

# The Nuclear Astrophysics' Curse on Nuclear Medicine

Ulli Köster

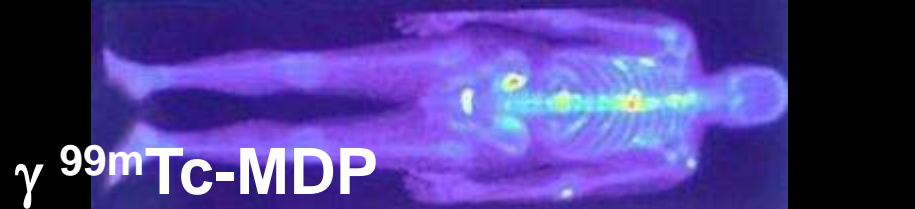
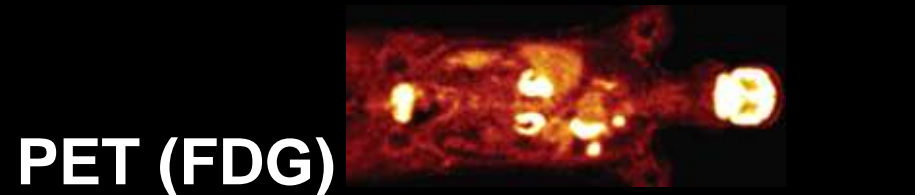
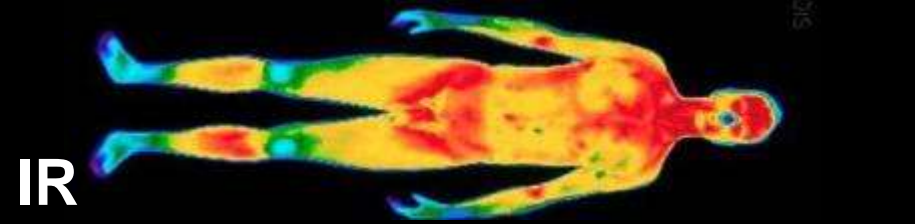
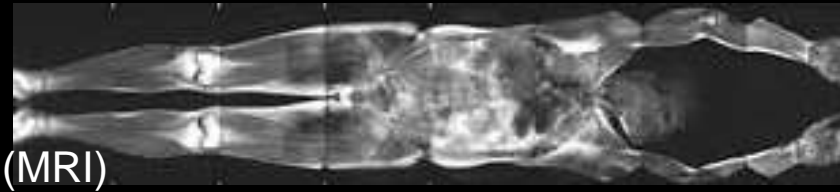
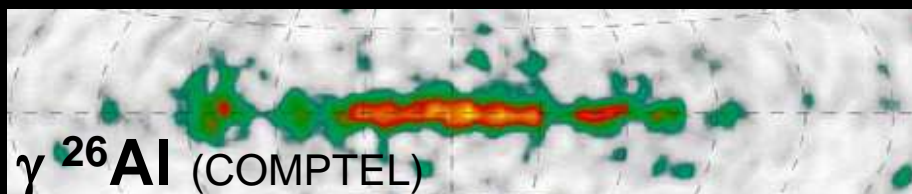
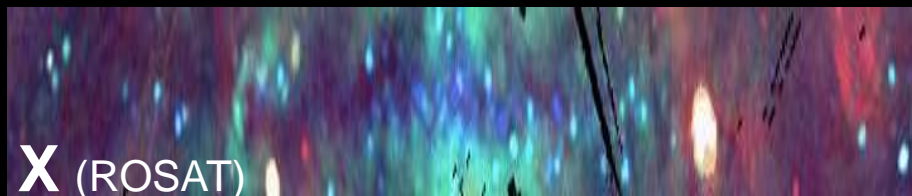
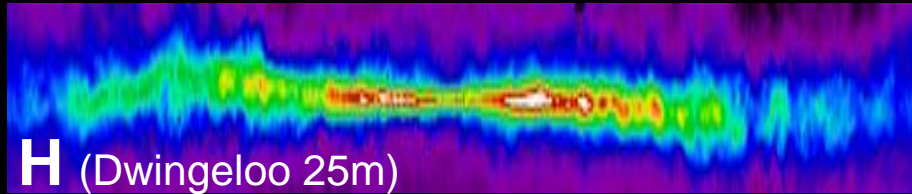
Institut Laue-Langevin, Grenoble



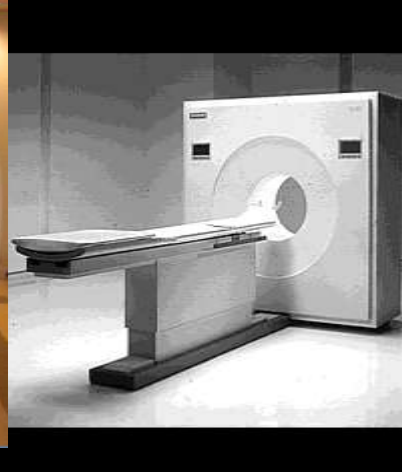
11<sup>th</sup> Russbach Workshop on Nuclear Astrophysics

11 March 2014

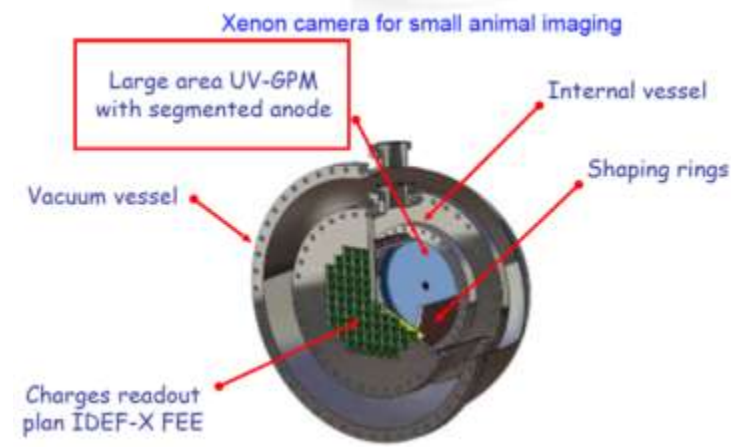
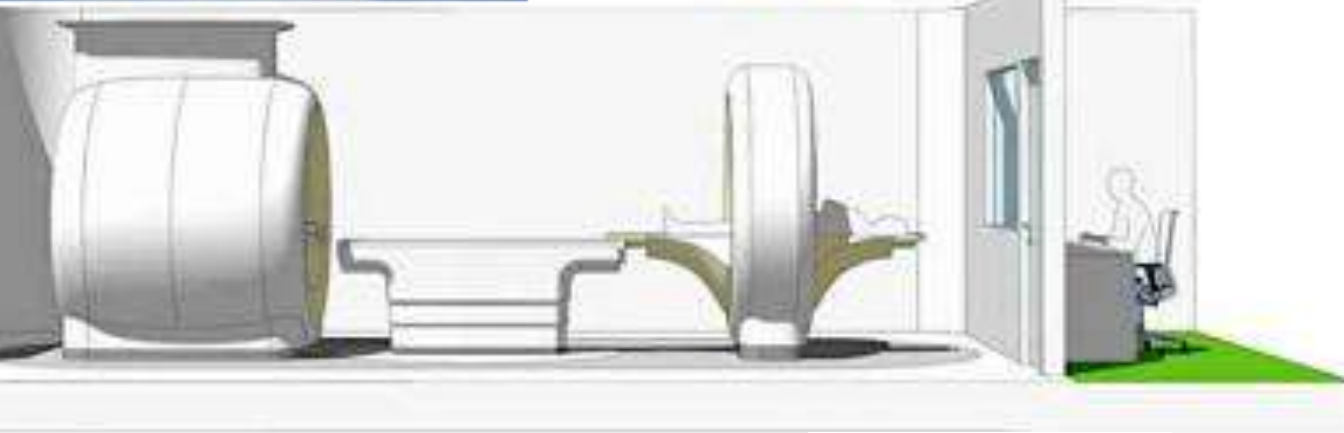
# Different views, different observables







PET





84th INTERNATIONAL

# MOJOR

6-16 MARCH 2014

# SHOW

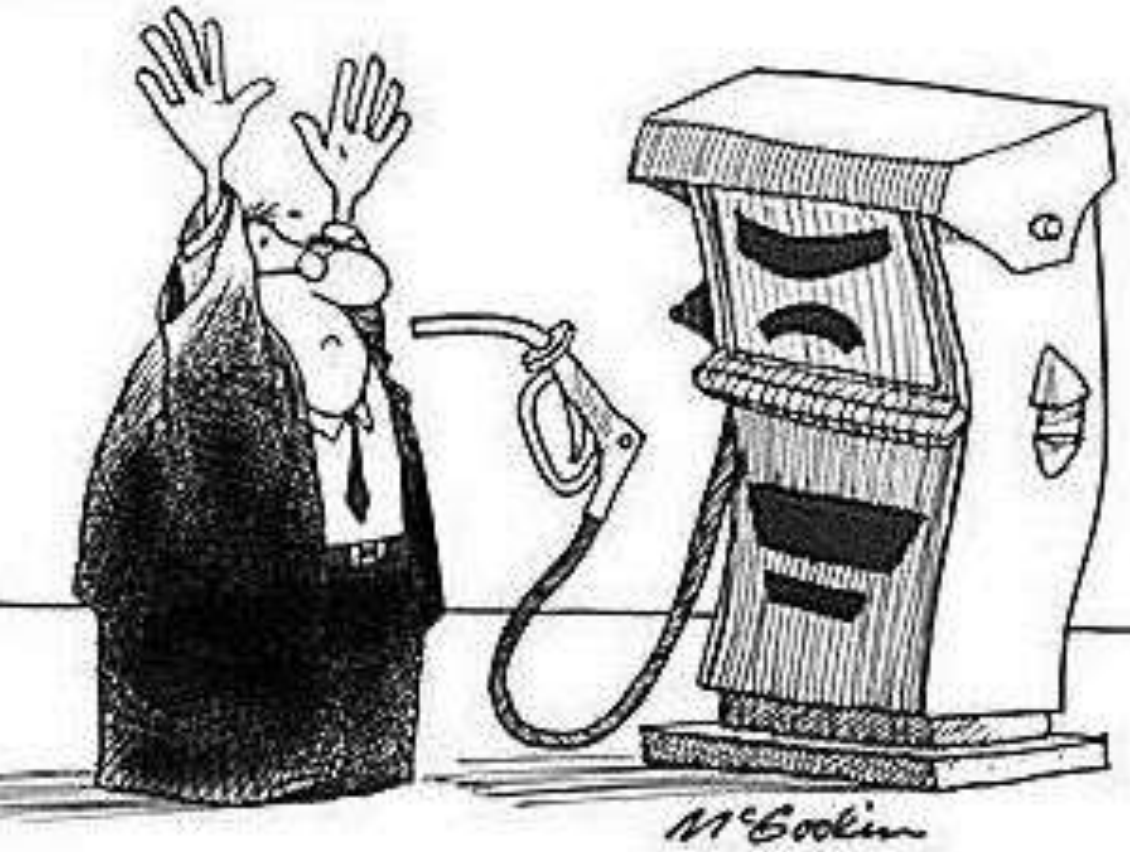
& ACCESSORIES

GENEVA  
PALEXPO





Don't forget the fuel!



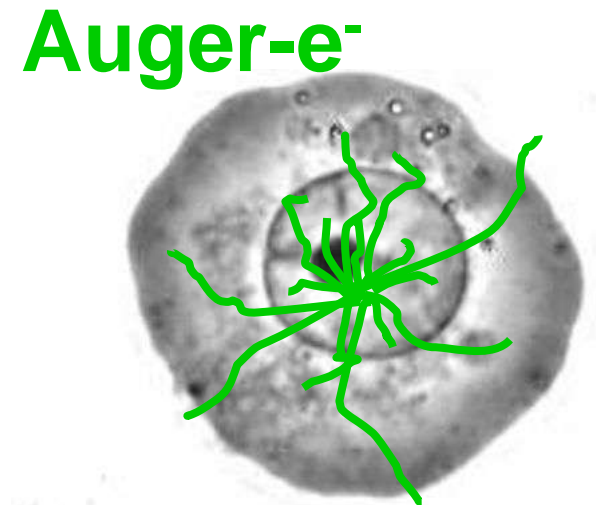
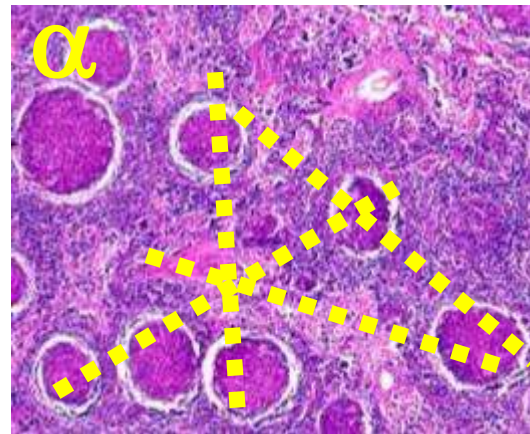
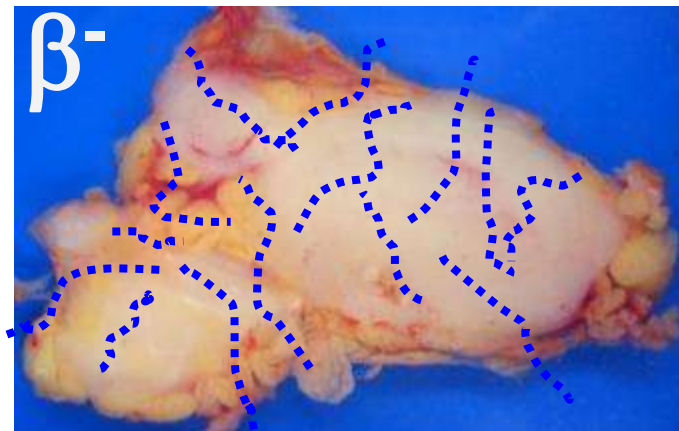
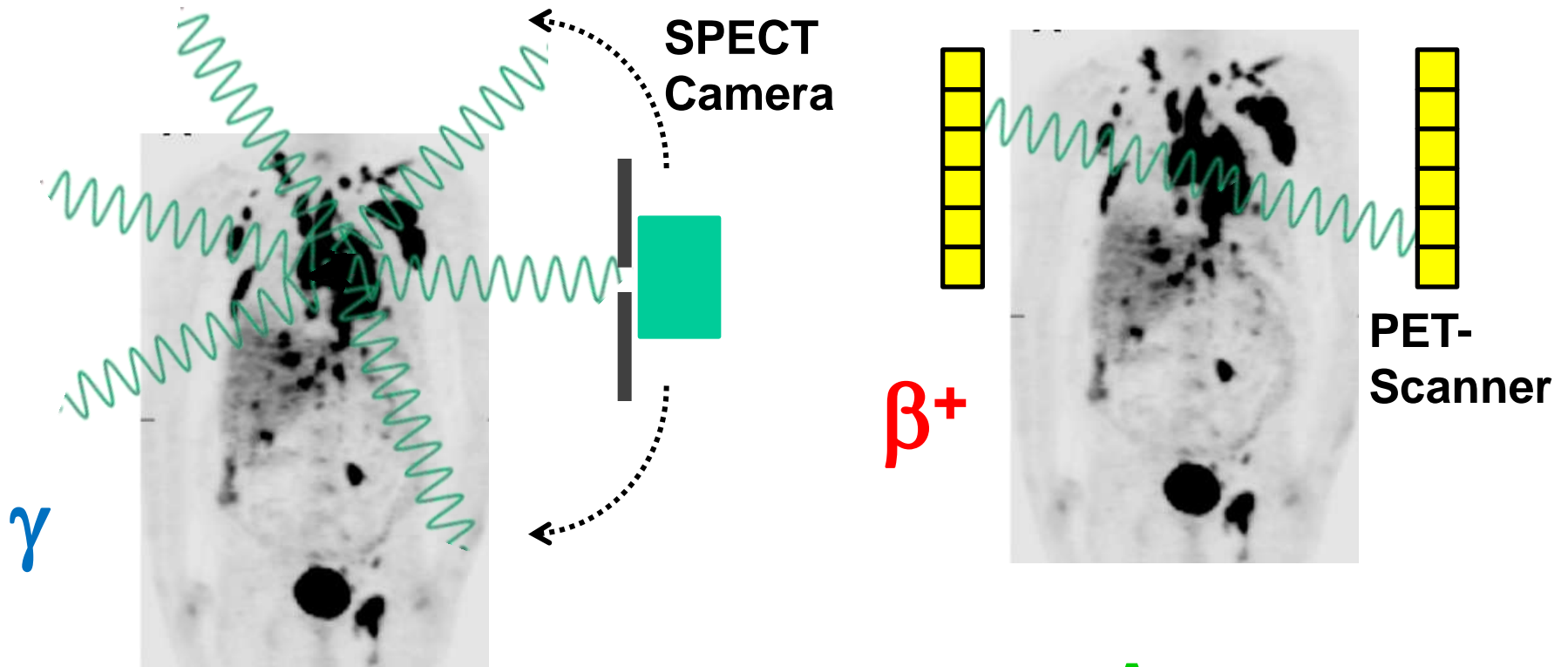
# Radioisotopes: the “fuel” for nuclear medicine

