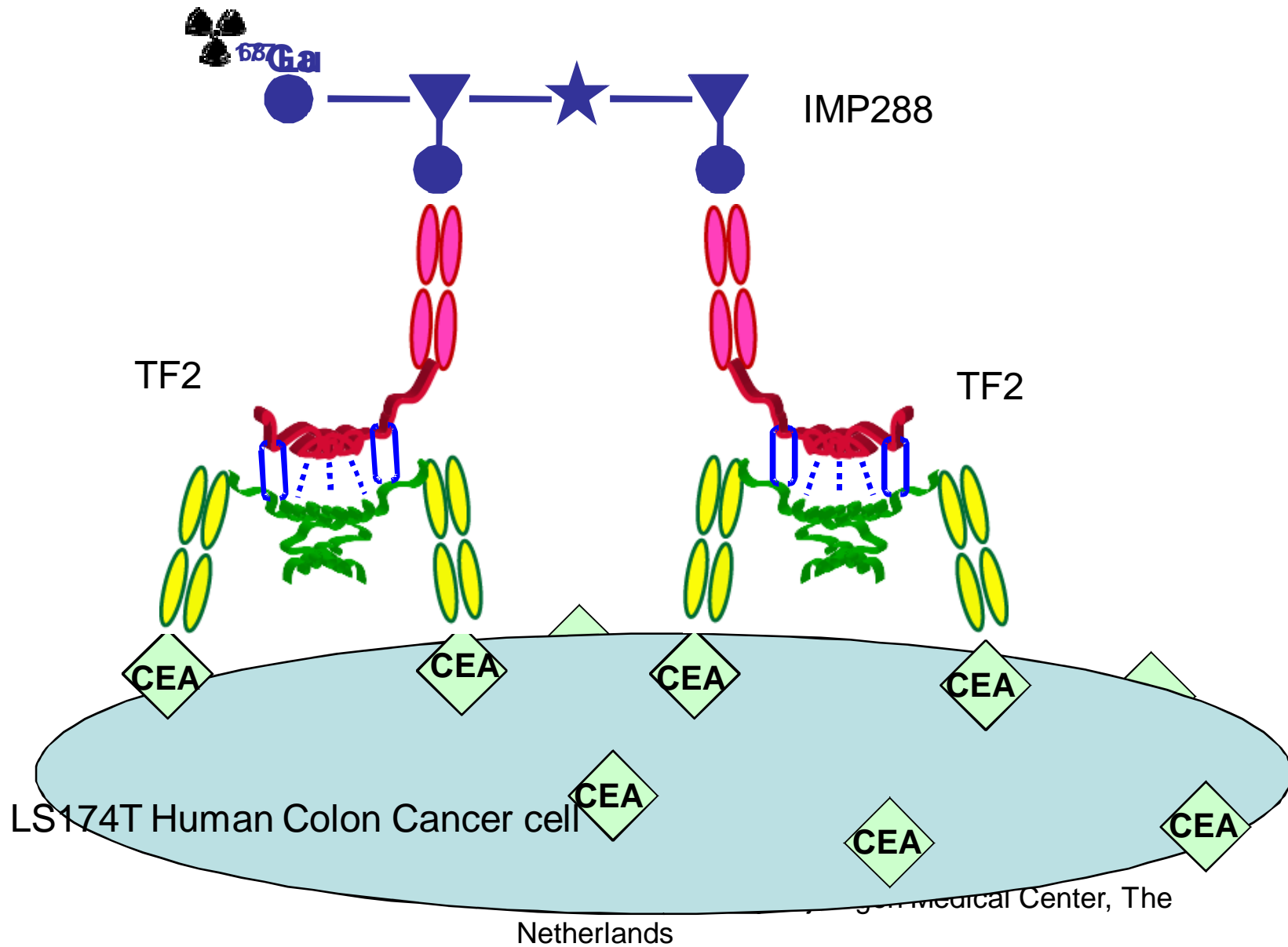
to therapy

Selectivity towards cancer cell

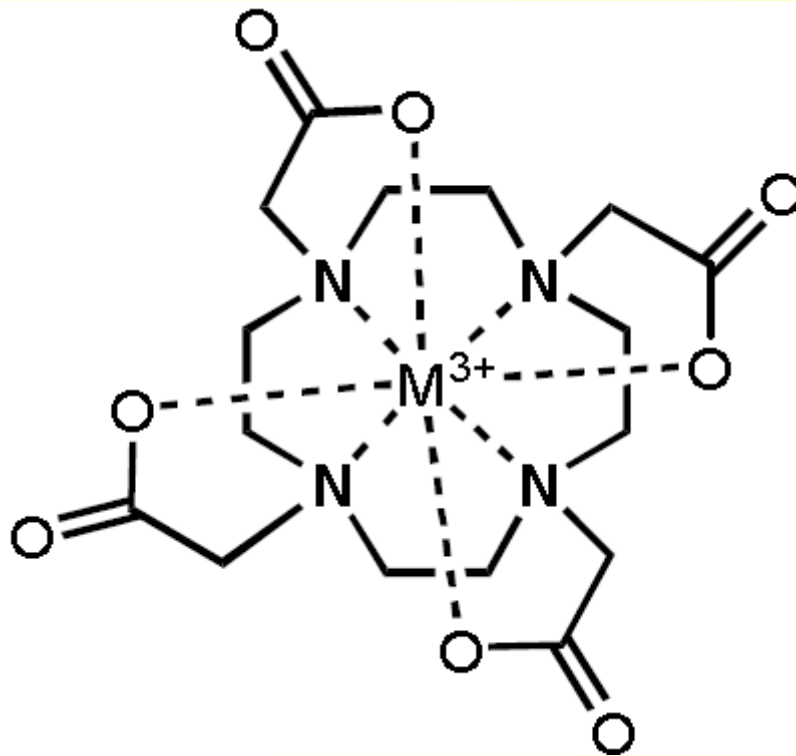
Biotracer	Example	Mass (u)
Element	I ⁻ (24 h), F ⁻ (1 h), Sr ²⁺ , Ra ²⁺	18 .. 223
Small molecule	TcO ₄ ²⁻ (20 min), FDG (1 h), MIBG	100..300
Peptides	DOTATOC, DOTATATE,... (1-4 h)	1000-1500
mab	Ibritumomab, Tositumomab, Rituximab, Cetuximab,... (days)	150000


slower **heavier**

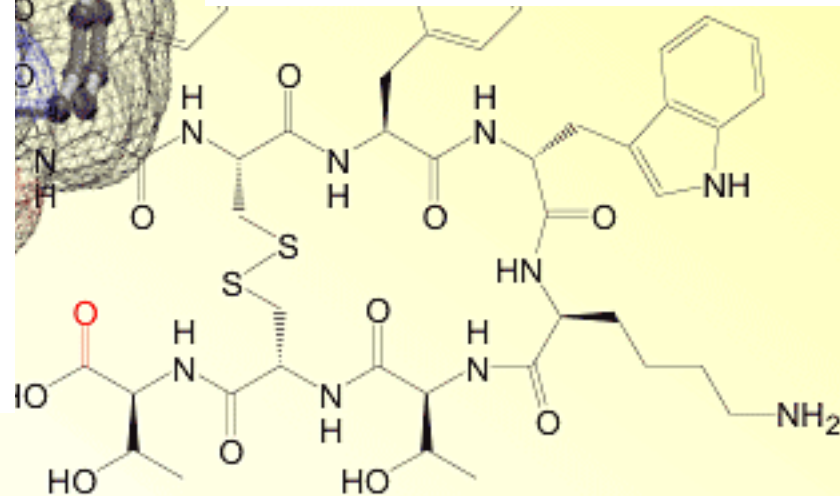
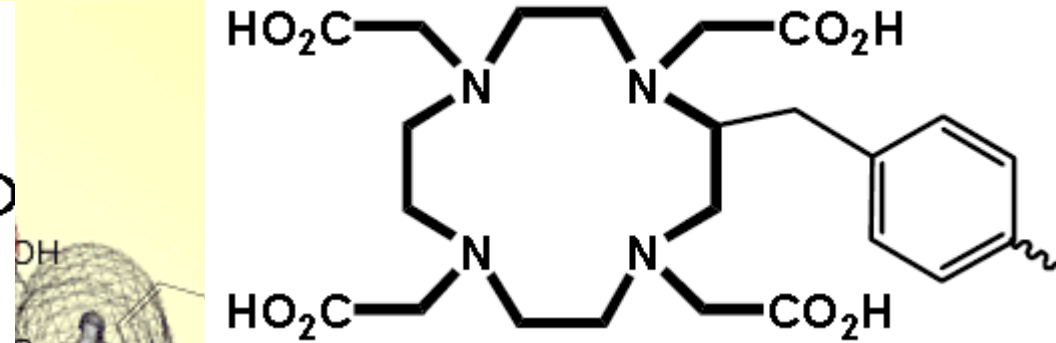
Pretargeted immunoPET imaging



Structural Formula of DOTA-TOC/TATE



DOTA-TATE



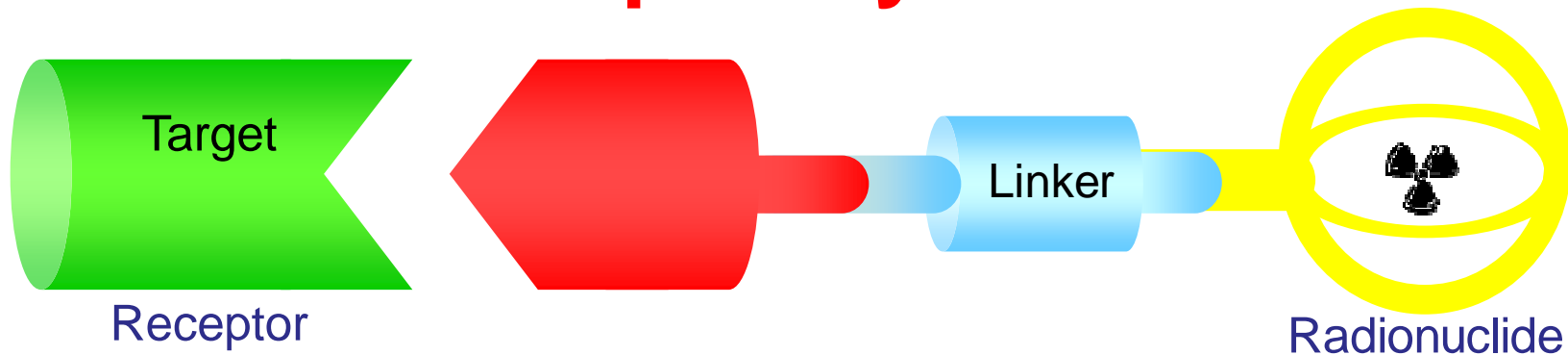
1,4,7,10-tetraazacyclododecantetraacetate

- ^{111}In ^{90}Y
- ^{67}Ga ^{177}Lu
- ^{68}Ga ^{213}Bi

$$IC_{50} (\text{Y}^{\text{III}}) = 1.6 \pm 0.4 \text{ nM}$$

Helmut Maecke, EANM-2007.

Interdisciplinary research



Structural biology

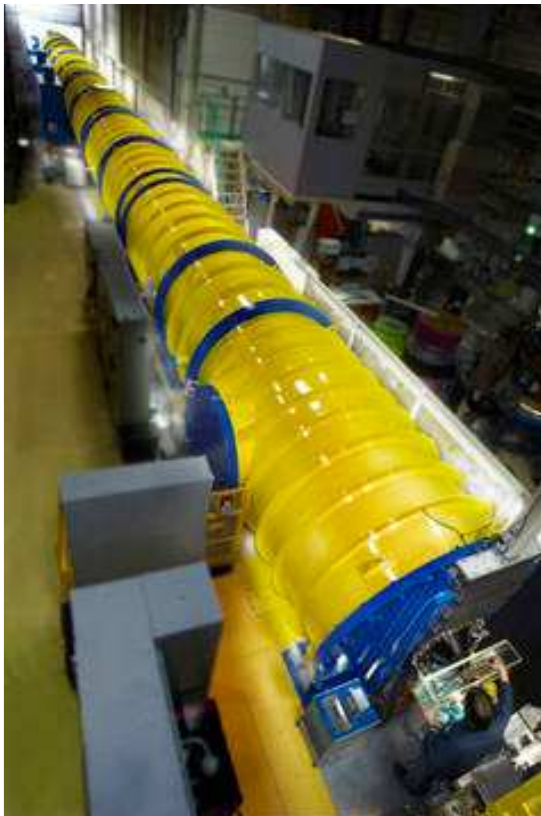
**Coordination
chemistry**

**Nuclear physics
and
radiochemistry**

- photon diffraction
- neutron diffraction

?