1. What is the optimum fuel for an application ?
2. Are we using the optimum fuel today ?
3. Where does this fuel come from ?

Nuclear medicine needs artificial transmutations.

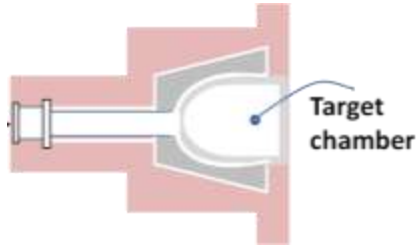
Nuclear astrophysics: “natural” transmutations  
in the universe.

# The Nuclear Medicine Alphabet

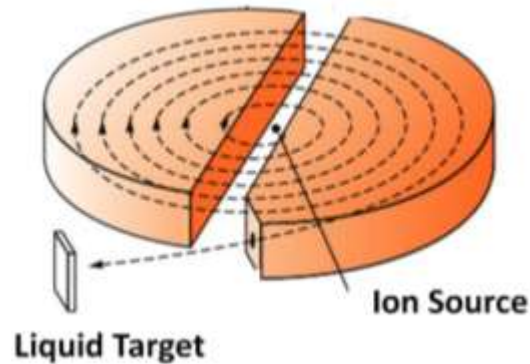




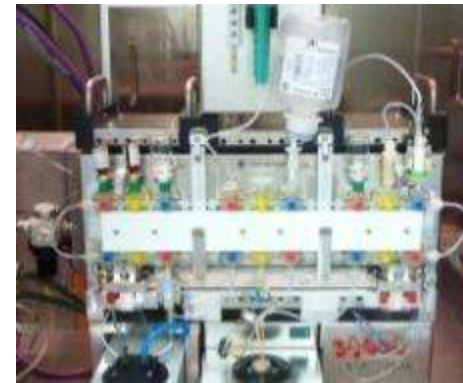
# Cyclotron versus reactor production



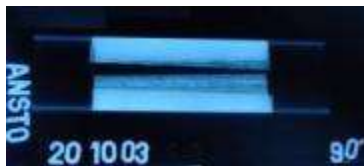
$\text{H}_2^{18}\text{O}$  water  
(liquid target)



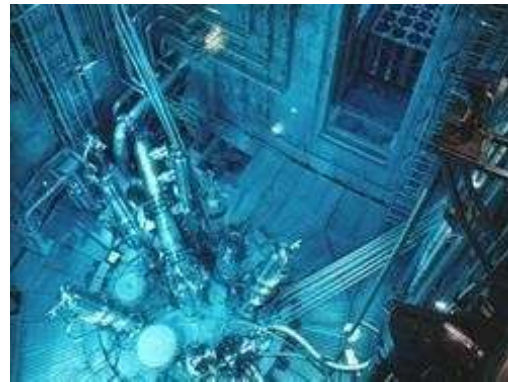
Cyclotron irradiation  
 $^{18}\text{O}(p,n)^{18}\text{F}$   
produces  $^{18}\text{F}$ fluoride



Transformation into FDG  
by automated synthesis  
modules in shielded hot cell



$^{235}\text{U}$   
(foil in Al capsule)



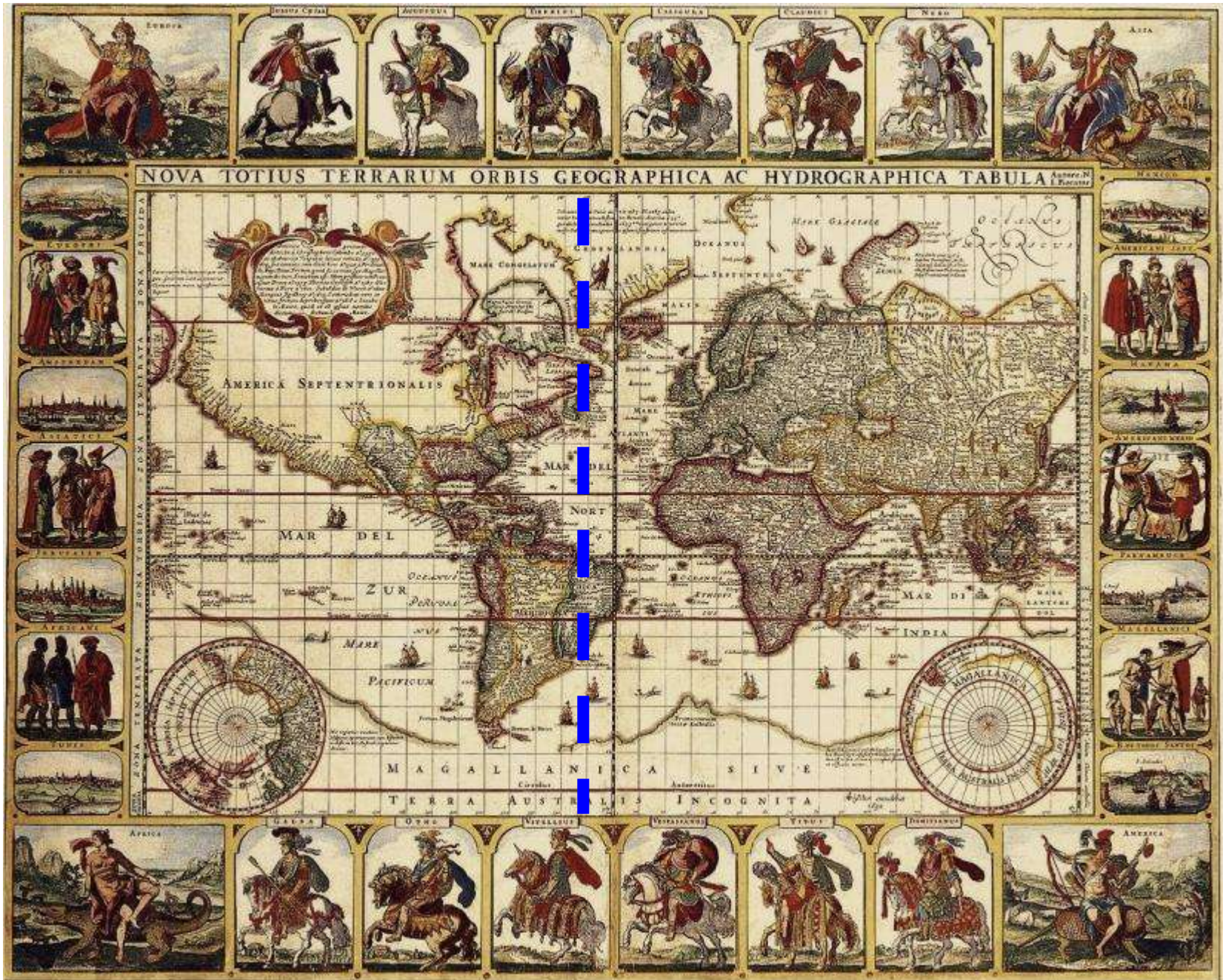
Reactor irradiation  
 $^{235}\text{U}(n,f)$   
produces many fission products



Radiochemical separation  
of Mo  
in shielded hot cells

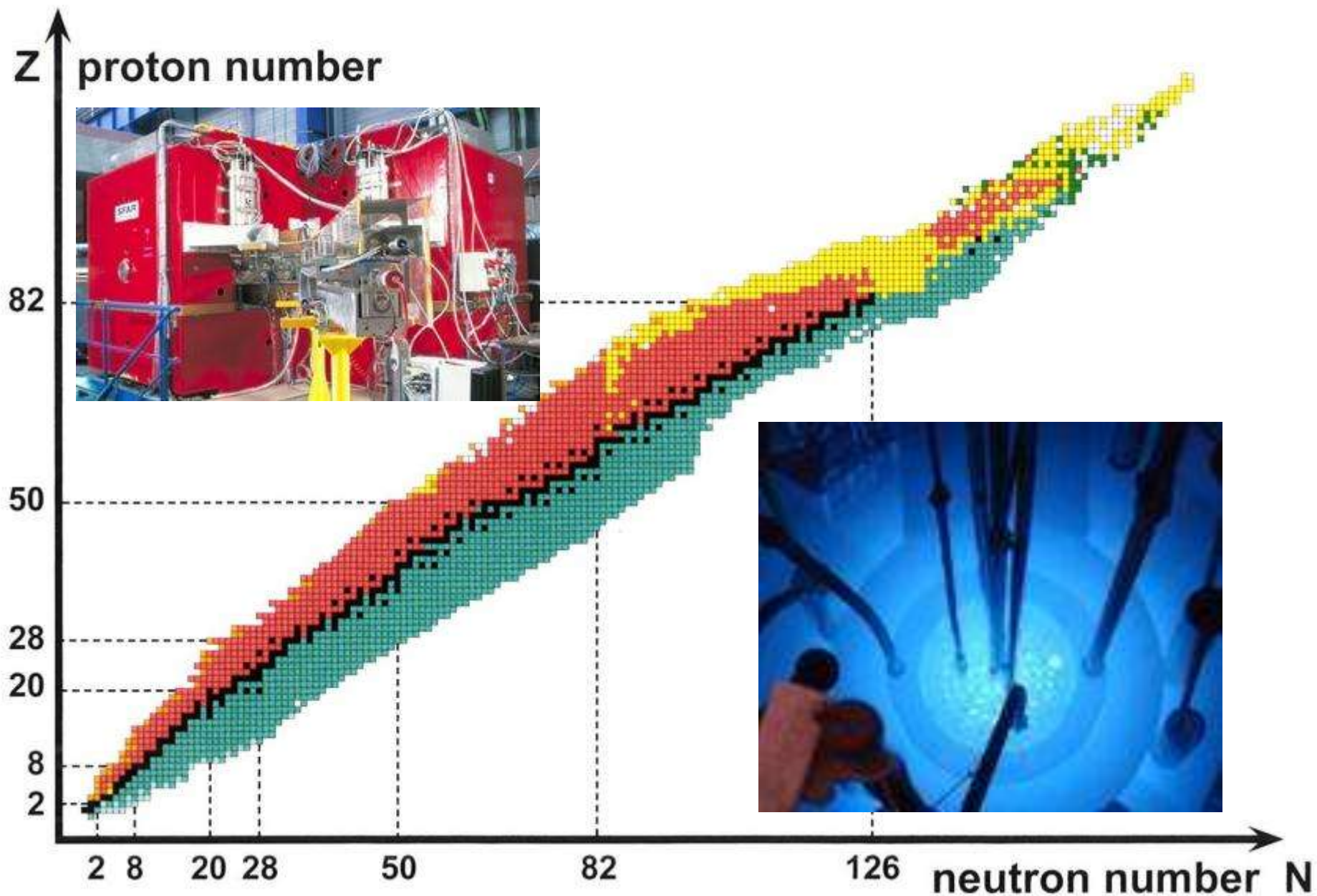


# The Tordesillas meridian





# The Tordesillas meridian of radioisotope production





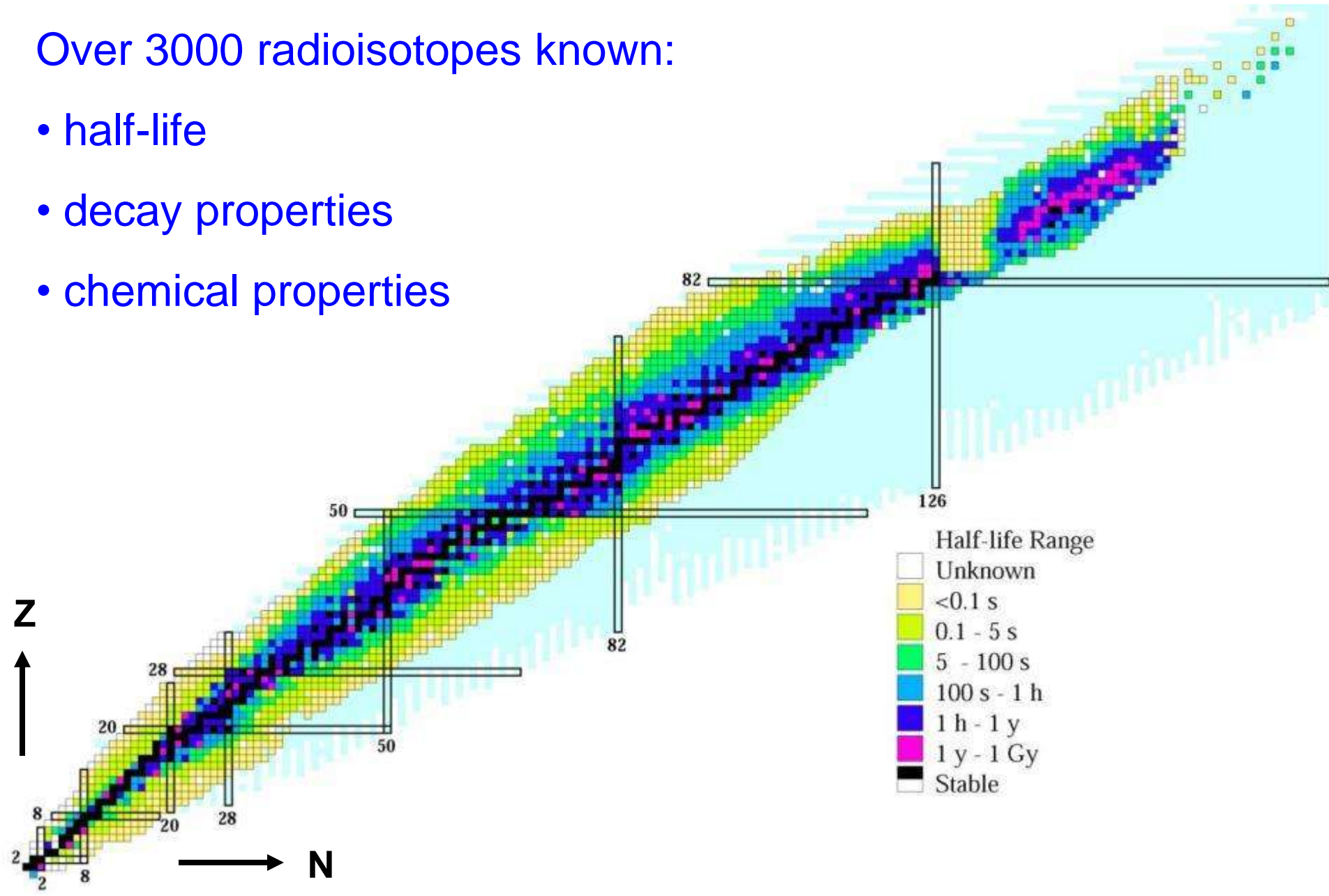
# Reactor vs. cyclotron

<b>Ge 64</b> 64 s $\beta^+$ 3.0, 3.3... $\gamma$ 427, 667 128...	<b>Ge 65</b> 31 s $\beta^+$ 4.6, 5.2... $\gamma$ 650, 62, 809 191... $\beta\beta$ 1.28...	<b>Ge 66</b> 2.3 h $\epsilon$ $\beta^+$ 0.7, 1.1... $\gamma$ 382, 44, 109 273...	<b>Ge 67</b> 18.7 m $\beta^+$ 3.0, 3.2... $\gamma$ 167, 1473...	<b>Ge 68</b> 270.82 d $\epsilon$ no $\beta^+$ no $\gamma$ $\sigma$ 1.0	<b>Ge 69</b> 39.0 h $\epsilon$ $\beta^+$ 1.2... $\gamma$ 1107, 574 872, 1336...	<b>Ge 70</b> 20.57 $\sigma$ 3.0	<b>Ge 71</b> 11.43 d $\epsilon$ no $\gamma$	<b>Ge 72</b> 27.45 $\sigma$ 0.9
<b>Ga 63</b> 31.4 s $\beta^+$ ~4.5... $\gamma$ 637, 627, 193 650...	<b>Ga 64</b> 2.62 m $\beta^+$ 2.9, 6.1... $\gamma$ 992, 808 3366, 1387 2195...	<b>Ga 65</b> 15 m $\beta^+$ 2.1, 2.2... $\gamma$ 115, 61, 153 752...	<b>Ga 66</b> 9.304 h $\beta^+$ 4.2... $\gamma$ 1039, 2752 834, 2190 4296...	<b>Ga 67</b> 78.278 h $\epsilon$ no $\beta^+$ $\gamma$ 93, 185, 300...	<b>Ga 68</b> 67.63 m $\beta^+$ 1.9... $\gamma$ 1077, (1833...)	<b>Ga 69</b> 60.108 $\sigma$ 1.68	<b>Ga 70</b> 21.15 m $\beta^-$ 1.7... $\epsilon$ $\gamma$ (1040, 176)	<b>Ga 71</b> 39.892 $\sigma$ 4.7
<b>Zn 62</b> 9.13 h $\epsilon$ $\beta^+$ 0.7 $\gamma$ 41, 597, 548 508...	<b>Zn 63</b> 38.1 m $\beta^+$ 2.3... $\gamma$ 670, 962 1412...	<b>Zn 64</b> 49.17 $\sigma$ 0.74 $\sigma_{n,\alpha}$ 1.1E-5 $\sigma_{n,p} < 1.2E-5$	<b>Zn 65</b> 244.3 d $\epsilon$ , $\beta^+$ 0.3 $\gamma$ 1115... $\sigma$ 66, $\sigma_{n,p} < 2.0$	<b>Zn 66</b> 27.73 $\sigma$ 0.9 $\sigma_{n,\alpha} < 2E-5$	<b>Zn 67</b> 4.04 $\sigma$ 6.9 $\sigma_{n,\alpha}$ 0.0004	<b>Zn 68</b> 18.45 $\sigma$ 0.072 + 0.8 $\sigma_{n,\alpha} < 2E-5$	<b>Zn 69</b> 13.8 h 56 m $\beta^-$ 439 $\gamma$ (574) $\beta^-$ 0.9... $\gamma$ (319...)	<b>Zn 70</b> 0.61 $\sigma$ 0.0081+0.083
<b>Cu 61</b> 3.4 h $\beta^+$ 1.2... $\gamma$ 283, 656, 67 1186...	<b>Cu 62</b> 9.74 m $\beta^+$ 2.9... $\gamma$ (1173...)	<b>Cu 63</b> 69.15 $\sigma$ 4.5	<b>Cu 64</b> 12.7004 h $\epsilon$ $\beta^-$ 0.6, $\beta^+$ 0.7 $\gamma$ (1346) $\sigma$ ~270	<b>Cu 65</b> 30.85 $\sigma$ 2.17	<b>Cu 66</b> 5.1 m $\beta^-$ 2.6... $\gamma$ 1039, (834...) $\sigma$ 140	<b>Cu 67</b> 61.9 h $\beta^-$ 0.4, 0.6... $\gamma$ 185, 93, 91...	<b>Cu 68</b> 3.8 m 30 s $\beta^-$ 526, 85 11... $\gamma$ 1077, 1077... $\beta^-$ 3.5 4.6... $\gamma$ 1077 1261...	<b>Cu 69</b> 3.0 m $\beta^-$ 2.5... $\gamma$ 1007, 834 531... g
<b>Ni 60</b> 26.223 $\sigma$ 2.9	<b>Ni 61</b> 1.1399 $\sigma$ 2.5 $\sigma_{n,\alpha}$ 3E-5	<b>Ni 62</b> 3.6346 $\sigma$ 15	<b>Ni 63</b> 100 a $\beta^-$ 0.07 no $\gamma$ $\sigma$ 20	<b>Ni 64</b> 0.9255 $\sigma$ 1.6	<b>Ni 65</b> 2.52 h $\beta^-$ 2.1... $\gamma$ 1482, 1115 366... $\sigma$ 22	<b>Ni 66</b> 54.6 h $\beta^-$ 0.2 no $\gamma$	<b>Ni 67</b> 21 s $\beta^-$ 3.8... $\gamma$ (1937, 1115 822...)	<b>Ni 68</b> 29 s $\beta^-$ $\gamma$ 758, 84 g
<b>Co 59</b> 100 $\sigma$ 20.7 + 16.5	<b>Co 60</b> 10.5 m 5.2711 a $\beta^-$ 0.3 1.5... $\gamma$ 1332 1173... $\sigma$ 58 $\sigma$ 2.0	<b>Co 61</b> 1.65 h $\beta^-$ 1.2... $\gamma$ 67, 909...	<b>Co 62</b> 14.0 m 1.5 m $\beta^-$ 2.9... 1163 1163 2302 2003... $\beta^-$ 4.1... 1173 1129...	<b>Co 63</b> 27.5 s $\beta^-$ 3.6... $\gamma$ 87, 982...	<b>Co 64</b> 0.3 s $\beta^-$ 7.0... $\gamma$ 1346, 931	<b>Co 65</b> 1.14 s $\beta^-$ 6.0... $\gamma$ 1141, 310 963...	<b>Co 66</b> 0.18 s $\beta^-$ 7.2, 8.5... $\gamma$ 1426, 1246 1805	<b>Co 67</b> 329 ms $\beta^-$ 8.0... $\gamma$ 694...

# The quest for the optimum isotope

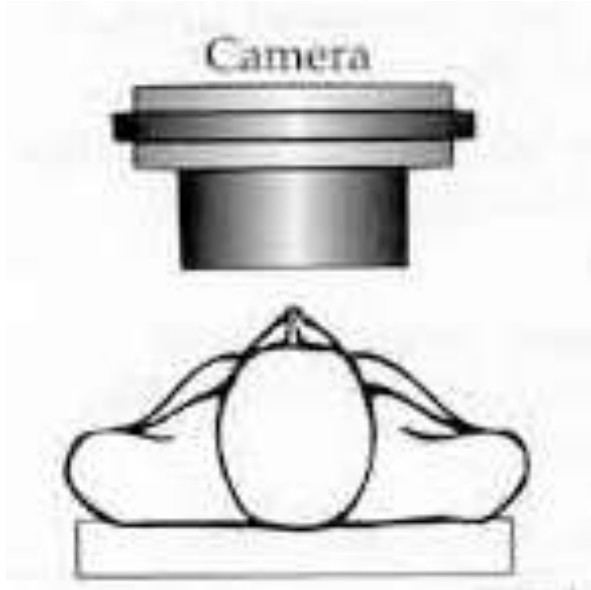
Over 3000 radioisotopes known:

- half-life
- decay properties
- chemical properties

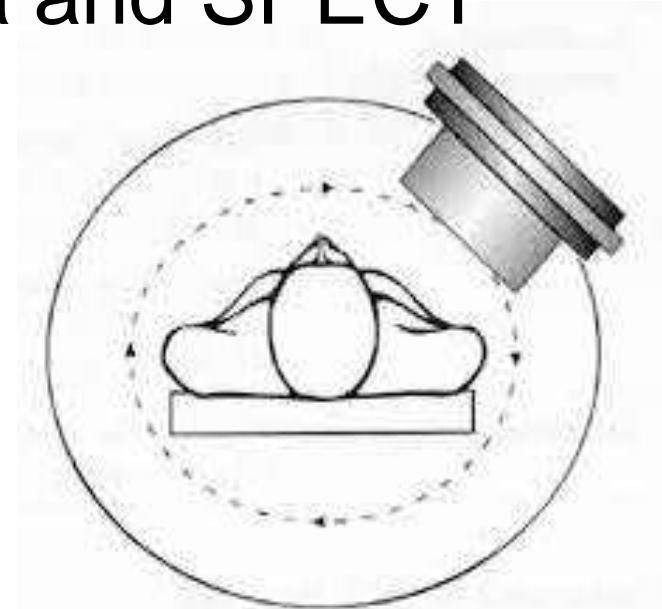




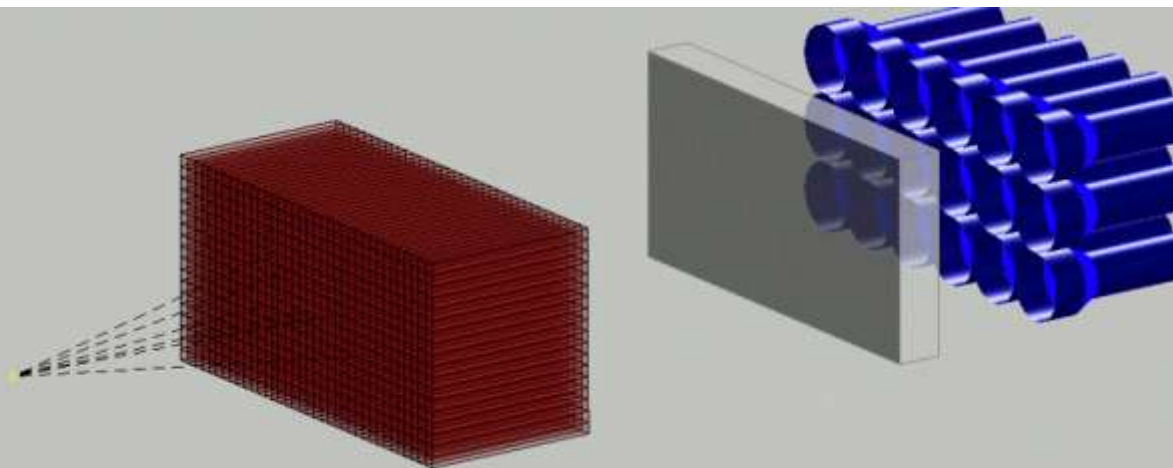
# Gamma camera and SPECT



**2D: planar scan**



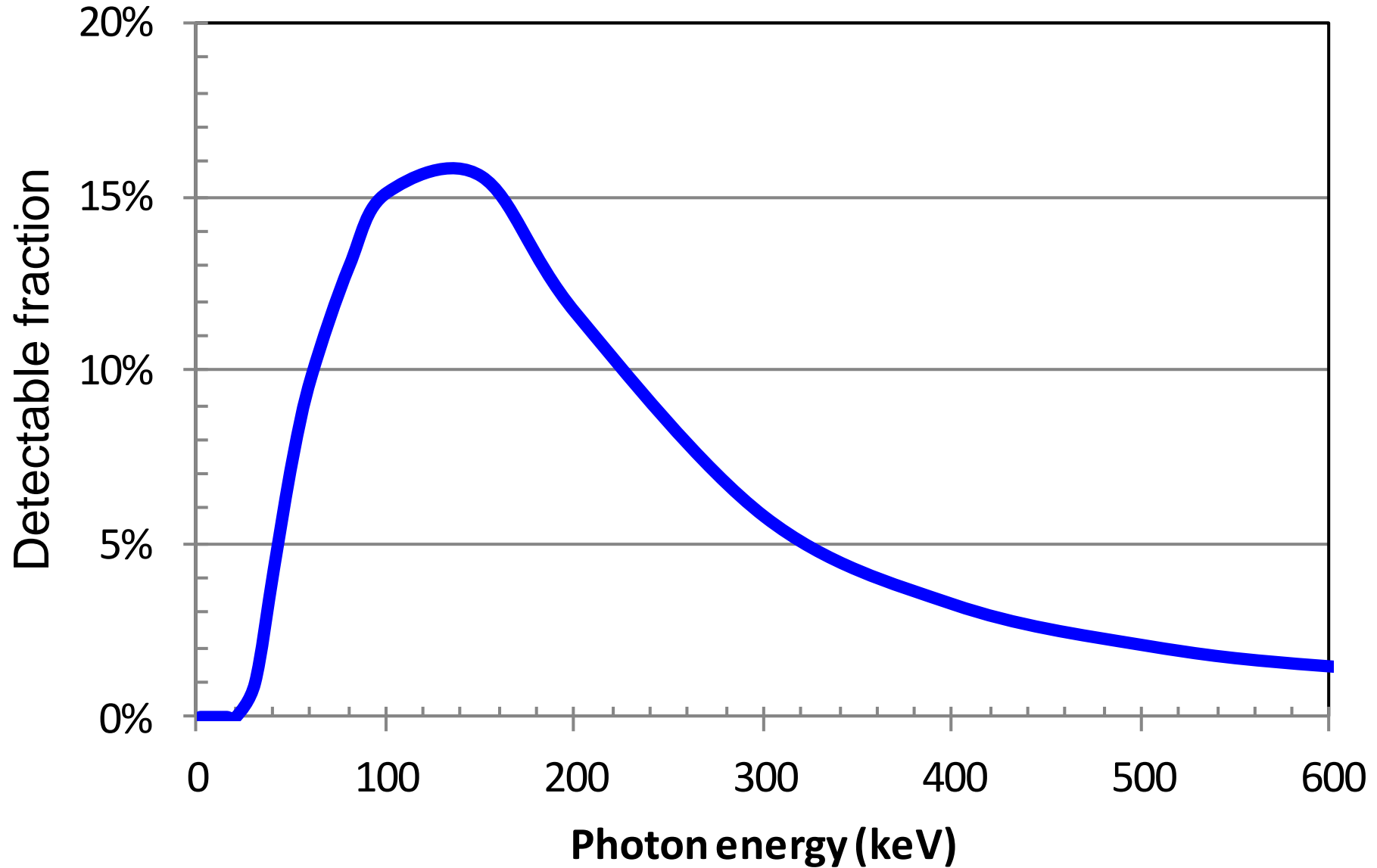
**3D: SPECT: Single Photon Emission  
Computer Tomography**