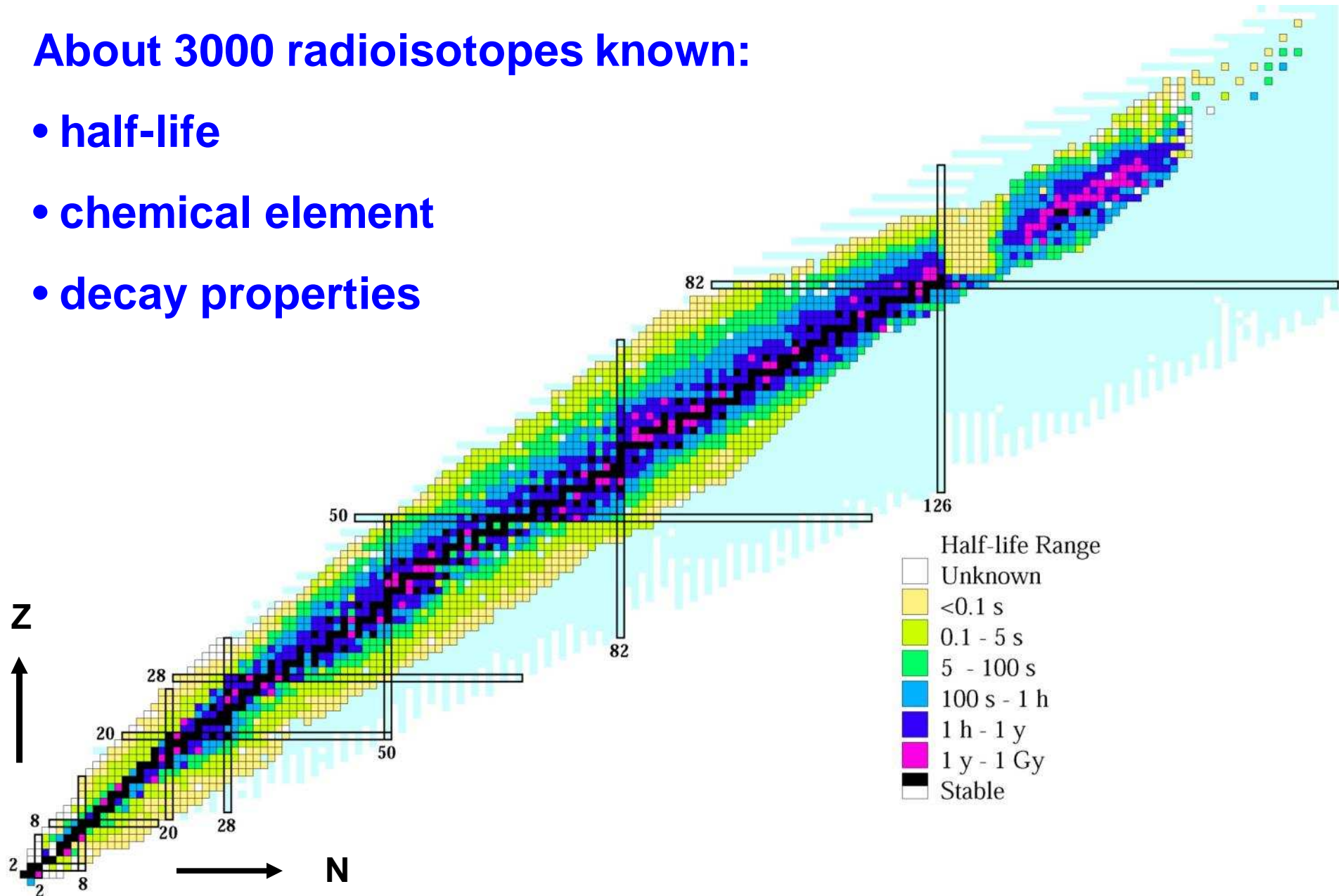
User facilities: ESRF, ILL, EMBL



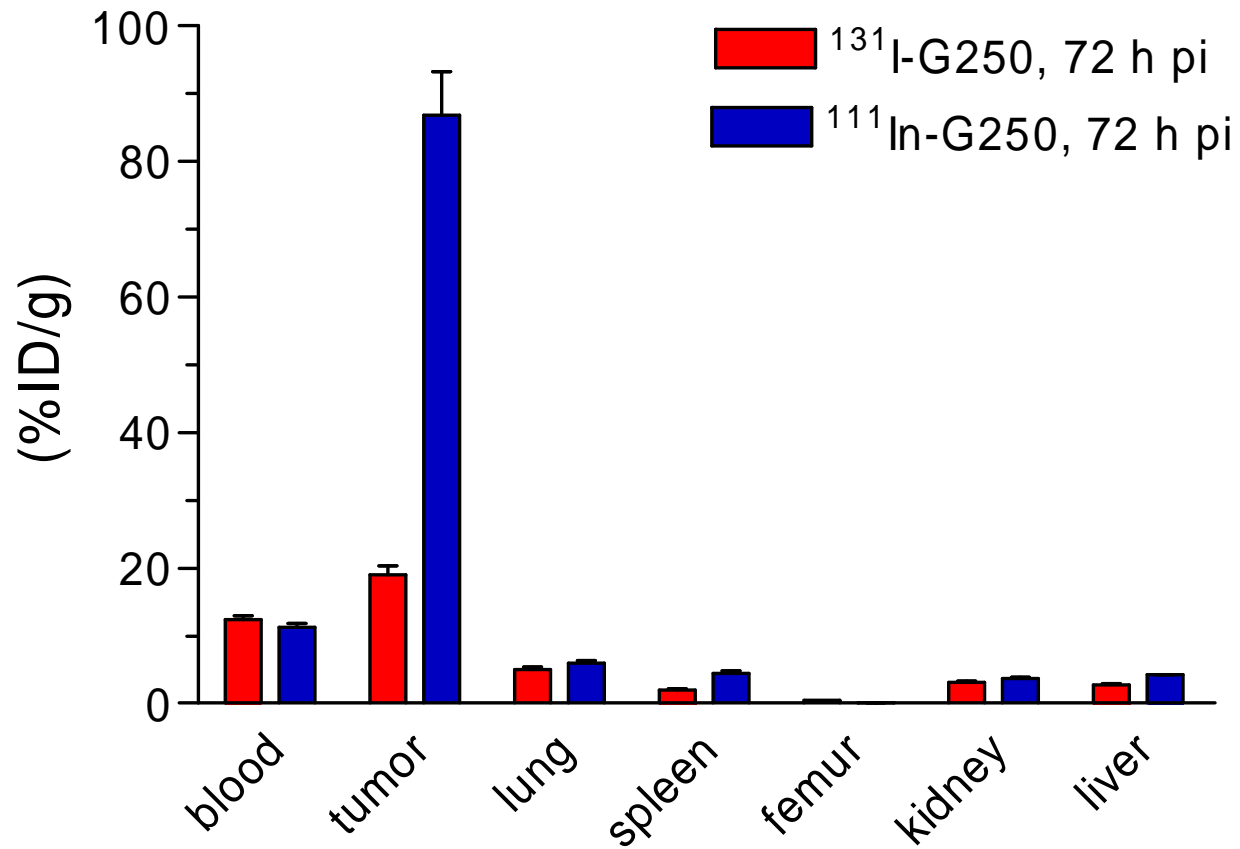
The quest for the optimum isotope

About 3000 radioisotopes known:

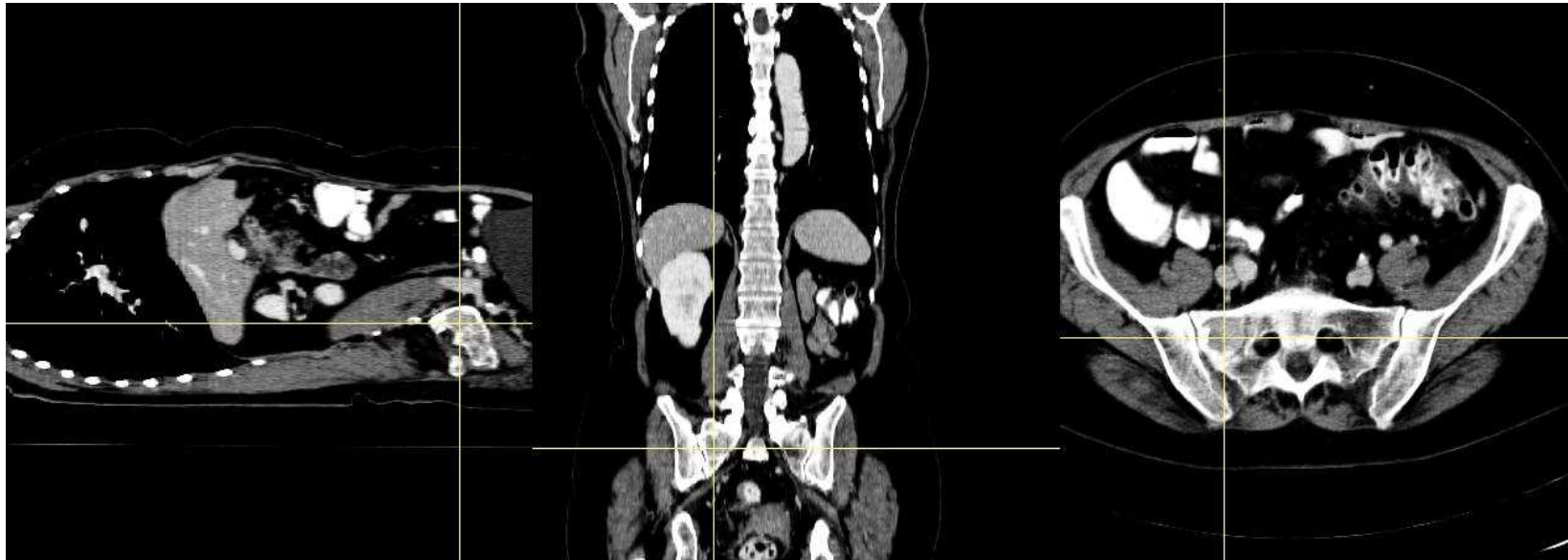
- half-life
- chemical element
- decay properties