$$E_{\gamma} > 60 \text{ keV}$$

$$E_{\gamma} < 300 \text{ keV}$$

# Ideal gamma ray energy for SPECT



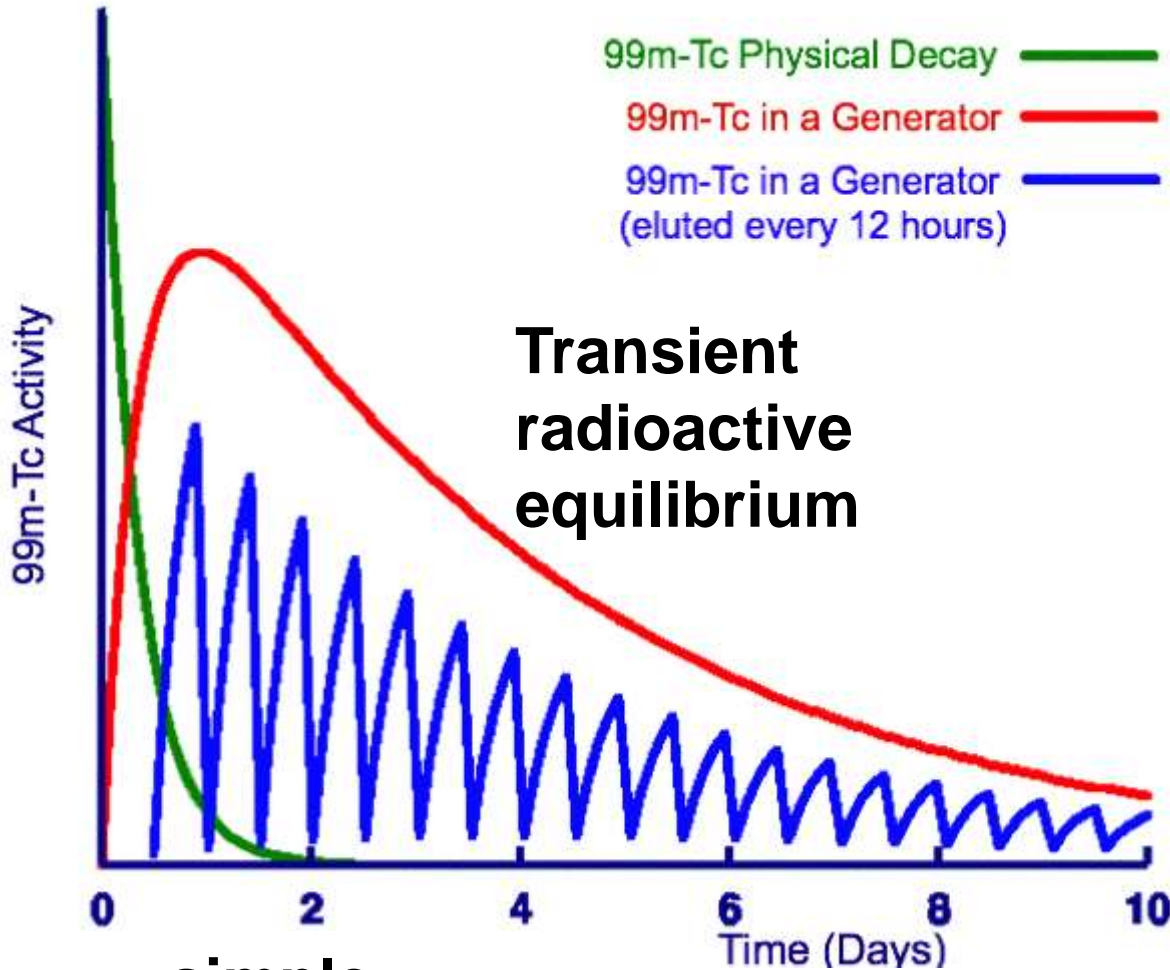


# $^{99m}\text{Tc}$ : ideal for SPECT and gamma cameras

Ru 98 1.87 $\sigma < 8$	Ru 99 12.76 $\sigma 4$	Ru 100 12.60 $\sigma 5.8$	Ru 101 17.06 $\sigma 5$	Ru 102 31.55 $\sigma 1.2$
Tc 97 92.2 d $4.0 \cdot 10^5 \text{ a}$ $I_{\gamma}(97)$ $e^{-}$ no $\gamma$	Tc 98 $4.2 \cdot 10^6 \text{ a}$ $\beta^{-} 0.4$ $\gamma 745; 652$ $\sigma 0.9 + ?$	Tc 99 6.0 h $2.1 \cdot 10^5 \text{ a}$ $I_{\gamma} 141 \dots$ $e^{-}$ $\beta^{-} \dots$ $\gamma (322 \dots)$ $\sigma 23$	Tc 100 15.8 s $\beta^{-} 3.4 \dots$ $\epsilon$ $\gamma 540; 591 \dots$	Tc 101 14.2 m $\beta^{-} 1.3 \dots$ $\gamma 307; 545 \dots$
Mo 96 16.68 $\sigma 0.5$	Mo 97 9.56 $\sigma 2.5$ $\sigma_{n, \alpha} 4E-7$	Mo 98 24.19 $\sigma 0.14$	Mo 99 66.0 h $\beta^{-} 1.2 \dots$ $\gamma 740; 182;$ 778... m; g	Mo 100 9.67 $1.15 \cdot 10^{19} \text{ a}$ $2 \beta^{-}$ $\sigma 0.19$

- IT with 89% 140.5 keV gamma ray,  $T_{1/2} = 6 \text{ h}$
- decays to quasi-stable daughter
- $^{99m}\text{Tc}$  fed in 88% of  $\beta^{-}$  decays of  $^{99}\text{Mo}$ ,  $T_{1/2} = 66 \text{ h}$
- produces nearly carrier-free product

# $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator



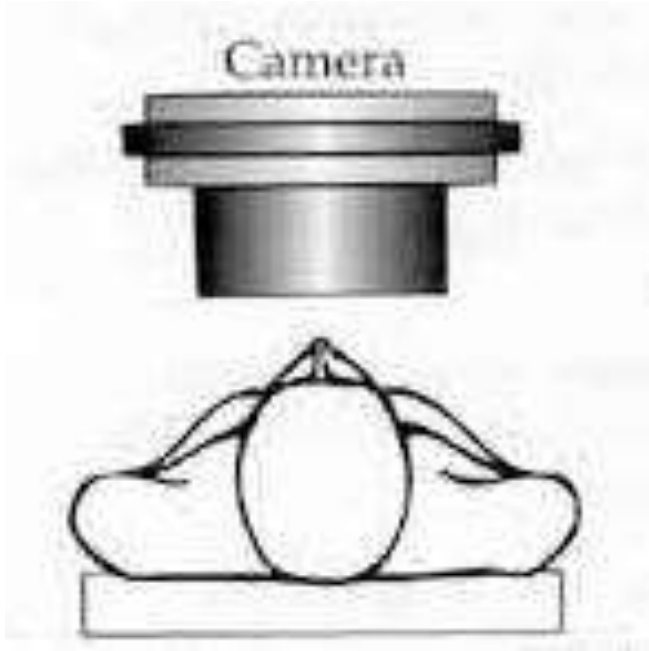
- simple
- reliable
- portable
- self-shielded



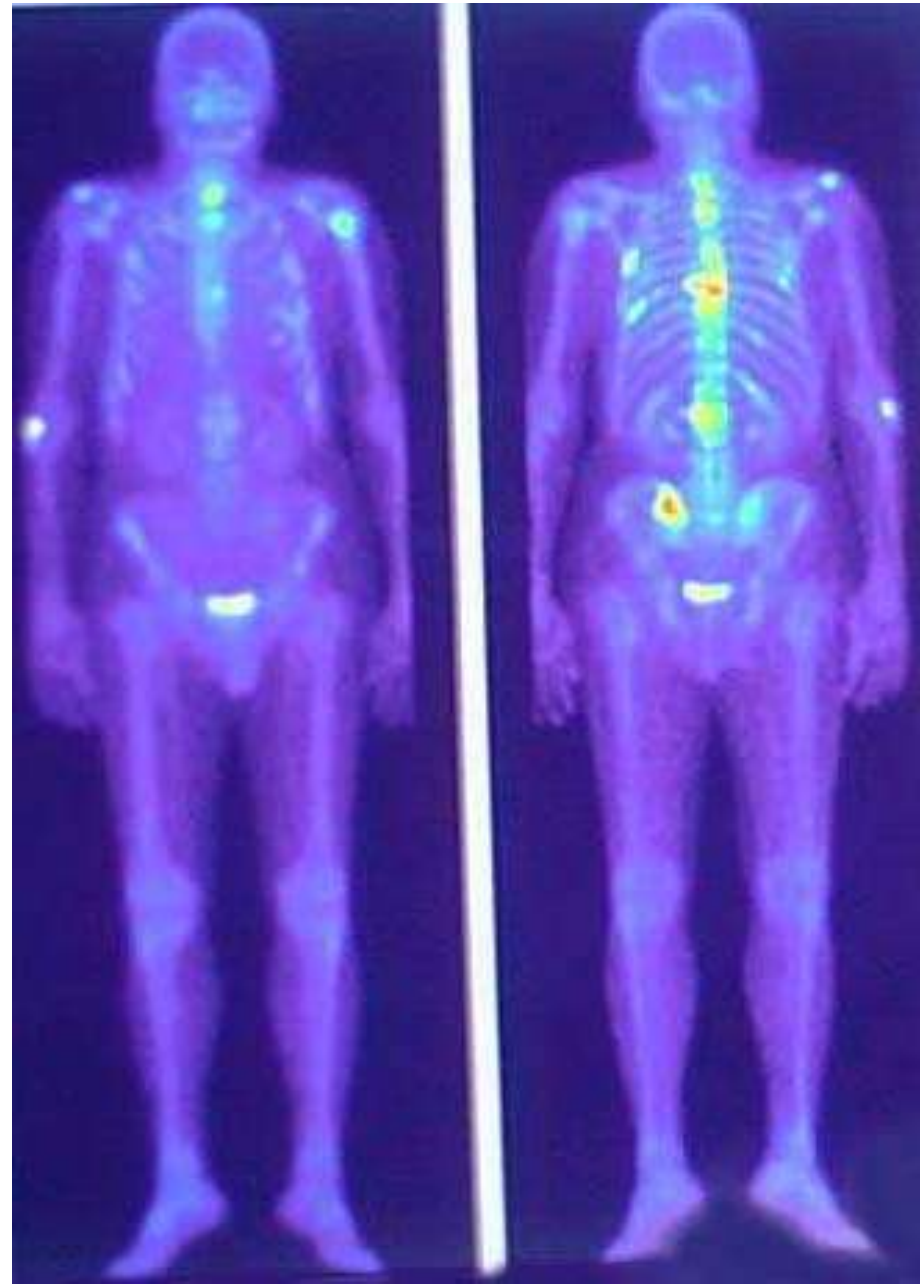




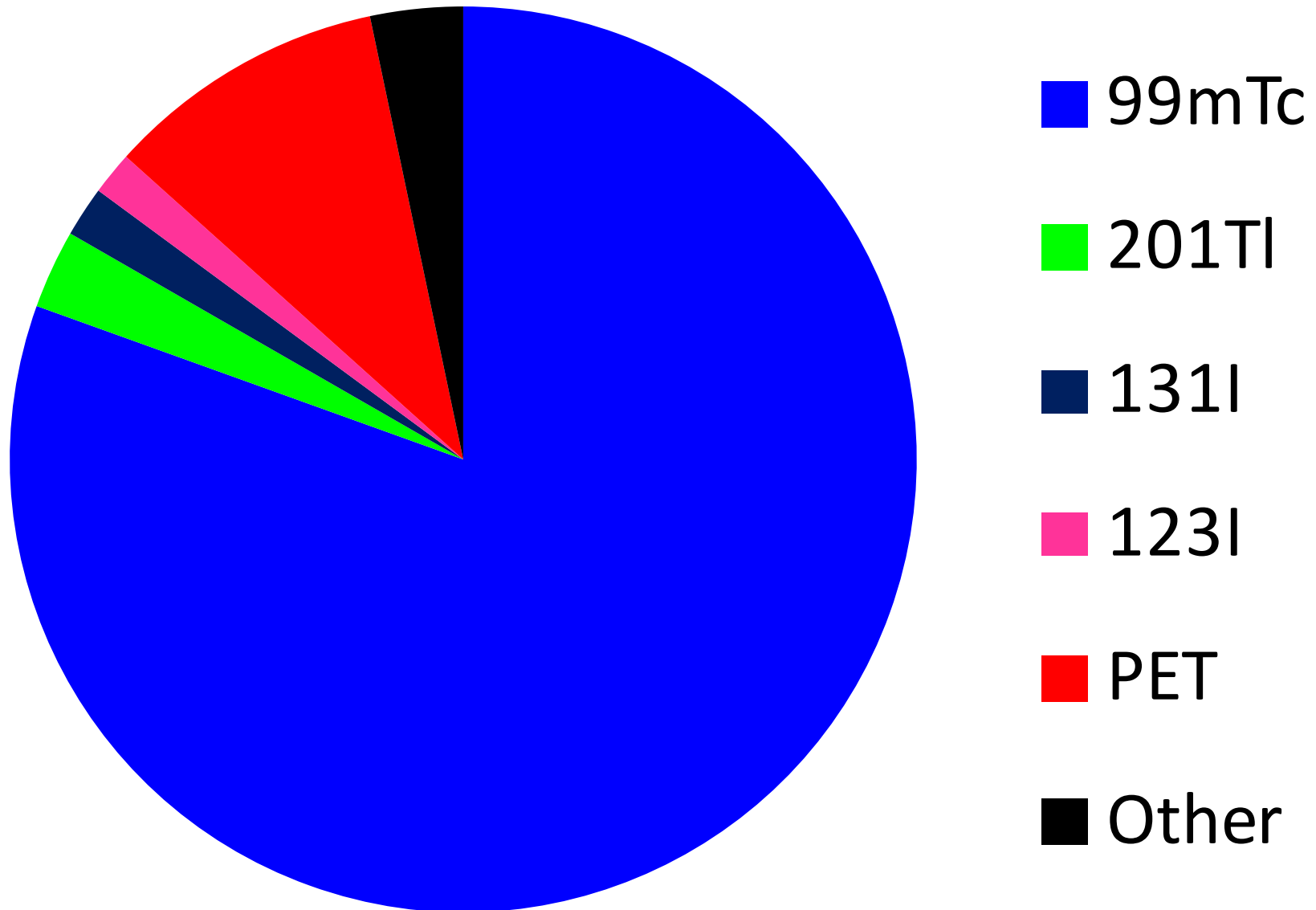
# Bone metastases from (prostate) cancer