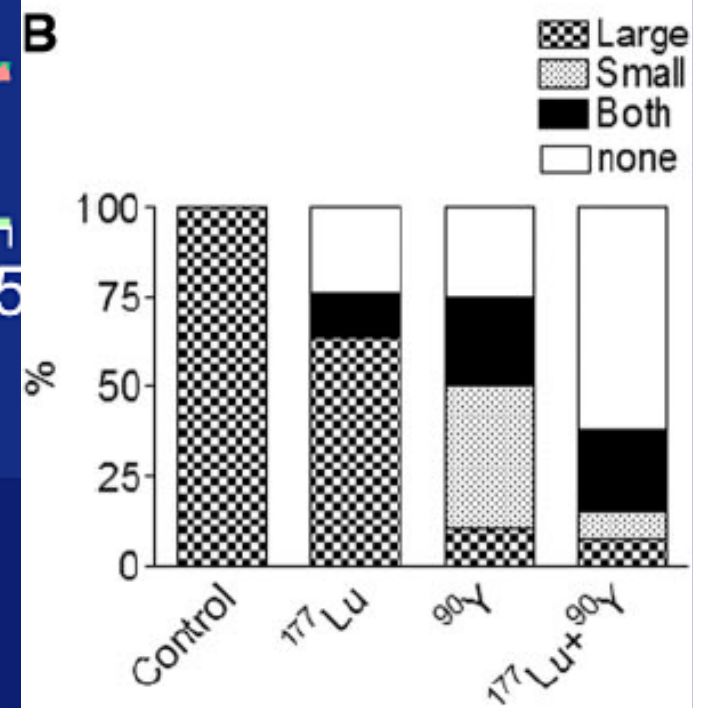
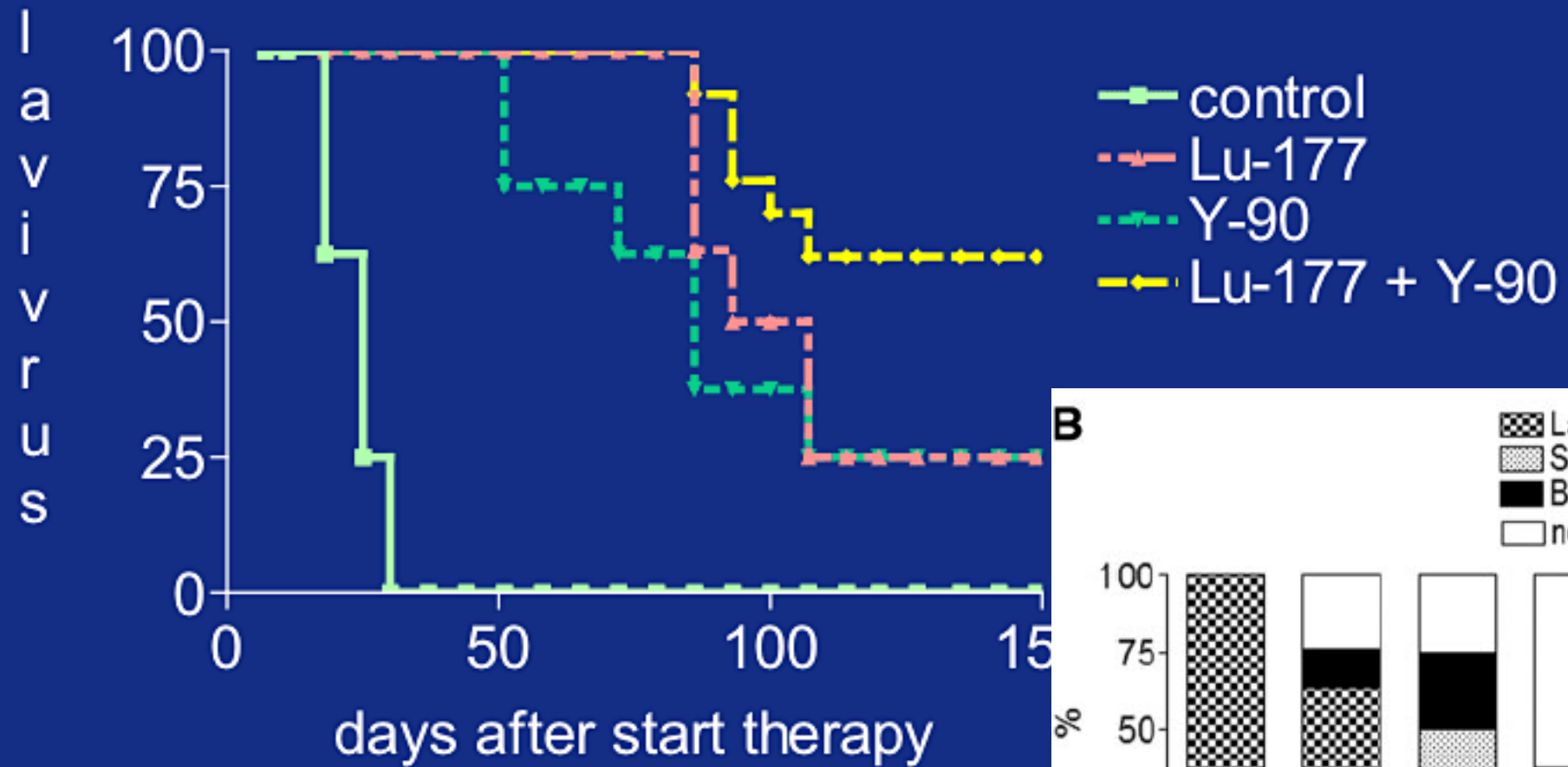
The Quest for the optimal radionuclide for RIT



Radioimmunotherapy of RCC with ^{177}Lu -cG250



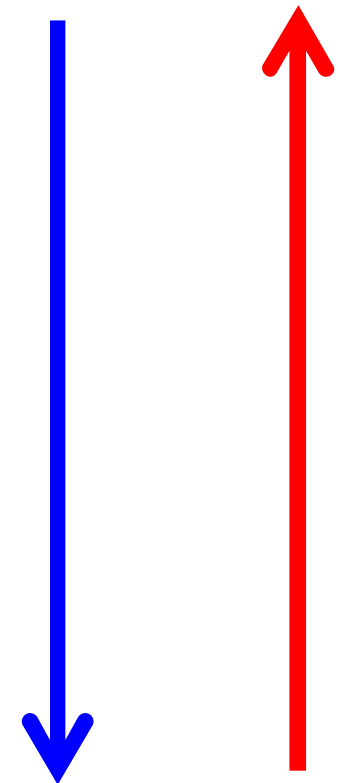
Survival



Radionuclides for radioimmunotherapy

Radio-nuclide	Half-life	E mean (keV)	E _γ (keV)	Range
Y-90	64 h	934 β	-	12 mm
Re-188	17 h	763 β	155	11 mm
I-131	8 days	182 β	364	3 mm
Lu-177	7 days	134 β	208, 113	2 mm
Tb-161	7 days	154 β 5, 17, 40 e ⁻	75	2 mm 1-30 μm
At-211	7.2 h	5870 α	-	45 μm
Tb-149	4.1 h	3967 α	165,..	25 μm

cross-fire



localized

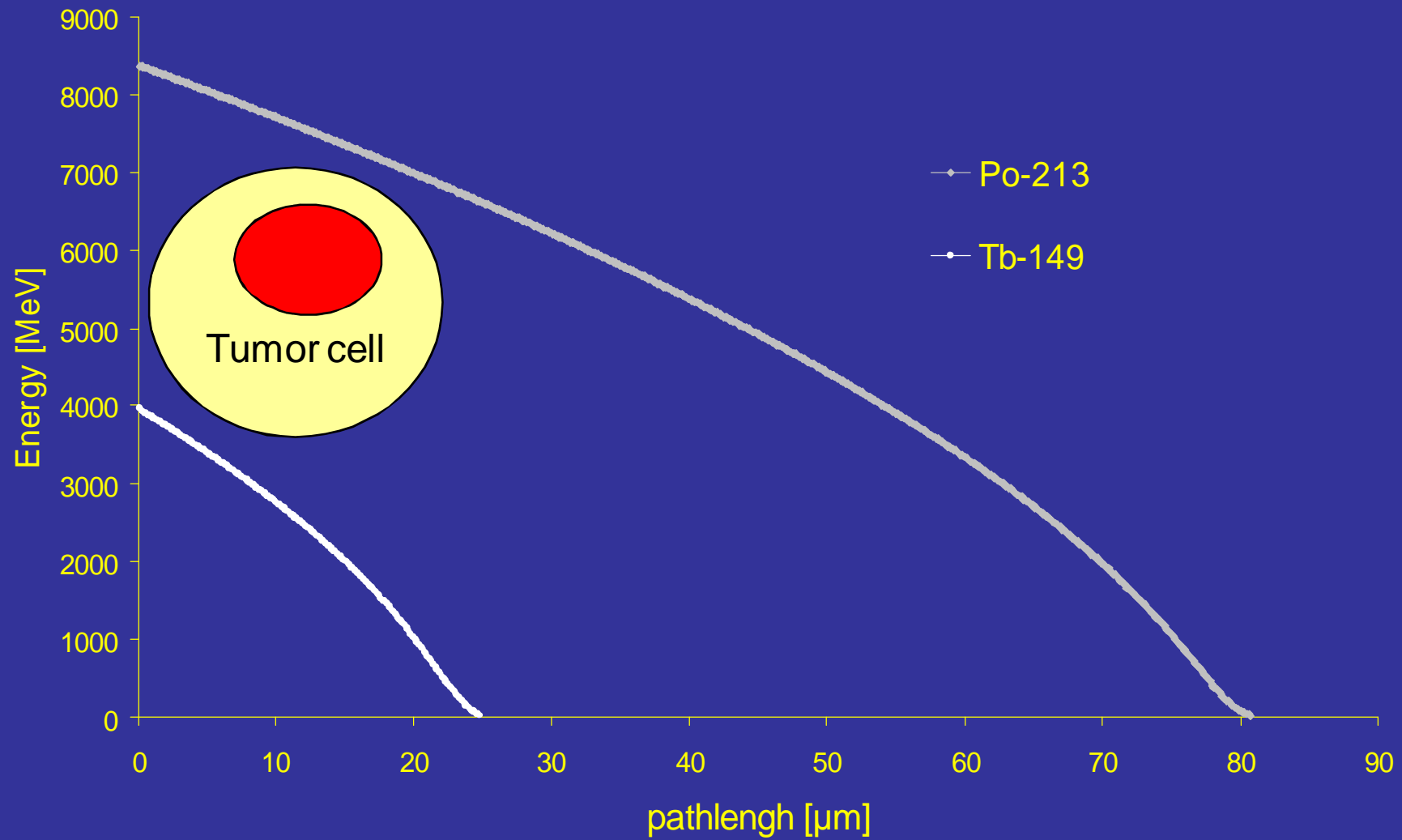
Isotopes for targeted alpha therapy

12	Ac 213 0.80 s	Ac 214 8.2 s	Ac 215 0.17 s	Ac 216 0.44 ms	Ac 217 0.74 μs	Ac 218 1.1 μs	Ac 219 11.8 μs	Ac 220 26 ms	Ac 221 52 ms	Ac 222 69 s	Ac 223 2.10 m	Ac 224 2.9 h	Ac 225 10.0 d	Ac 226 29 m
11	Ra 212 13.0 s	Ra 213 7.1 ms	Ra 214 2.46 s	Ra 215 1.67 ms	Ra 216 2.1 s	Ra 217 1.6 μs	Ra 218 25.6 μs	Ra 219 10 ms	Ra 220 25 ms	Ra 221 28 s	Ra 222 38 s	Ra 223 11.43 d	Ra 224 3.66 d	Ra 225 14.8 d
10	Fr 211 3.10 m	Fr 212 20.0 m	Fr 210 34.8 s	Fr 214 335 ms	Fr 215 0.09 μs	Fr 216 3.70 μs	Fr 217 16 μs	Fr 218 22 ms	Fr 219 21 ms	Fr 220 27.4 s	Fr 221 4.9 m	Fr 222 14.2 m	Fr 223 21.8 m	Fr 224 3.3 m
09	Rn 210 2.4 h	Rn 211 14.6 h	Rn 212 24 m	Rn 213 19.5 ms	Rn 214 15 ns	Rn 215 2.3 μs	Rn 216 45 μs	Rn 217 0.54 ms	Rn 218 35 ms	Rn 219 3.96 s	Rn 220 55.6 s	Rn 221 25 m	Rn 222 3.825 d	Rn 223 23.2 m
08	At 209 5.4 h	At 210 8.3 h	At 211 7.22 h	At 212 119 m	At 213 0.11 μs	At 214 0.76 μs	At 215 0.1 ms	At 216 1 s	At 217 32.3 ms	At 218 -2 s	At 219 0.9 m	At 220 3.7 m	At 221 2.3 m	At 222 54 s
07	Po 208 2.678 s	Po 209 102 s	Po 210 138.38 d	Po 211 89.2 s	Po 212 0.11 s	Po 213 4.2 μs	Po 214 164 μs	Po 215 1.78 ms	Po 216 0.15 s	Po 217 1.53 s	Po 218 3.05 m	Po 219 >300 ns	Po 220 >300 ns	
06	Bi 207 31.55 a	Bi 208 3.68 · 10 ⁻⁴ a	Bi 209 ICO	Bi 210 5.012 d	Bi 211 2.17 m	Bi 212 20.3 m	Bi 213 45.6 m	Bi 214 16.9 m	Bi 215 33.0 s	Bi 216 3.07 m	Bi 217 98.6 s	Bi 218 33 s		136
05	Pb 203 24.1	Pb 207 22.1	Pb 200 52.4	Pb 209 3.253 h	Pb 210 22.3 a	Pb 211 35.1 m	Pb 212 10.84 h	Pb 213 16.2 m	Pb 214 26.5 m					134
04	Tl 206 70.4 d	Tl 208 3.7 m	Tl 207 1.33 a	Tl 209 4.77 m	Tl 209 3.053 m	Tl 209 2.16 m	Tl 210 1.30 m	Tl 211 >207 ns	Tl 212 >370 ns					132

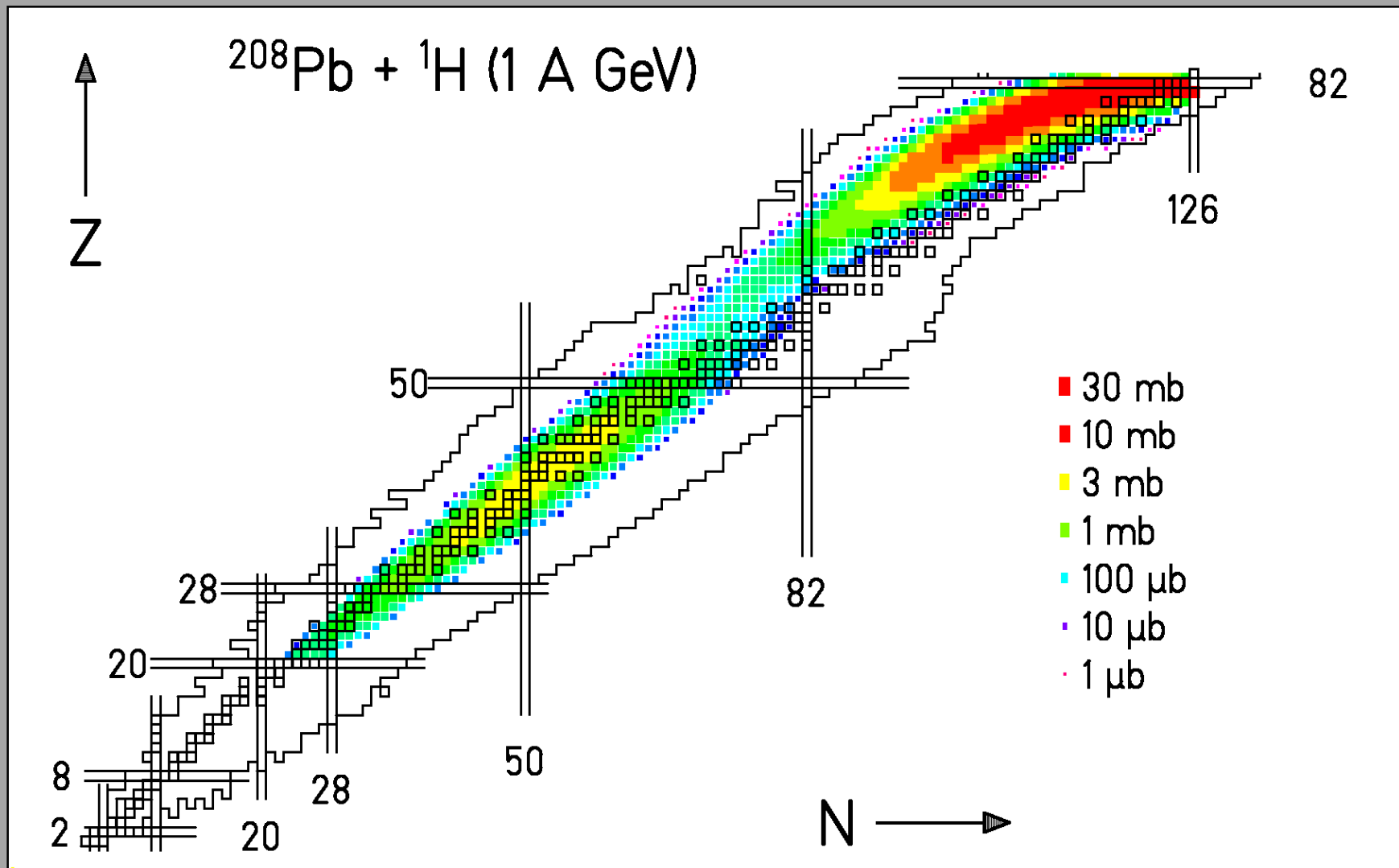
^{149}Tb for targeted alpha therapy

Er 148 4.8 s	Er 149	Er 150 18.5 s	Er 151	Er 152 10.3 s	Er 153 37.1 s	Er 154 5.73 m	Er 155 5.3 m	Er 156 18.6 m	Er 157 18.66 m	Er 158 2.25 h	Er 159 36 m	Er 160 28.6 h	Er 161 5.24 h	Er 162 0.139	Er 163 75 m	Er 164 1.001
Ho 147 5.8 s	Ho 148	Ho 149	Ho 150	Ho 151	Ho 152	Ho 153	Ho 154	Ho 155 48 m	Ho 156	Ho 157 12.6 m	Ho 158	Ho 159	Ho 160	Ho 161	Ho 162	Ho 163
Dy 146 29 s	Dy 147	Dy 148 3.1 m	Dy 149	Dy 150 7.2 m	Dy 151 17 m	Dy 152 2.4 h	Dy 153 6.29 h	Dy 154 3.0 · 10 ⁴ a	Dy 155 10.0 h	Dy 156 0.056	Dy 157 8.1 h	Dy 158 0.085	Dy 159 144.4 d	Dy 160 2.329	Dy 161 13.889	Dy 162 25.475
Tb 145	Tb 146	Tb 147	Tb 148	Tb 149	Tb 150	Tb 151	Tb 152	Tb 153	Tb 154	Tb 155 5.32 d	Tb 156	Tb 157	Tb 158	Tb 159 100	Tb 160 72.3 d	Tb 161 690 d
Gd 144 4.5 m	Gd 145	Gd 146 48.3 d	Gd 147 38.1 h	Gd 148 74.6 a	Gd 149 9.28 d	Gd 150 1.8 · 10 ⁴ a	Gd 151 120 d	Gd 152 0.20	Gd 153 239.47 d	Gd 154 2.18	Gd 155 14.80	Gd 156 20.47	Gd 157 15.65	Gd 158 24.84	Gd 159 16.48 h	Gd 160 21.88
Eu 143 2.6 m	Eu 144 10.2 s	Eu 145 5.93 d	Eu 146 4.51 d	Eu 147 24.6 d	Eu 148 65.6 d	Eu 149 93.1 d	Eu 150	Eu 151 47.81	Eu 152	Eu 153 52.19	Eu 154	Eu 155 4.761 a	Eu 156 15.2 h	Eu 157 15.18 h	Eu 158 46 m	Eu 159 1.81 m
Sm 142 72.4 m	Sm 143	Sm 144 3.07	Sm 145 340 d	Sm 146 1.03 · 10 ⁴ a	Sm 147 14.99	Sm 148 11.24	Sm 149 13.82	Sm 150 7.38	Sm 151 93 a	Sm 152 26.75	Sm 153 46.27 h	Sm 154 22.75	Sm 155 22.4 m	Sm 156 9.4 h	Sm 157 8.11 m	Sm 158 5.51 m
Pm 141 20.9 m	Pm 142 40.5 s	Pm 143 265 d	Pm 144 1.0 a	Pm 145 17.7 s	Pm 146 0.53 a	Pm 147 2.62 a	Pm 148	Pm 149 33.1 h	Pm 150 2.7 h	Pm 151 28.4 h	Pm 152 5.3 m	Pm 153	Pm 154	Pm 155 41.5 s	Pm 156 26.7 s	Pm 157 10.6 s
Nd 140 3.37 d	Nd 141	Nd 142 27.2	Nd 143 12.2	Nd 144 23.8	Nd 145 8.3	Nd 146 17.2	Nd 147 10.38 d	Nd 148 5.7	Nd 149 1.73 h	Nd 150 5.6	Nd 151 12.4 m	Nd 152 18.4 m	Nd 153 28.9 s	Nd 154 25.9 s	Nd 155 8.9 s	Nd 156 5.5 s
Pr 139 4.5 h	Pr 140 3.4 m	Pr 141 106	Pr 142	Pr 143 13.67 d	Pr 144	Pr 145 5.98 h	Pr 146 24.0 m	Pr 147 13.6 m	Pr 148	Pr 149 2.25 m	Pr 150	Pr 151 18.9 s	Pr 152 3.8 s	Pr 153 4.3 s	Pr 154 2.3 s	Pr 155 >300 ns
Ce 138 0.251	Ce 139	Ce 140 88.450	Ce 141 32.60 d	Ce 142 11.114	Ce 143 33.0 h	Ce 144 284.8 d	Ce 145 2.98 m	Ce 146 13.5 m	Ce 147 57 s	Ce 148 48 s	Ce 149 5 s	Ce 150 4.1 s	Ce 151 1.0 s	Ce 152 1.4 s	Ce 153 >300 ns	Ce 154 >300 ns

Alpha track in relation to cancer cells

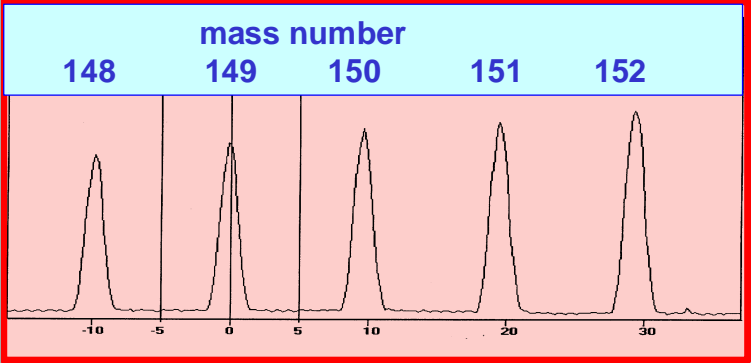
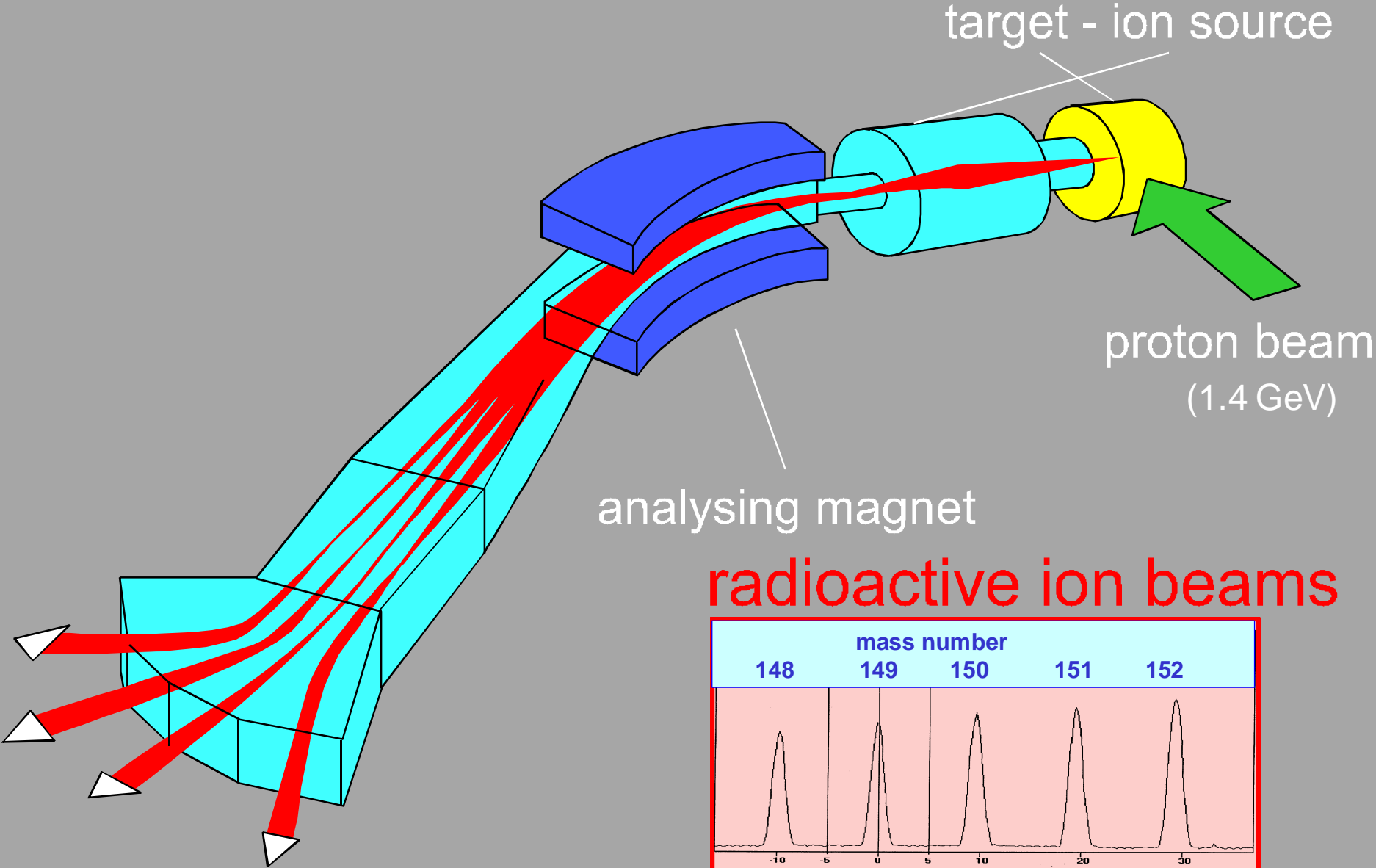