- planar or SPECT scan for bone metastases
- differentiate between local and generalized disease
- decide on treatment options: surgery or brachytherapy versus systemic therapy



# The leading radioisotopes for nuclear medicine

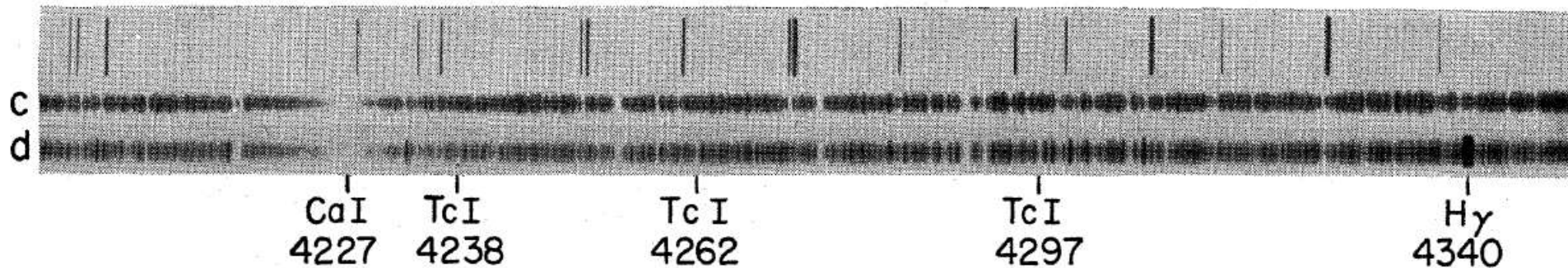


Dose Datamed 2 project; update by NuPECC working group.



# Technetium ( $^{99}\text{Tc}$ ): “proof” of the s-process

stars (Ca55, Fo55). The presence of technetium in the atmospheres of S-type stars, observed by Merrill (Me52), and also to a lesser extent in carbon and M-type stars, affords conclusive evidence that nuclear activity involving neutron capture is currently going on in the interiors of these stars. This element is being both




*P.W. Merrill, Science 1952;115:484.  
B<sup>2</sup>FH 1957.*

## MEMORANDUM

# Recognizing the prospects of "new" radioisotopes ?

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."

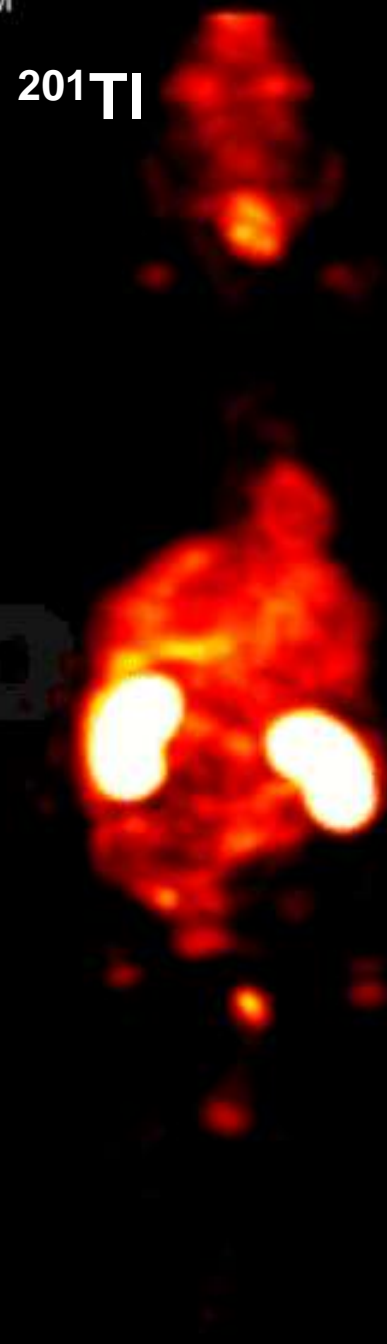
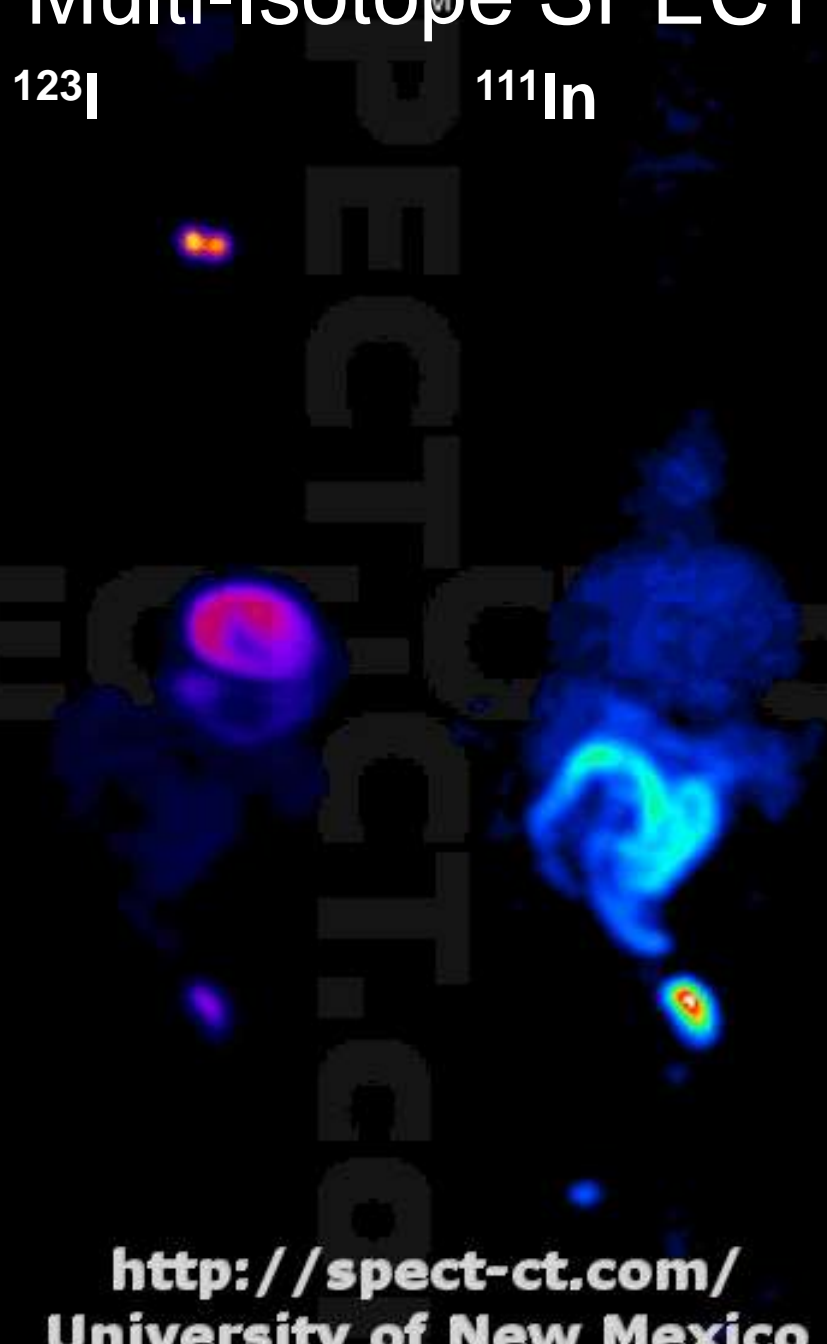
# M Multi-Isotope SPECT M

M  
 $^{99m}\text{Tc}$

M  
 $^{123}\text{I}$

M  
 $^{111}\text{In}$

M  
 $^{201}\text{Tl}$

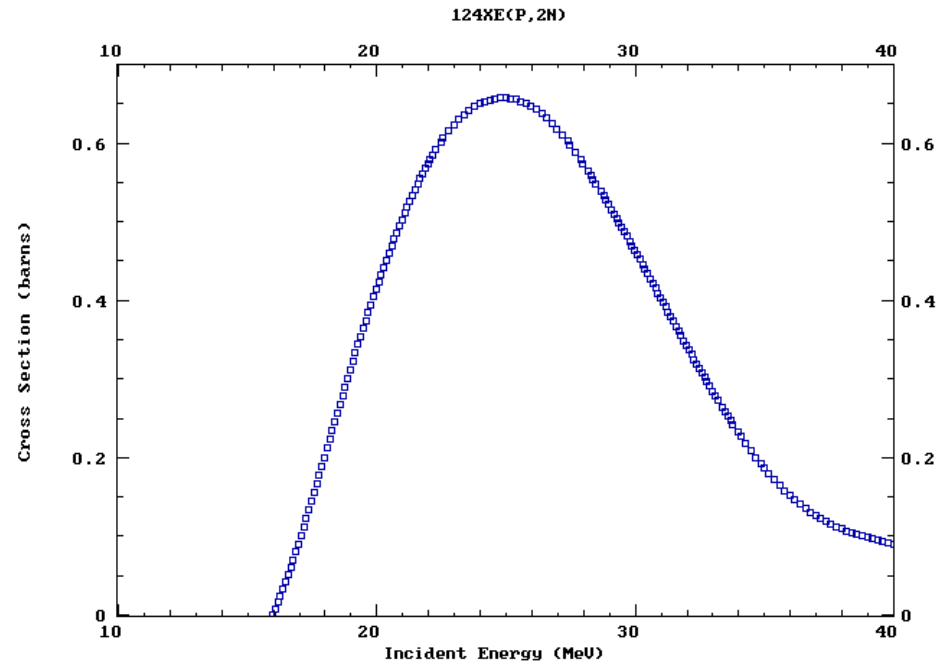


<http://spect-ct.com/>  
University of New Mexico



# Production of $^{123}\text{I}$ by $^{124}\text{Xe}(p,2n)^{123}\text{Cs}(\beta^+)^{123}\text{Xe}(\beta^+)^{123}\text{I}$

<b>Cs 123</b> 1.6 s $\beta^+ 3.1$ $\gamma 97$ $\gamma 95, 64$	<b>Cs 124</b> 6.3 s $\beta^+ 4.9$ $\gamma 212, 90$ $\gamma 354, 915$ $\gamma 493$	<b>Cs 125</b> 46.7 m $\beta^+ 3.1$ $\gamma 526, 412$ g	<b>Cs 126</b> 1.6 m $\beta^+ 3.8$ $\gamma 389, 491$ $\gamma 925$	<b>Cs 127</b> 6.25 h $\epsilon, \beta^+ 0.7, 1.1$ $\gamma 411, 125$ $\gamma 462$ g
<b>Xe 122</b> 20.1 h $\epsilon$ $\gamma 350, 149$ $\gamma 417$	<b>Xe 123</b> 2.08 h $\epsilon$ $\beta^+ 1.5$ $\gamma 149, 178$ $\gamma 330$	<b>Xe 124</b> 0.0952 $\epsilon$ $\gamma 28 + 137$	<b>Xe 125</b> 57 s 16.9 h $\epsilon$ $\beta^+ 188, 243$ $\gamma 55$ $\sigma_{tot} -0.05$	<b>Xe 126</b> 0.0890 $\sigma 0.45 + 3.0$
<b>I 121</b> 2.12 h $\epsilon$ $\beta^+ 1.1$ $\gamma 212$ g	<b>I 122</b> 3.6 m $\beta^+ 3.1$ $\gamma 564$	<b>I 123</b> 13.224 h $\epsilon$ no $\beta^+$ $\gamma 159$ g	<b>I 124</b> 4.15 d $\epsilon$ $\beta^+ 2.1$ $\gamma 603, 1691$ $\gamma 723$	<b>I 125</b> 59.407 d $\epsilon$ $\gamma 35, e^-$ g $\sigma 894$
<b>Te 120</b> 0.09 $\sigma 1 + 5$	<b>Te 121</b> 164.2 d 19.16 d $\beta^+$ $\gamma 212$ $\gamma 573$ $\gamma 908$ $\gamma 1102$	<b>Te 122</b> 2.55 $\sigma 0.4 + 3$	<b>Te 123</b> 0.89 119.7 d $\beta^+$ $\gamma 159$ $e^-$	<b>Te 124</b> 4.74 1.24 $\cdot 10^{13}$ a $\epsilon$ no $\gamma$ $\sigma 370$ $\sigma_{tot} 5E-5$