High-energy proton induced reactions

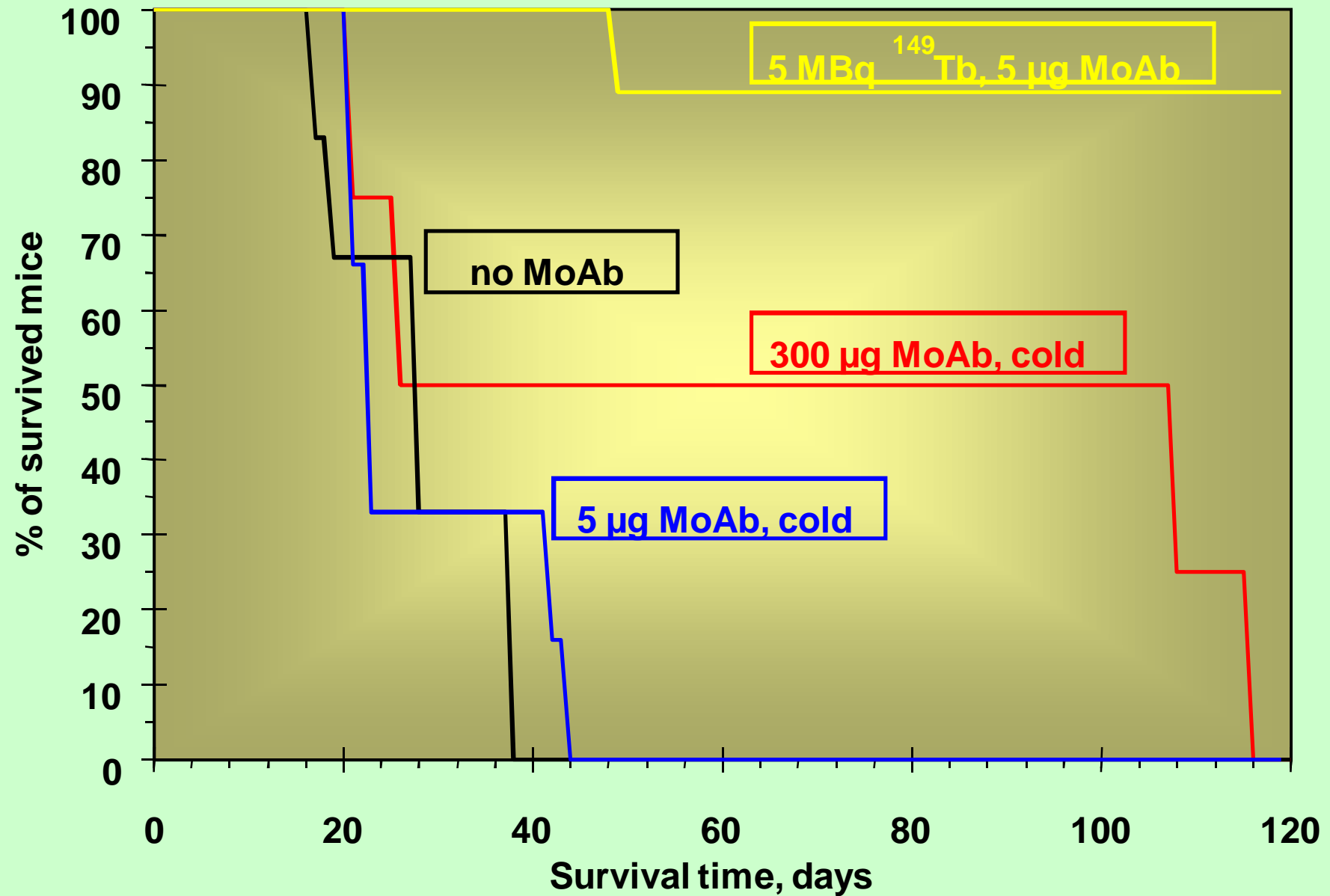


High-energy proton induced reactions can produce most of the isotopes of the chart of nuclides.

Isotope Separation On-Line



Survival of SCID mice



Terbium: a unique element

Dy 150 72 m	Dy 151 7 m	Dy 152 2.4 h	Dy 153 6.2 h	Dy 154 3.0 · 10 ⁶ a	Dy 155 10.0 d	Dy 156 0.366	Dy 157 6.1 d	Dy 158 0.095	Dy 159 144.3 d	Dy 160 2.329	Dy 161 18.055	Dy 162 25.075
Tb 149	Tb 150	Tb 151	Tb 152	Tb 153	Tb 154	Tb 155	Tb 156	Tb 157	Tb 158	Tb 159	Tb 160	Tb 161
Gd 148 74.6 a	Gd 149 52.8 d	Gd 150 1.3 · 10 ⁶ a	Gd 151 100 d	Gd 152 0.30	Gd 153 338.47 d	Gd 154 2.18	Gd 155 14.80	Gd 156 20.47	Gd 157 5.45	Gd 158 24.84	Gd 159 15.70 h	Gd 160 21.80

ID101
¹⁴⁹Tb
α-RIT

ID92
¹⁵²Tb
PET

¹⁵⁵Tb
SPECT

ID97
¹⁶¹Tb
β/e⁻ RIT
SPECT

Radioisotopes available at ISOLDE-CERN

Isotopes on-line separated at ISOLDE																					
Long-lived isotopes available at ISOLDE																					
Decay daughters of ISOLDE beams																					
1																	2				
H																	He				
3	4															5	6	7	8	9	10
Li	Be															B	C	N	O	F	Ne
11	12															13	14	15	16	17	18
Na	Mg															Al	Si	P	S	Cl	Ar
19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36				
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr				
37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54				
Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe				
55	56	57	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86				
Cs	Ba	La	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn				
87	88	89	104	105	106	107	108	109	110	111	112	113	114	115	116		118				
Fr	Ra	Ac	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg											

58	59	60	61	62	63	64	65	66	67	68	69	70	71
Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
90	91	92	93	94	95	96	97	98	99	100	101	102	103
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Currently available: more than 1000 different radioisotopes
 Saturation activities of longer-lived radioisotopes: GBq and more
 Unique radiochemical techniques (e.g. P. Hoff et al., NIM 221 (1984) 313.)

Isotopes for targeted alpha therapy

The image displays a periodic table of isotopes, color-coded by half-life and decay mode. Red arrows point to isotopes suitable for targeted alpha therapy: Ra-223, Rn-222, Po-212, and Bi-212. Blue arrows point to other isotopes of interest: Pb-209, Bi-209, and Tl-209. The table includes atomic number, element symbol, isotope name, and half-life.

Atomic Number	Element	Isotope	Half-life
88	Radium	Ra-223	11.43 d
86	Rn	Rn-222	14.2 m
84	Po	Po-212	0.3 μs
83	Bi	Bi-212	2.14 m
82	Pb	Pb-209	3.4 h
81	Tl	Tl-209	>10 ¹² a

Thomson Reuters

Algeta soars on \$800 million Bayer drug alliance

09.03.09, 09:13 AM EDT

FRANKFURT, Sept 3 (Reuters) –

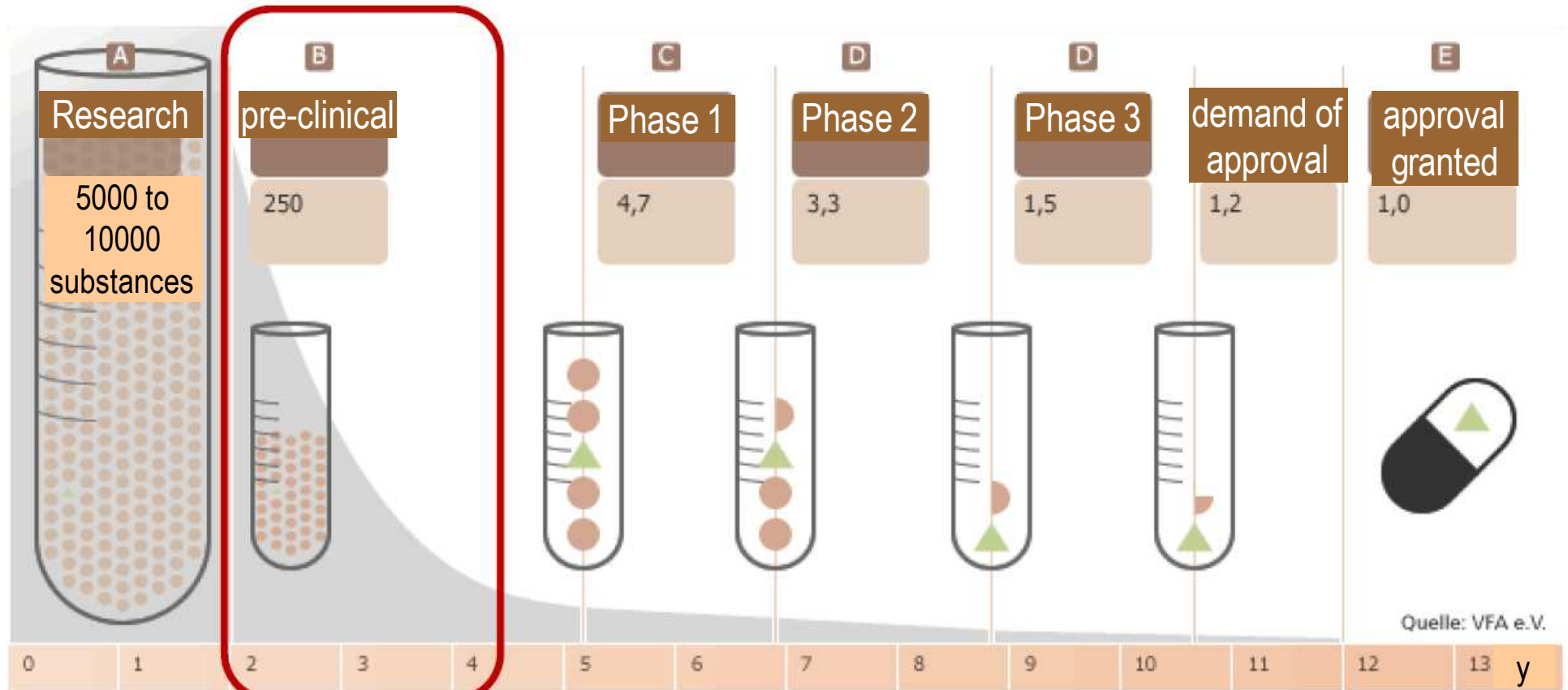
Norwegian biotech company Algeta clinched an \$800 million licensing deal for its main experimental drug with German drugmaker [Bayer](#), sending its shares soaring on Thursday.

Algeta expects **peak annual global sales of \$1.3-\$1.9 billion** for the cancer drug, dubbed **Alpharadin**, which clings to **cancerous bone cells** because it has some properties of calcium and **destroys them via alpha rays**.

The deal is potentially worth 560 million euros (\$800 million) to Algeta, including an upfront payment of 42.5 million from Bayer and payments depending on development and commercial milestones, the two companies said.

Algeta, founded in 1997 by two **Norwegian radiochemistry researchers**, will also get double-digit royalties on future sales. It also has an option in the U.S. market, by far the largest for Alpharadin, to switch from royalties to sharing profit equally with Bayer.