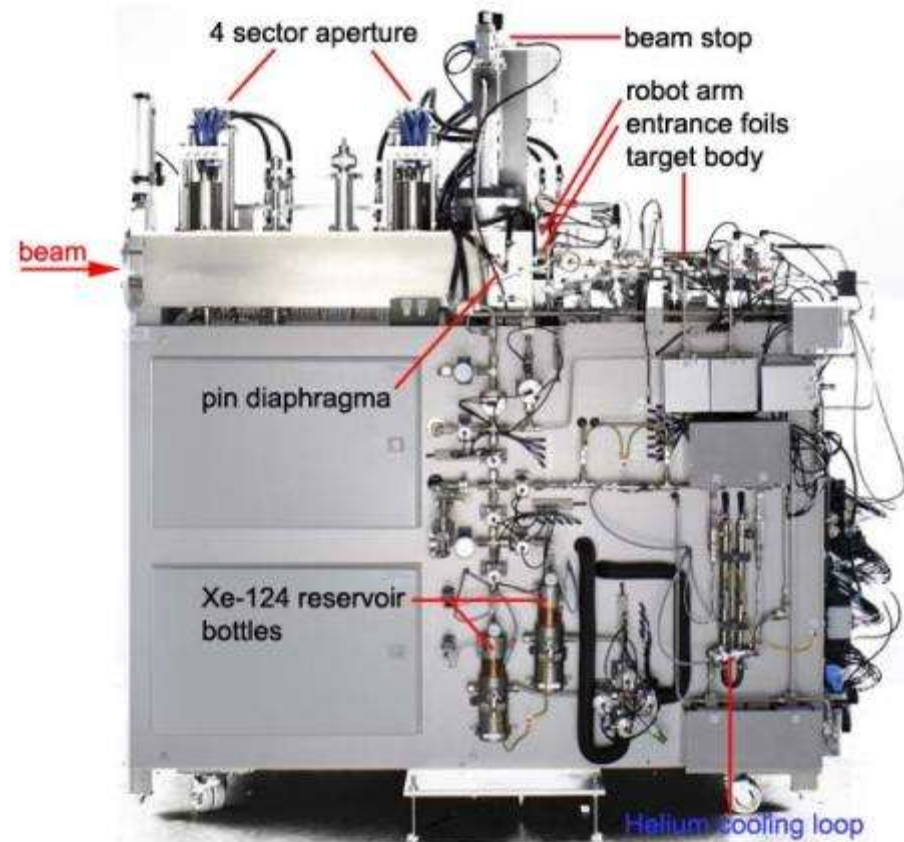


# Question

Why is  $^{124}\text{Xe}$  so rare ?

$$^{124}\text{Xe}/\text{Xe} = 9.5\text{E-}4$$

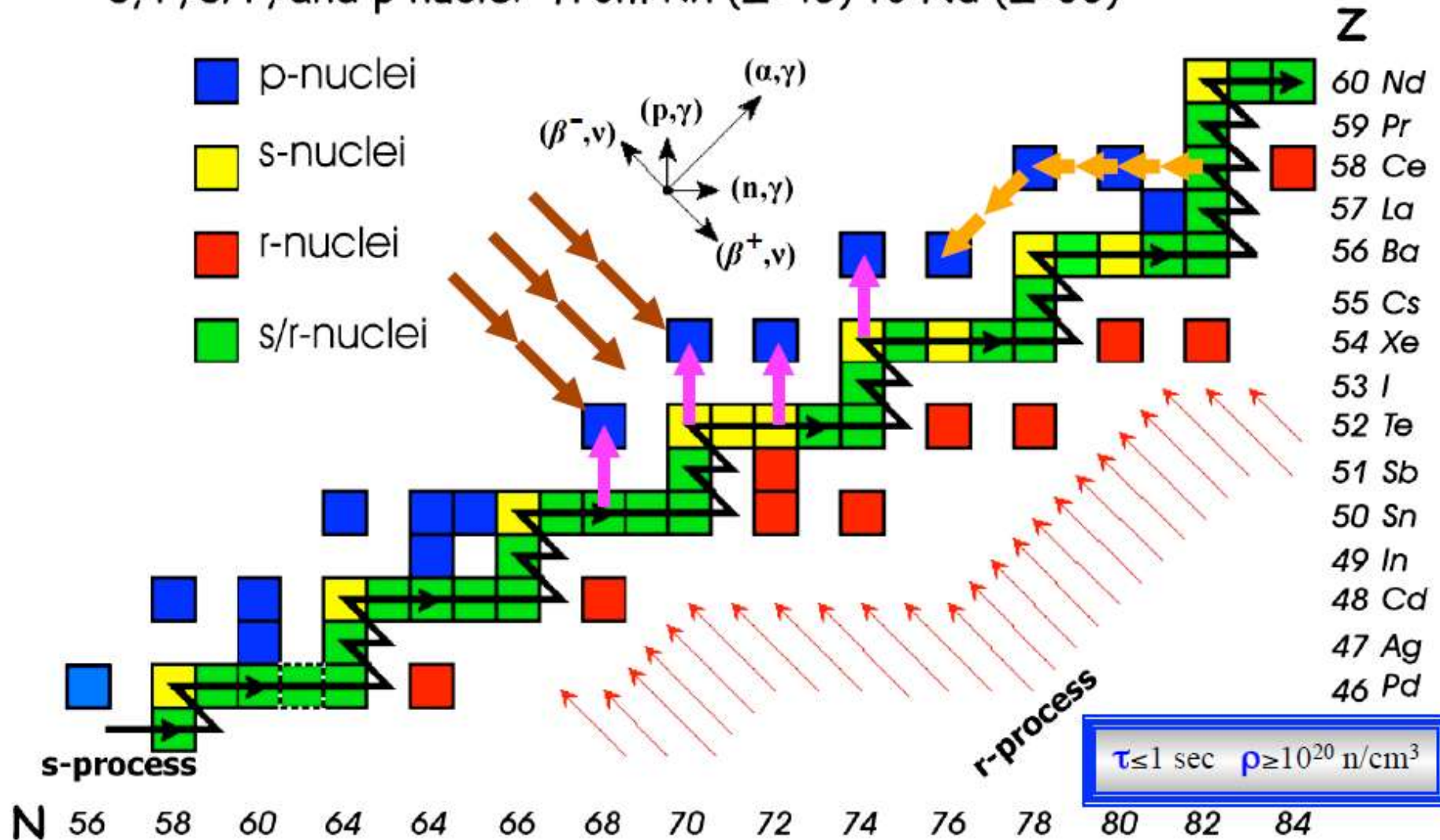
<b>Cs 123</b> 1.6 s 5.9 m $\beta^+$ 3.1... $\gamma$ 97... $\gamma$ 597... ly 95, 64...	<b>Cs 124</b> 6.3 s 30.8 s $\beta^+$ 4.9... $\gamma$ 212, 90 $\gamma$ 354, 915 $\gamma$ 493...	<b>Cs 125</b> 46.7 m $\epsilon$ , $\beta^+$ 2.1... $\gamma$ 526, 112 $\gamma$ 412... g	<b>Cs 126</b> 1.6 m $\beta^+$ 3.8... $\gamma$ 389, 491 $\gamma$ 925...	<b>Cs 127</b> 6.25 h $\epsilon$ , $\beta^+$ 0.7, 1.1... $\gamma$ 411, 125 $\gamma$ 462... g
<b>Xe 122</b> 20.1 h $\epsilon$ $\gamma$ 350, 149 $\gamma$ 417...	<b>Xe 123</b> 2.08 h $\epsilon$ $\beta^+$ 1.5... $\gamma$ 149, 178 $\gamma$ 330...	<b>Xe 124</b> 0.0952 $\sigma$ 28 + 137	<b>Xe 125</b> 57 s 16.9 h $\epsilon$ , $\beta^+$ $\gamma$ 188, 243 $\gamma$ 55... $\sigma_{\text{tot}}$ -0.05	<b>Xe 126</b> 0.0890 $\sigma$ 0.45 + 3.0
<b>I 121</b> 2.12 h $\epsilon$ $\beta^+$ 1.1... $\gamma$ 212... g	<b>I 122</b> 3.6 m $\beta^+$ 3.1... $\gamma$ 564...	<b>I 123</b> 13.224 h $\epsilon$ no $\beta^+$ $\gamma$ 159... g	<b>I 124</b> 4.15 d $\epsilon$ $\beta^+$ 2.1... $\gamma$ 603, 1691 $\gamma$ 723...	<b>I 125</b> 59.407 d $\epsilon$ $\gamma$ 35, $e^-$ g $\sigma$ 894
<b>Te 120</b> 0.09 $\sigma$ 1 + 5	<b>Te 121</b> 164.2 d 19.16 d $\beta^+$ 1.1... $\gamma$ 212... $\gamma$ 1102...	<b>Te 122</b> 2.55 $\sigma$ 0.4 + 3	<b>Te 123</b> 0.89 119.7 d $\beta^+$ 1.24 $\cdot 10^{13}$ a $\epsilon$ $\sigma$ 370 $\sigma_{\text{tot}}$ 5E-5 $e^-$	<b>Te 124</b> 4.74 $\sigma$ 1 + 6





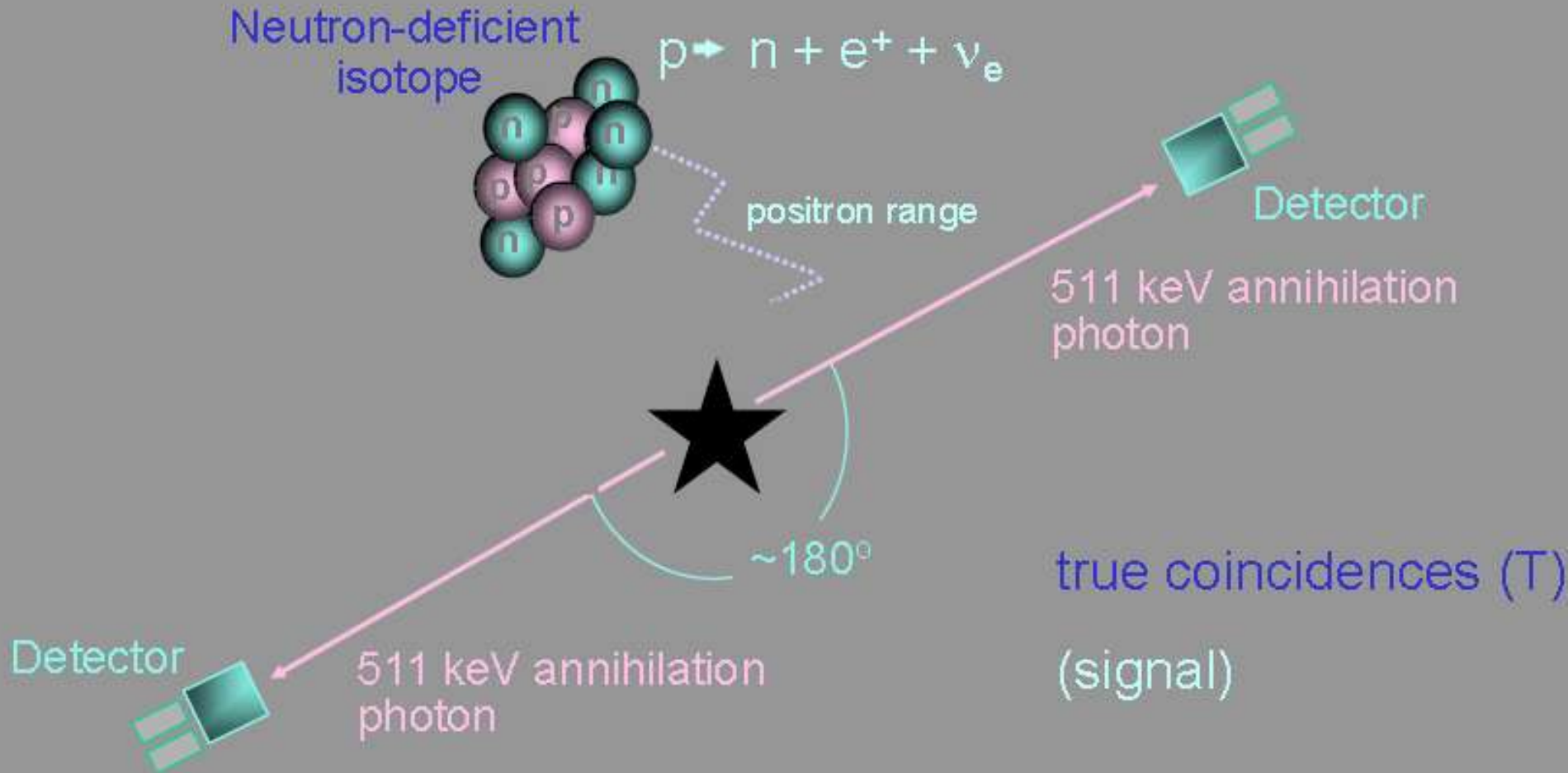
# Answer: $^{124}\text{Xe}$ is a p-nucleus

s, r, s/r, and p nuclei from Rh (Z=45) to Nd (Z=60)