Development of pharmaceuticals



Screening

**in vitro tests
animal exp.**

tests with humans

**toxicity
side effects**

wanted effect

**comparison
with standard**

**20-80 healthy
volunteers** **100-300 patients** **x00-x000 patients**

Pre-clinical studies (1)



Pre-clinical studies (2)



Pre-clinical studies (3)





Control



Treated



Control



Treated



Control



Treated



Control



Treated

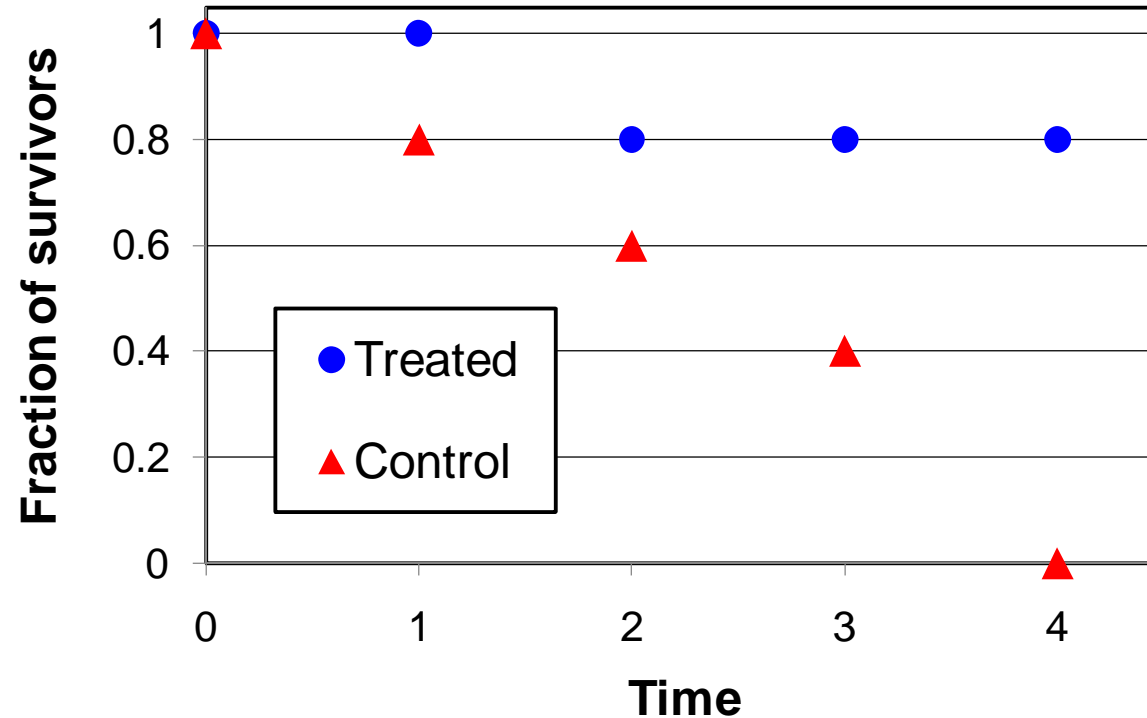


Control

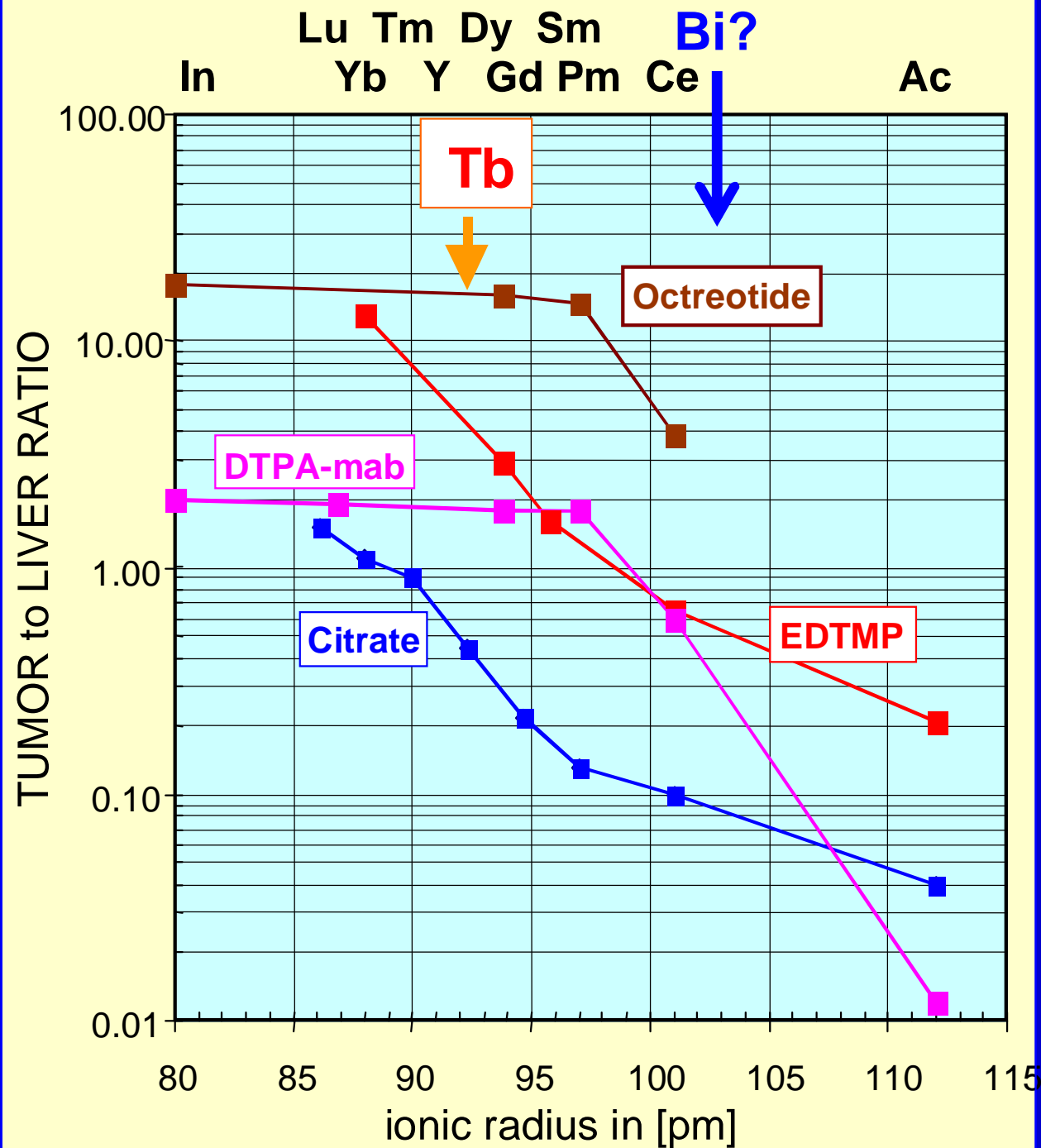


Treated

Survival curve



- medium survival time, median survival time, survival benefit
- shows final benefit but not detailed mechanism
- more information from **bio-distribution studies**
- preferentially **on-line with suitable radiotracers**
and small animal SPECT or PET



Comparison

of the
bio-distribution
of different
tumor seeking tracers
labeled with
radio-lanthanides,
 ^{225}Ac and ^{111}In

free chelates:

Citrate
EDTMP

specific tracers:

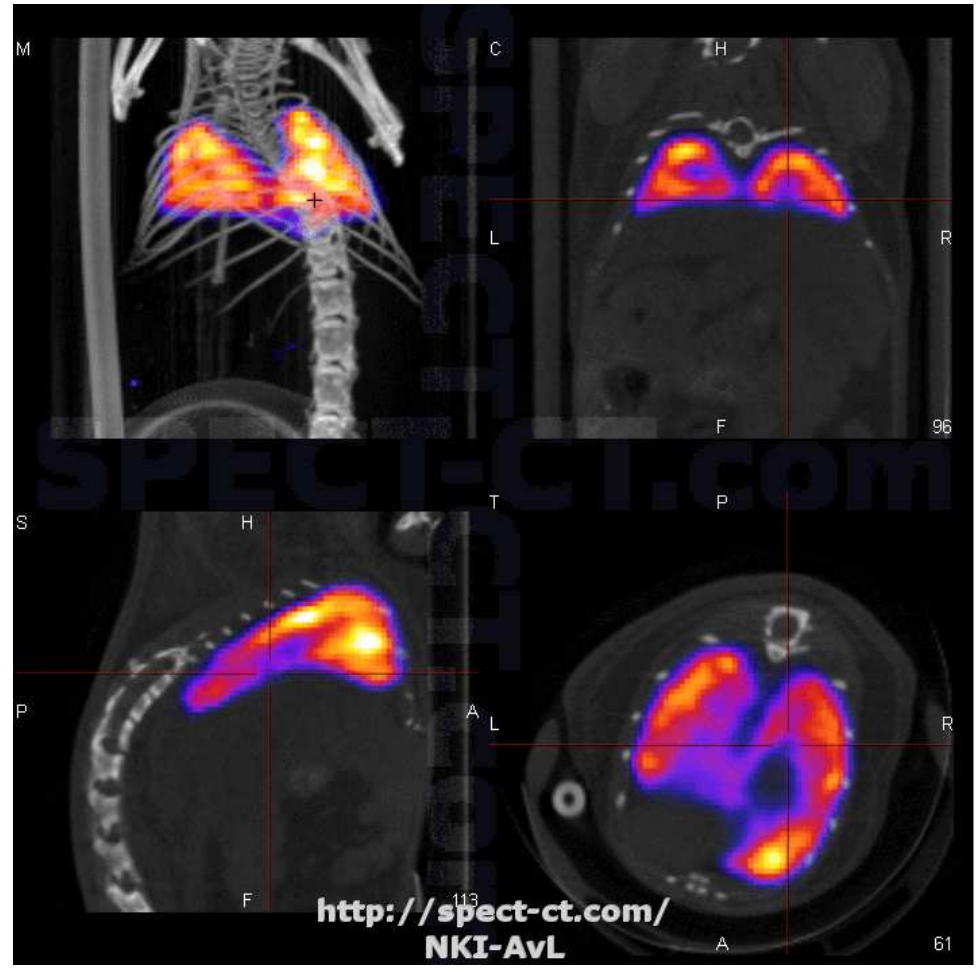
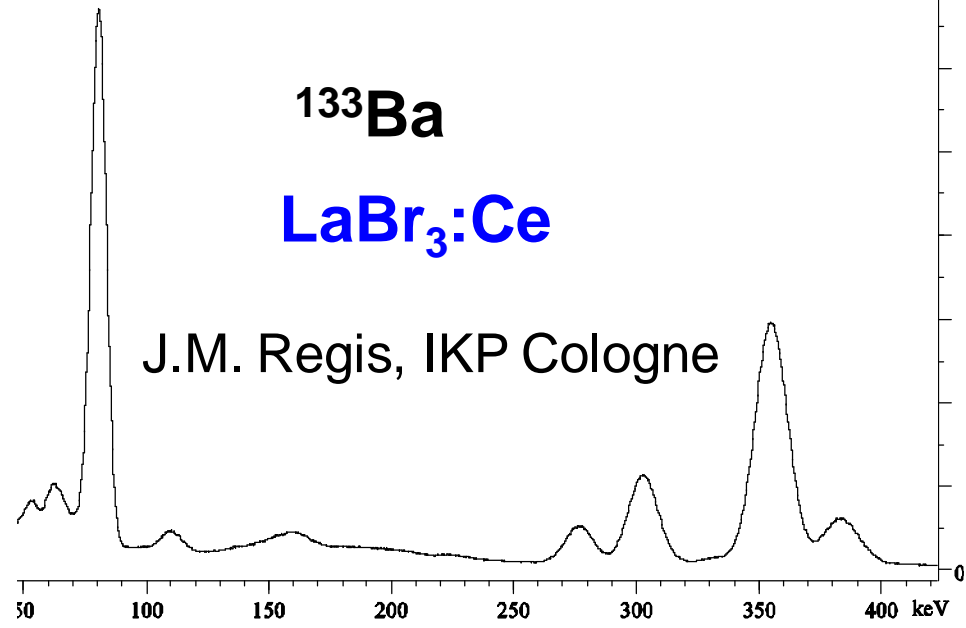
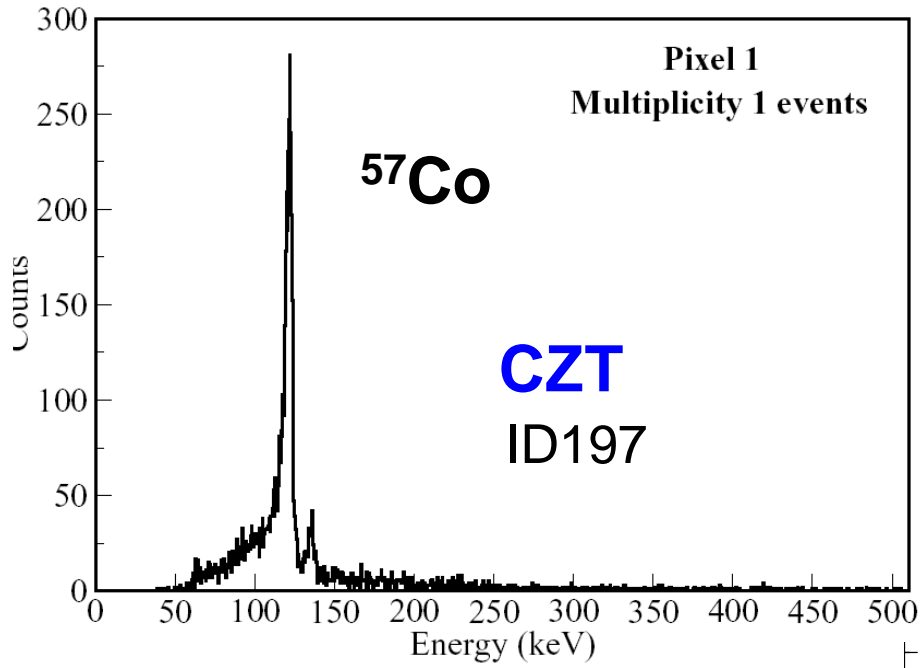
Octreotide
and
Mab

Linker:

Aminobenzyl-DTPA

G.J.Beyer, Hyperfine Interactions 129 (2000) 529.

New generation of small animal SPECT



systematic biodistribution studies with different radiotracers become possible with dedicated small animal SPECT

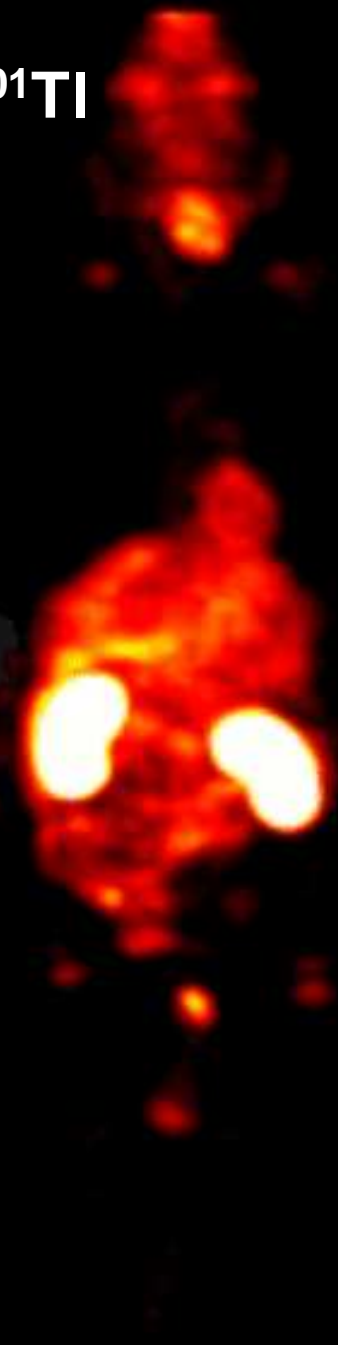
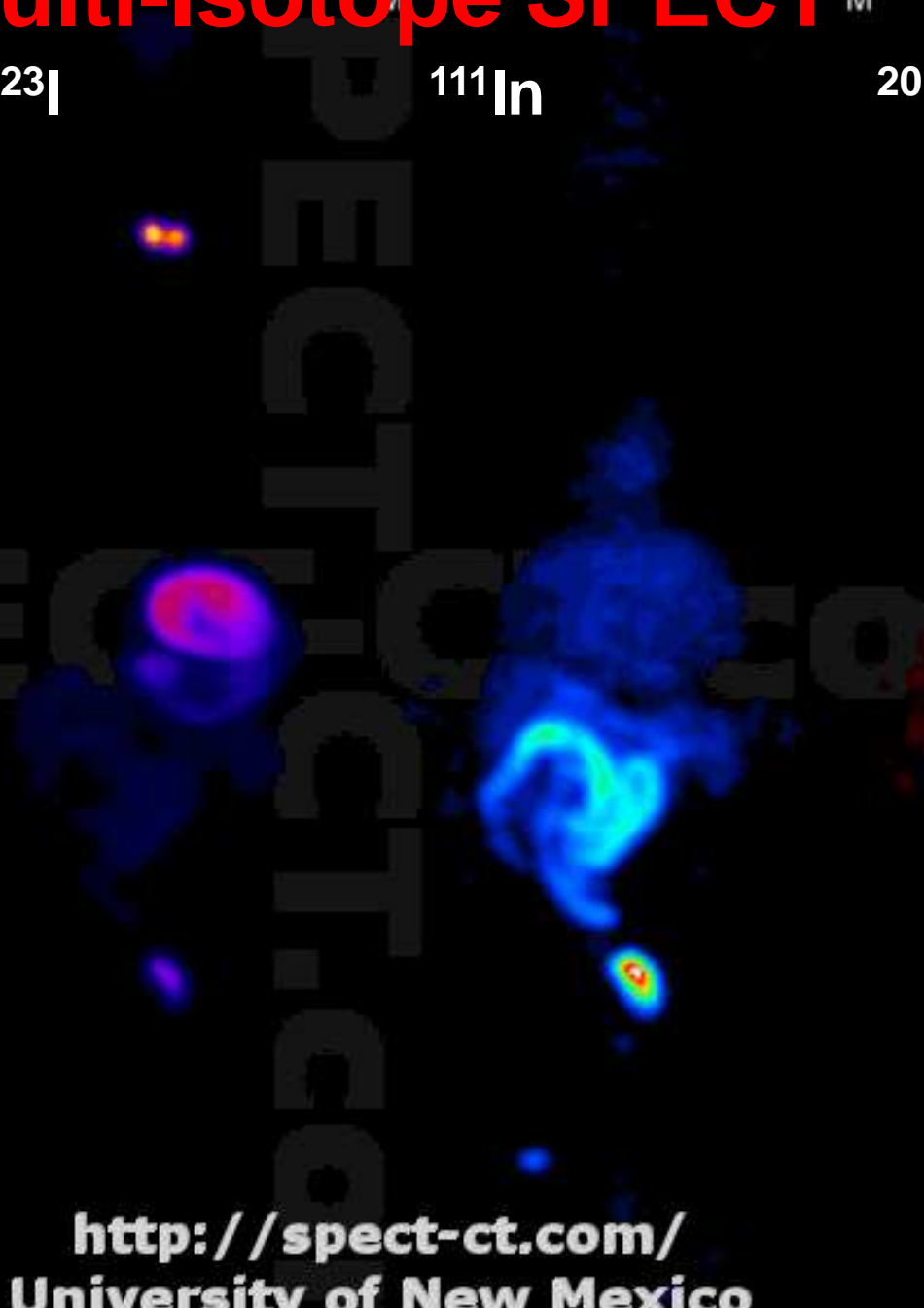
Multi-Isotope SPECT