A. Lagoyannis, Russbach 2013.  
Artemis Spyrou: Thursday

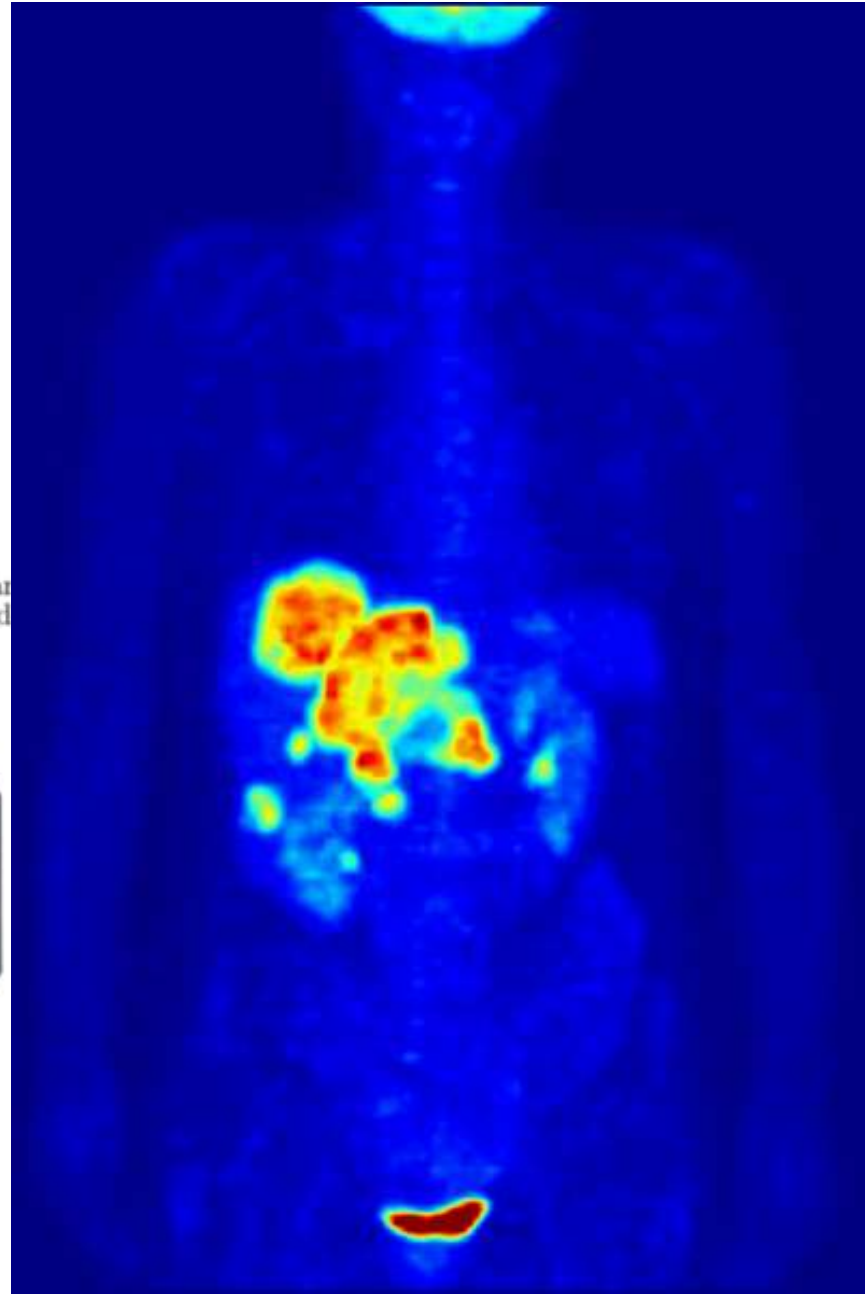
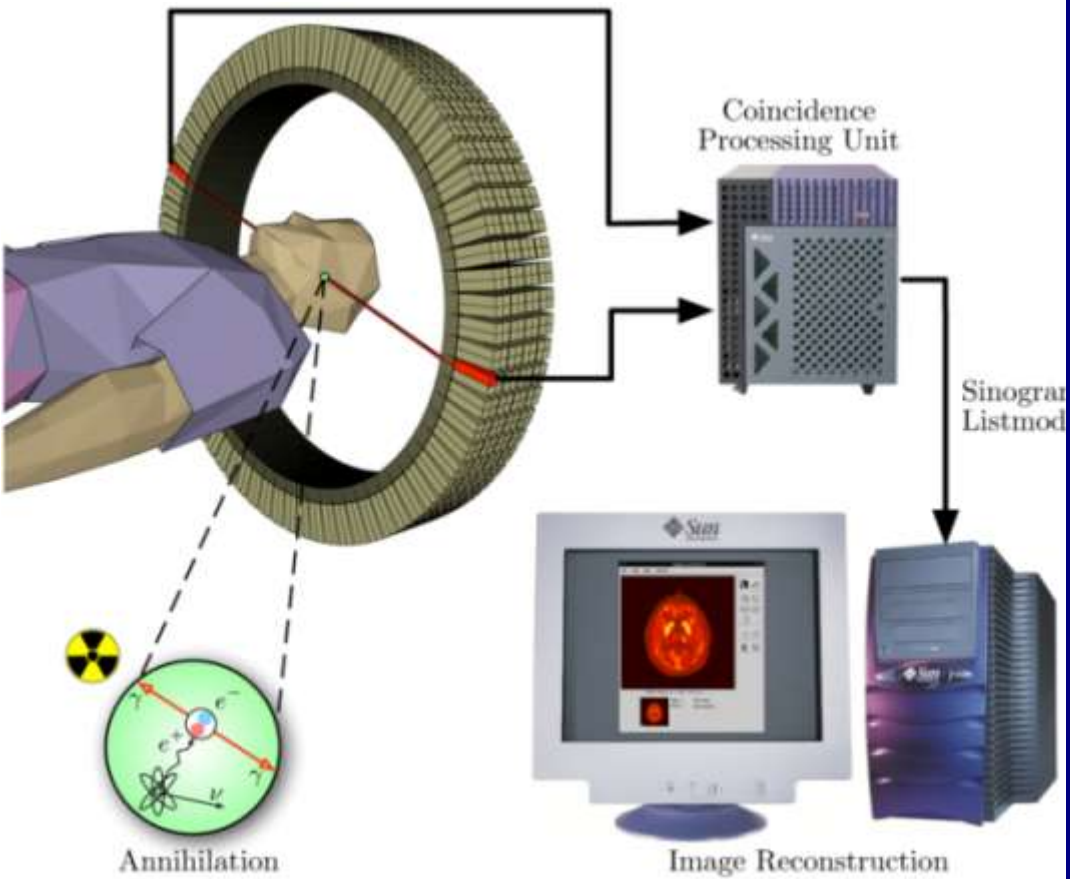
# PET: Positron Emission Tomography



Low  $\beta^+$  energy to minimize range > better spatial resolution.



# Positron Emission Tomography



# PET isotopes

<b>Radio-nuclide</b>	<b>Half-life (h)</b>	<b>Intensity <math>\beta^+</math> (%)</b>	<b>E mean (MeV)</b>	<b>Range (mm)</b>
<b>C-11</b>	<b>0.34</b>	<b>99.8</b>	<b>0.39</b>	<b>1.3</b>
<b>N-13</b>	<b>0.17</b>	<b>99.8</b>	<b>0.49</b>	<b>1.8</b>
<b>O-15</b>	<b>0.03</b>	<b>99.9</b>	<b>0.74</b>	<b>3.2</b>
<b>F-18</b>	<b>1.83</b>	<b>96.7</b>	<b>0.25</b>	<b>0.7</b>
<b>Ga-68</b>	<b>1.13</b>	<b>89.1</b>	<b>0.83</b>	<b>3.8</b>
<b>Rb-82</b>	<b>0.02</b>	<b>95.4</b>	<b>3.38</b>	<b>20</b>



**$^{99m}\text{Tc}$ -MDP planar**



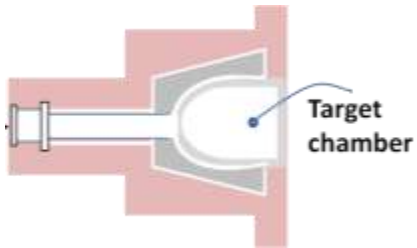
**$^{99m}\text{Tc}$ -MDP SPECT**



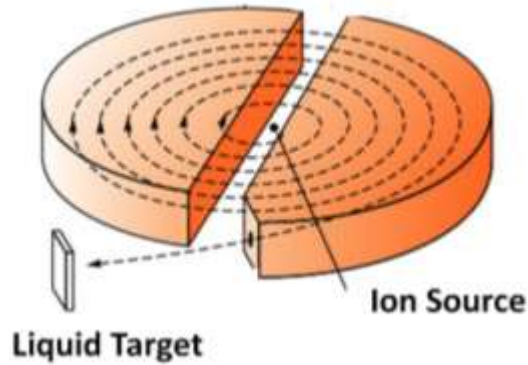
**$^{18}\text{F}$ - PET**



# $^{18}\text{F}$ production by $^{18}\text{O}(p,n)$



$\text{H}_2^{18}\text{O}$  water

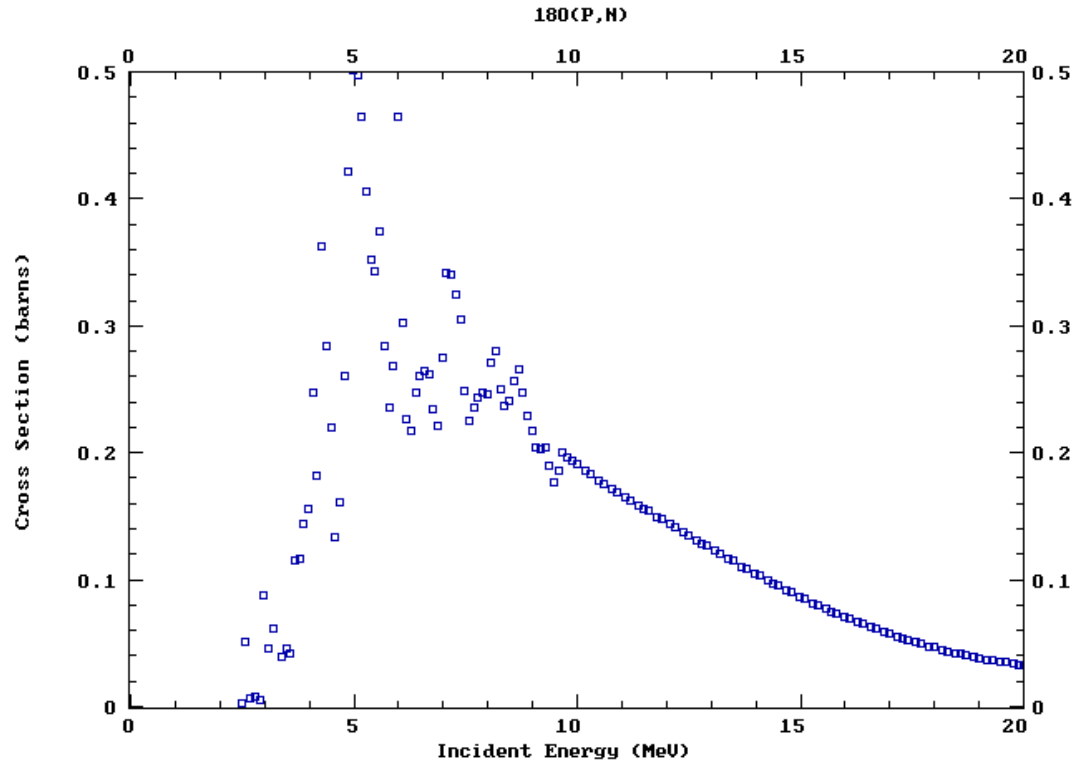


Cyclotron irradiation



Transformation into FDG

<b>Ne 18</b> 1.67 s $\beta^+$ 3.4... $\gamma$ 1042...	<b>Ne 19</b> 17.22 s $\beta^+$ 2.2... $\gamma$ (110, 197, 1357)	<b>Ne 20</b> 90.48 $\sigma$ 0.039
<b>F 17</b> 64.8 s $\beta^+$ 1.7 no $\gamma$	<b>F 18</b> 109.728 m $\beta^+$ 0.633 no $\gamma$	<b>F 19</b> 100 $\sigma$ 0.0095
<b>O 16</b> 99.757 $\sigma$ 0.00019	<b>O 17</b> 0.038 $\sigma$ 0.00054 $\sigma_{n,\alpha}$ 0.257	<b>O 18</b> 0.205 $\sigma$ 0.00016



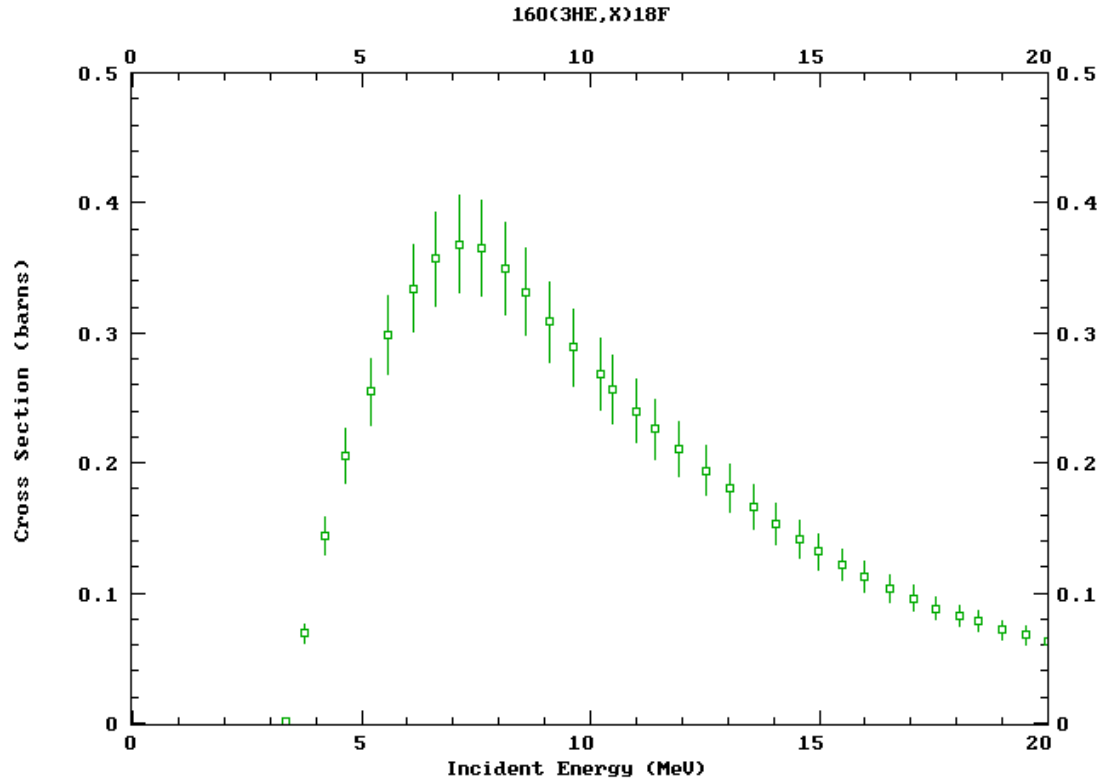
# Question

Why is  $^{18}\text{O}$  so rare?  $^{18}\text{O}/^{16}\text{O} = 2\text{E}-3$

$\text{O } 16$ 99.757 $\sigma$ 0.00019	$\text{O } 17$ 0.038 $\sigma$ 0.00054 $\sigma_{n,\alpha}$ 0.257	$\text{O } 18$ 0.205 $\sigma$ 0.00016
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# $^{18}\text{F}$ production by $^{16}\text{O}(^3\text{He},n)^{18}\text{Ne}(\beta^+)$