^{99m}Tc

^{123}I

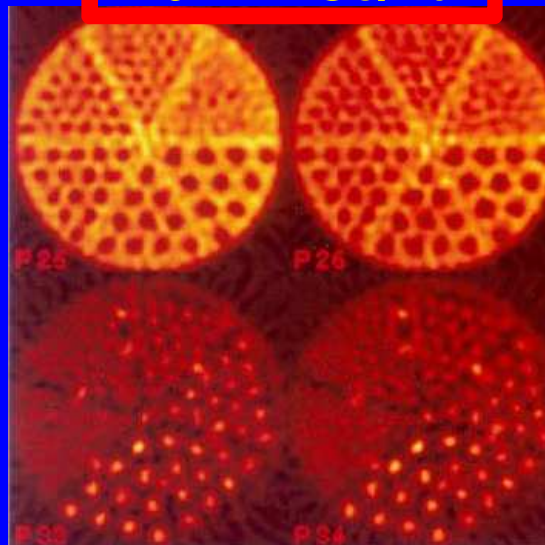
^{111}In

^{201}Tl

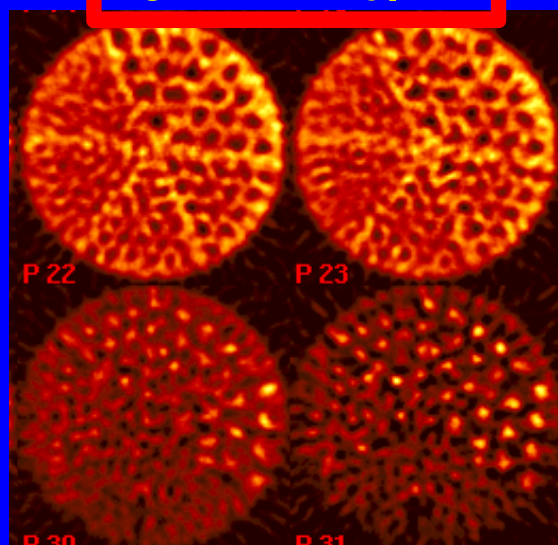


<http://spect-ct.com/>
University of New Mexico

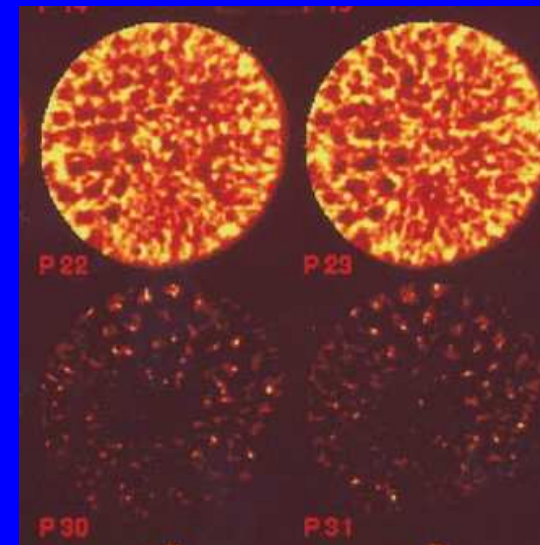
76 h $^{134}\text{Ce}/\text{La}$



81 h $^{140}\text{Nd}/\text{Pr}$



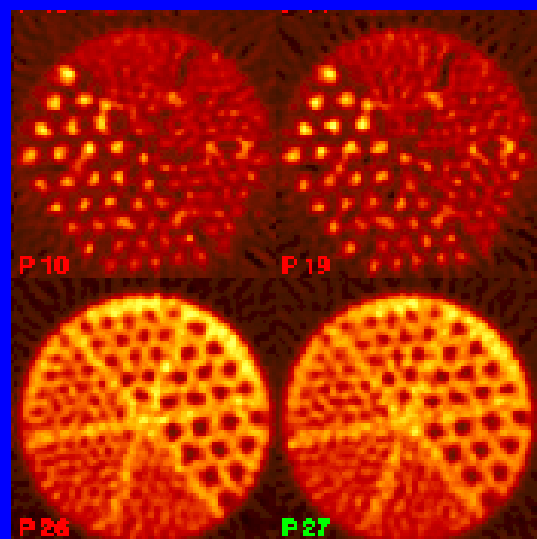
^{149}Tb



Positron emitting radiolanthanides

PET phantom studies

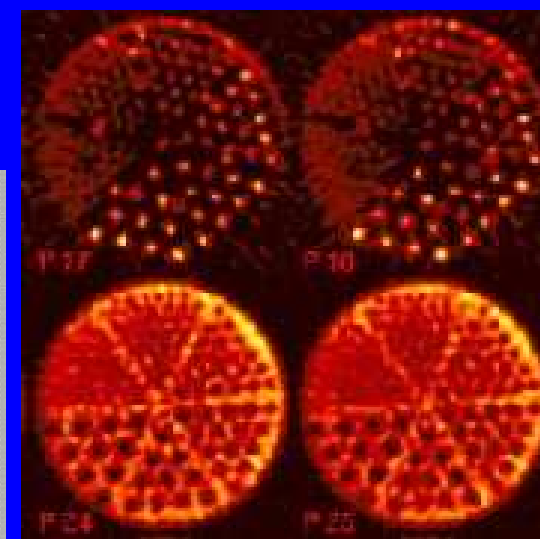
$^{142}\text{SmEDTMP}$ in vivo study



$^{138}\text{Nd}/\text{Pr}$

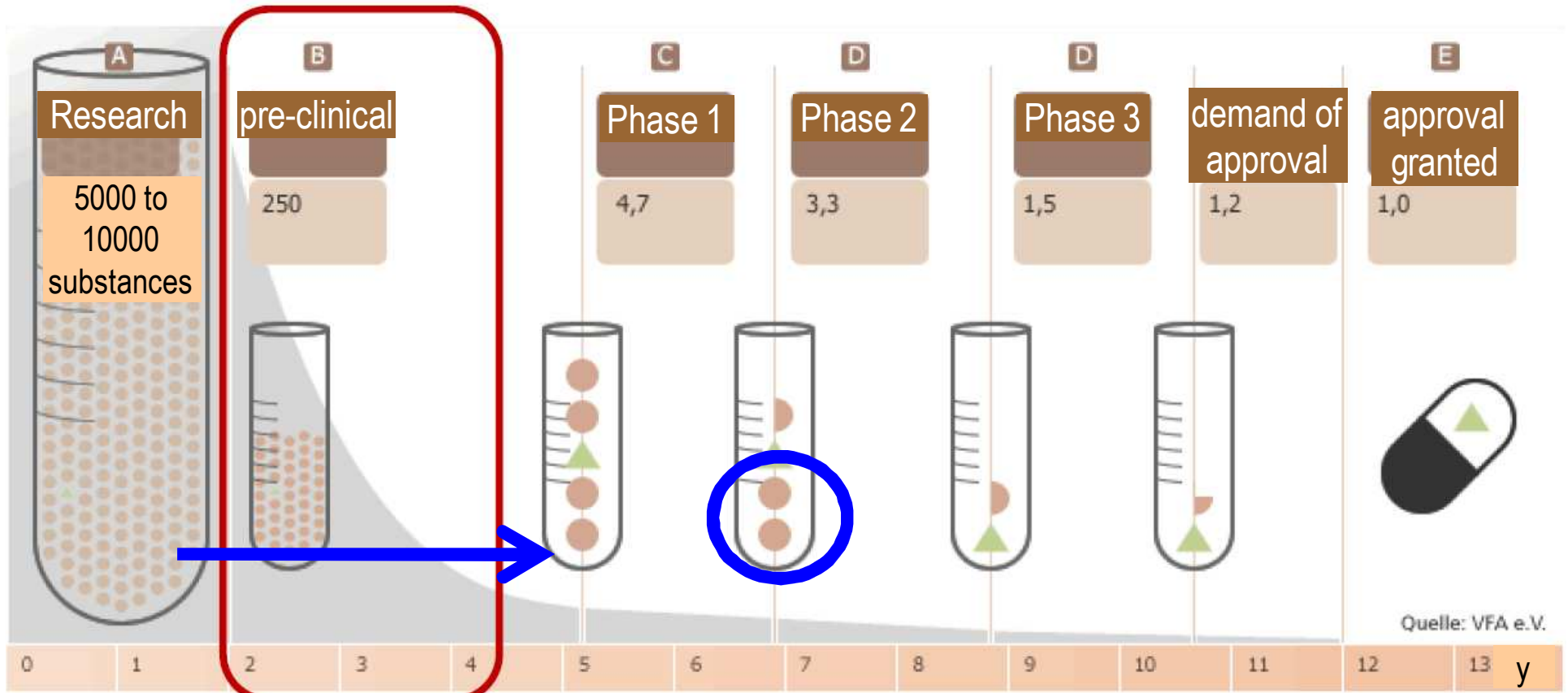


$^{142}\text{Sm}/\text{Pm}$



17.5 h ^{152}Tb

Development of pharmaceuticals



Quelle: VFA e.V.

Screening

in vitro tests
animal exp.

- Multi-isotope studies
- Long-lived PET tracer

tests with humans

toxicity
side effects

wanted effect

comparison
with standard

20-80 healthy
volunteers

100-300 patients

x00-x000 patients

Classification of Isotopes for Medicine

1. Established isotopes

^{99m}Tc , ^{18}F , $^{123,125,131}\text{I}$, ^{111}In , ^{90}Y

supply security

optimization of production/scale effects > cost reduction

“industrial” suppliers

2. Emerging isotopes

^{68}Ga , ^{82}Rb , ^{89}Zr , ^{177}Lu , ^{188}Re

quality, GMP, certification

“small” innovative suppliers

3. R&D isotopes

$^{44,47}\text{Sc}$, $^{64,67}\text{Cu}$, ^{134}Ce , ^{140}Nd ,

$^{149,152,155,161}\text{Tb}$, ^{166}Ho , ^{195m}Pt ,

^{211}At , $^{212,213}\text{Bi}$, ^{223}Ra , ^{225}Ac ,...

availability at affordable cost

research labs

**“Small” innovative suppliers
in tight collaboration
with universities & research labs**

AAA CERN, Uni Geneva, Uni Lausanne, CERIMED,...

ITG FRM2, TU Munich

ITD FZR, TU Dresden

(ARRONAX Subatech, Univ. Nantes)

Classification of Isotopes for Medicine

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availability at affordable cost

research labs

Innovative Radioisotopes for Medicine

Proposal for a **European user facility providing R&D isotopes for (pre-)clinical studies + logistics.**

Potential Suppliers:

- **ILL Grenoble** ($1.5 \cdot 10^{15}$ n./cm²/s high flux reactor):
 ^{161}Tb , ^{166}Ho , ^{169}Er , ^{186}Re , $^{195\text{m}}\text{Pt}$,... highest spec. activity
- **ISOLDE-CERN** (1.4 GeV protons + mass separation):
 $^{149,152,155}\text{Tb}$, ^{140}Nd , ^{134}Ce ,... + many others carrier-free!
- **PSI Villigen** (1 MW SINQ + cyclotron + radiochemistry):
 $^{44}\text{Ti}/^{44}\text{Sc}$, $^{64,67}\text{Cu}$, $^{117\text{m}}\text{Sn}$,...
- **ARRONAX Nantes** (70 MeV high power cyclotron):
 $^{44,47}\text{Sc}$, $^{64,67}\text{Cu}$, ^{211}At ,...
- Open for additional contributors...

Opportunity and duty for large scale research infrastructures!

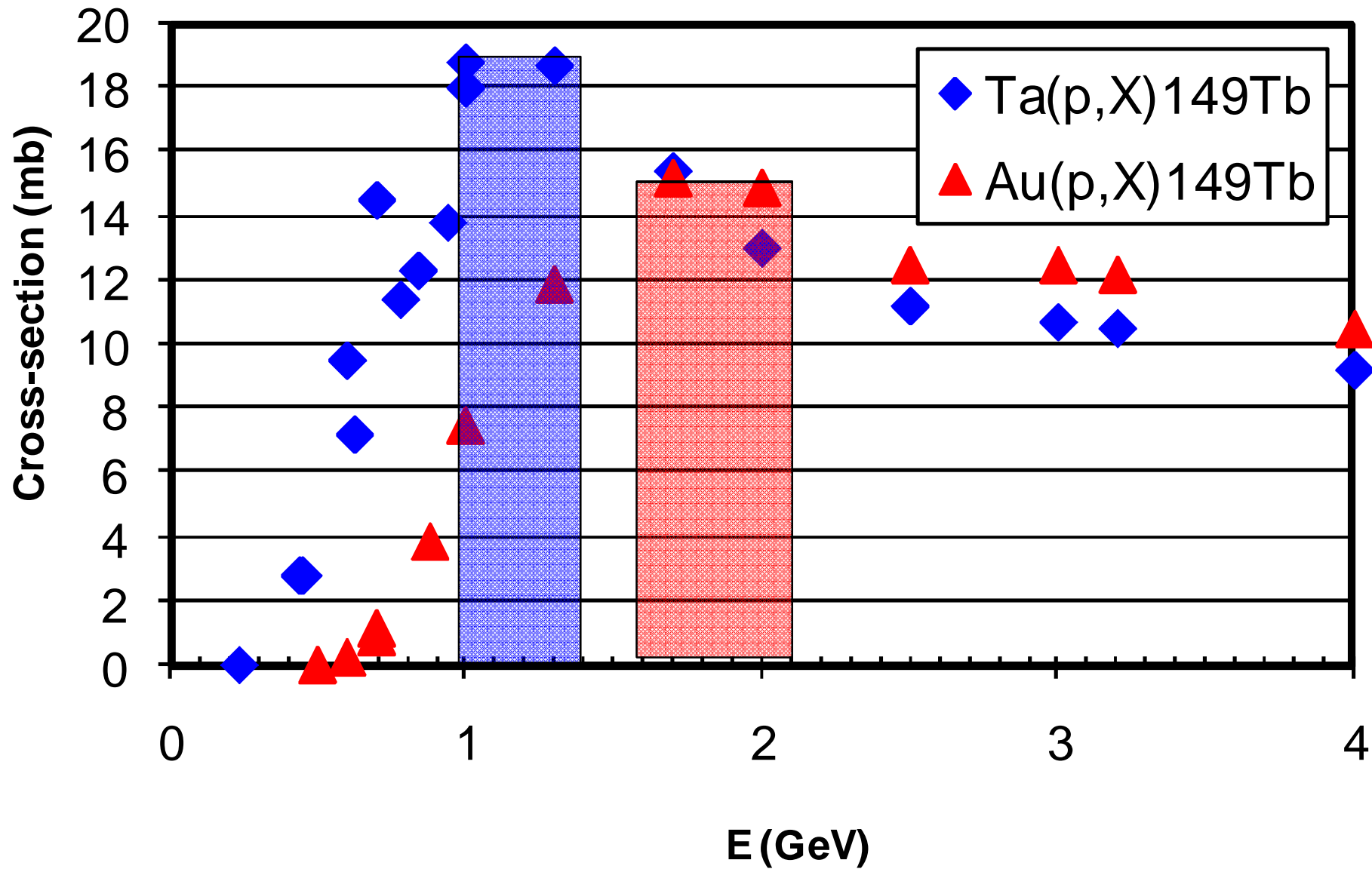
Future of ISOLDE Isotopes for Nuclear Medicine

What should be done at CERN:

- **Launch a new European collaboration for bio-medical and nuclear medicine studies with carrier-free radioisotopes from ISOLDE and other sources.**
- **Rebuild a radiochemical laboratory at ISOLDE for on-site chemical purification of radioisotopes.**
- **Prepare technological solutions for larger-scale isotope production with coming accelerator upgrades (LINAC4, SPL).**

Radio-isotope	Half-life $T_{1/2}$	X-section (mb)	Production rate (per s)	Alternative production processes		Applications
192-Ir	74 d	2.58E+00	1.0E+14	(n, γ)	reactor	Sealed sources for industry and cancer therapy
188-W/Re	69 d	6.90E-02	2.7E+12	(2n, γ)	HFR	Radio-immuno-therapy with 188-Re
178-W/Ta	22 d	8.08E+00	3.1E+14	(p,4n)	accelerator	Generator with potential in PET
177-Lu	6.7 d	6.31E-02	2.4E+12	(n, γ)	reactor	Therapy with labelled antibodies and peptides
166-Ho	25.8 h	5.30E-03	2.0E+11	(n, γ)	reactor	Therapy with labelled antibodies and peptides
149-Tb	4.12 h	9.21E-01	3.5E+13			Targeted Alpha Therapy, single cancer cell targeting
148-Gd	74.6a	5.31E-01	2.1E+13	spallation	accelerator	Low-energy alpha sources
153-Sm	46.75 h	1.41E-03	0.6E+11	(n, γ)	reactor	Therapy of bone metastases
127-Xe	76.4 d	9.22E-02	3.5E+12	(p,x...)	accelerator	SPECT, lung ventilation and brain perfusion
117m-Sn	13.6 d	1.78E-01	0.7E+13	(n, γ)	HFR	Systemic radionuclide therapy
99-Mo/99m-Tc	66 h	2.78E-01	0.6E+13	(n, f)	reactor	Most important radionuclide for nuclear medical imaging
89-Sr	50.5 d	5.39E-01	2.1E+13	(n, γ), (n,p)	reactor	Palliative therapy of bone metastases
82-Sr/Rb	25.5 d	1.36E-01	0.5E+13	(p,4n)	accelerator	Generator, PET, myocardial perfusion
68-Ge/Ga	288 d	9.38E-02	3.6E+12	(p,2n), spall.	accelerator	Different PET imaging procedures, calibration of PET
67-Cu	61.9 h	3.83E-01	1.5E+13	(p, γ)	accelerator	Therapy with labelled antibodies and peptides
44-Ti/Sc	47.3 y	1.77E-03	0.7E+11	spallation	accelerator	Generator, great potential for PET
32-Si	101 y	3.03E-02	1.2E+12			Important isotope for R&D and technical application
26-Al	7.16e5 y	6.05E-03	2.3E+11	(p,n)	cyclotron	Important isotope for R&D and technical application
28-Mg	20.9 h	1.45E-02	0.6E+12			Important isotope for R&D

Spallation production of ^{149}Tb




BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

Which radioisotopes will
we need in 2030?

DATE: December 4, 1958

TO: Addressees Below

FROM: Daniel M. Schaeffer, Head 
BNL Patent Office

SUBJECT: P-701 and P-702 - PREPARATION OF
CARRIER-FREE MOLYBDENUM AND OF
TECHNETIUM FROM FISSION PRODUCTS

The New York Patent Group has carefully studied the information available relative to the above-identified item. The AEC does not at present desire to prepare a patent application on this item for the following reason:

"The method of producing carrier-free molybdenum-99 from fission products is disclosed in U. S. Patent Application S.N. 732,108, Green, Powell, Samos & Tucker (BNL Pat No. 58-17). It is noted that molybdenum-99 may be separated from its radioactive daughter, technetium-99, by absorption of a solution of molybdenum-99 on alumina and subsequent elution of its daughter with .1 nitric acid. While this method is probably novel, it appears that the product will probably be used mostly for experimental purposes in the laboratory. On this basis, no further patent action is believed warranted."

■■■
believe that this attitude is significant. We are not aware of a potential market for technetium-99 great enough to encourage one to undertake the risk of patenting in hopes of successful and rewarding licensing. We would recommend against filing on the Tucker, Greene and Murrenhoff separation process."