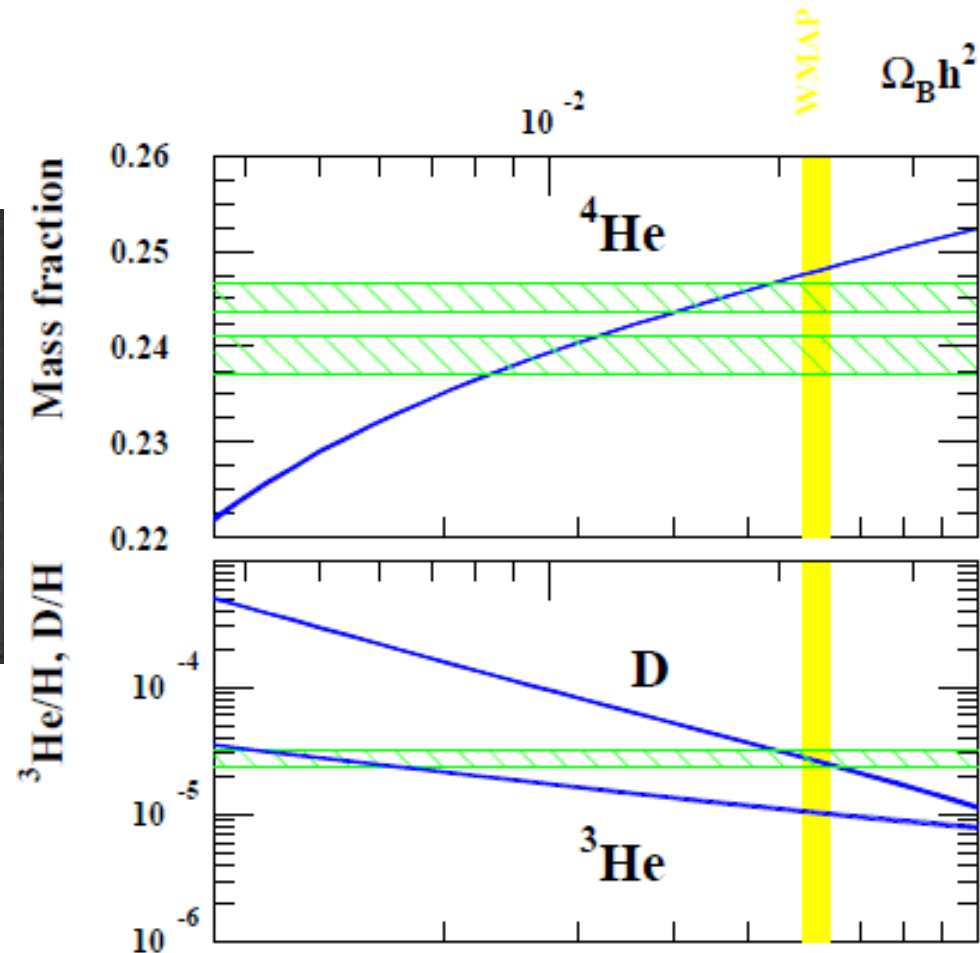
<b>Ne 18</b> 1.67 s $\beta^+$ 3.4... $\gamma$ 1042...	<b>Ne 19</b> 17.22 s $\beta^+$ 2.2... $\gamma$ (110, 197, 1357)	<b>Ne 20</b> 90.48
<b>F 17</b> 64.8 s $\beta^+$ 1.7 no $\gamma$	<b>F 18</b> 109.728 m $\beta^+$ 0.633 no $\gamma$	<b>F 19</b> 100
<b>O 16</b> 99.757 $\sigma$ 0.00019	<b>O 17</b> 0.038 $\sigma$ 0.00054 $\sigma_{n,\alpha}$ 0.257	<b>O 18</b> 0.205 $\sigma$ 0.00016





# Question

Why is  ${}^3\text{He}/{}^4\text{He}$  lower on Earth compared to BBN ?  
1.3E-6 versus 4E-5  $\Rightarrow$  factor 30 depletion !

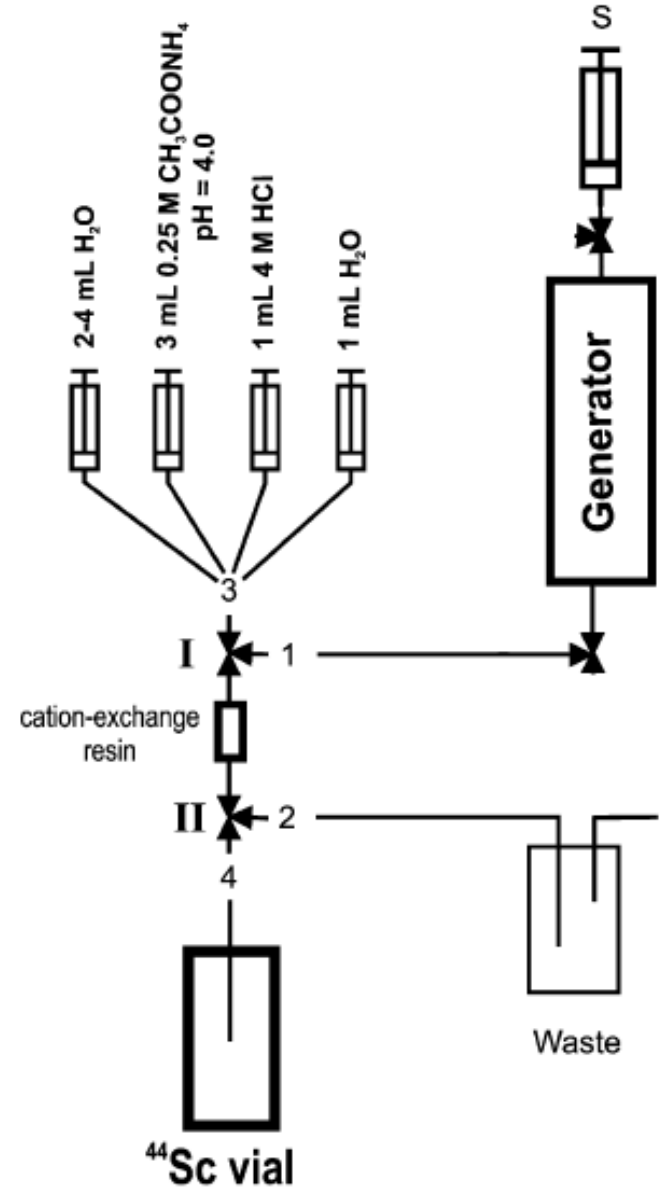


# Longer-lived PET isotopes

<b>Radio-nuclide</b>	<b>Half-life (h)</b>	<b>Intensity <math>\beta^+</math> (%)</b>	<b>E mean (MeV)</b>	<b>Range (mm)</b>
<b>Sc-44</b>	<b>3.97</b>	<b>94.3</b>	<b>0.63</b>	<b>2.5</b>
<b>Cu-64</b>	<b>12.7</b>	<b>17.6</b>	<b>0.28</b>	<b>0.8</b>
<b>Br-76</b>	<b>16.2</b>	<b>55</b>	<b>1.18</b>	<b>6</b>
<b>Y-86</b>	<b>14.7</b>	<b>31.9</b>	<b>0.66</b>	<b>2.6</b>
<b>Zr-89</b>	<b>78.4</b>	<b>22.7</b>	<b>0.40</b>	<b>1.4</b>
<b>I-124</b>	<b>100</b>	<b>22.8</b>	<b>0.82</b>	<b>3.8</b>

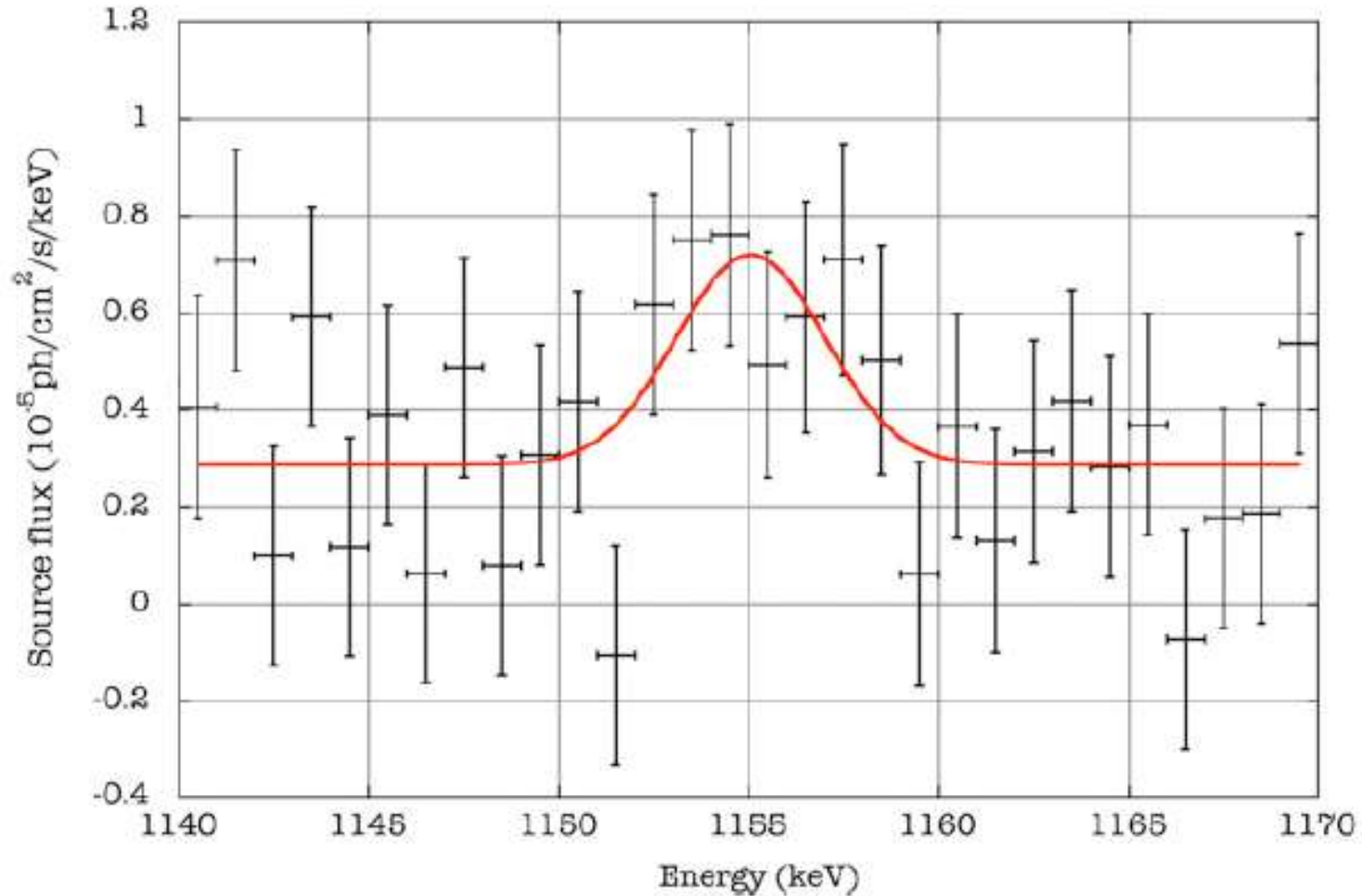
# $^{44}\text{Sc}$ from $^{44}\text{Ti}$ generator

<b>Ti 44</b> 58.9 a $\epsilon$ $\gamma$ 78, 68..., g $\sigma$ 1.1	<b>Ti 45</b> 3.08 h $\beta^+$ 1.0... $\gamma$ (720...)	<b>Ti 46</b> 8.25 $\sigma$ 0.6
<b>Sc 43</b> 3.89 h $\beta^+$ 1.2... $\gamma$ 373...	<b>Sc 44</b> 58.61 d 3.92 h $\gamma$ 271 $\epsilon$ $\gamma$ (1002, 1261, 1157) $\beta^+$ 1.5... $\gamma$ 1157...	<b>Sc 45</b> 100 $\sigma$ 10 + 17

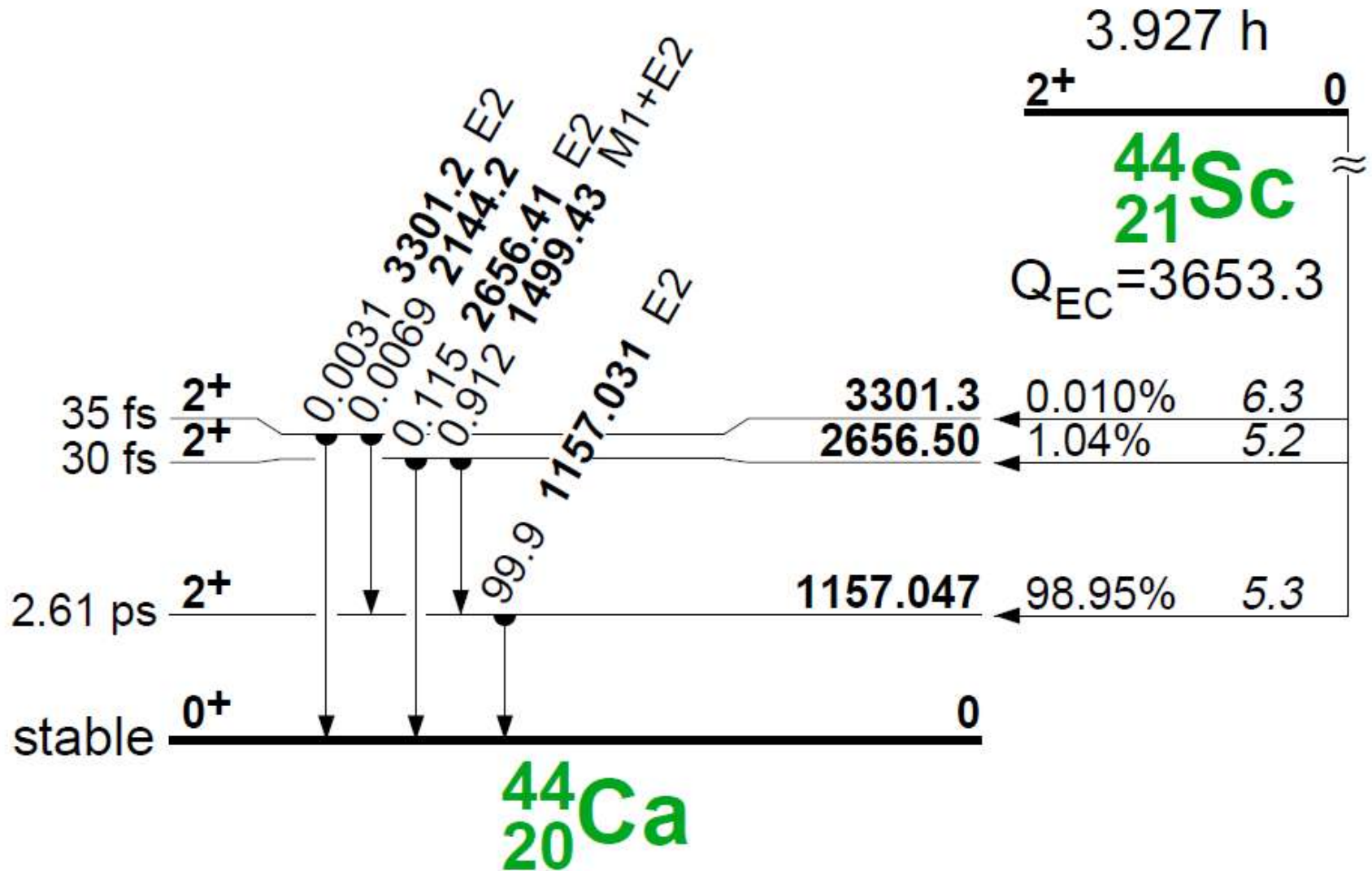




# $^{44}\text{Sc}$ in the universe



# $^{44}\text{Sc}$ in the universe



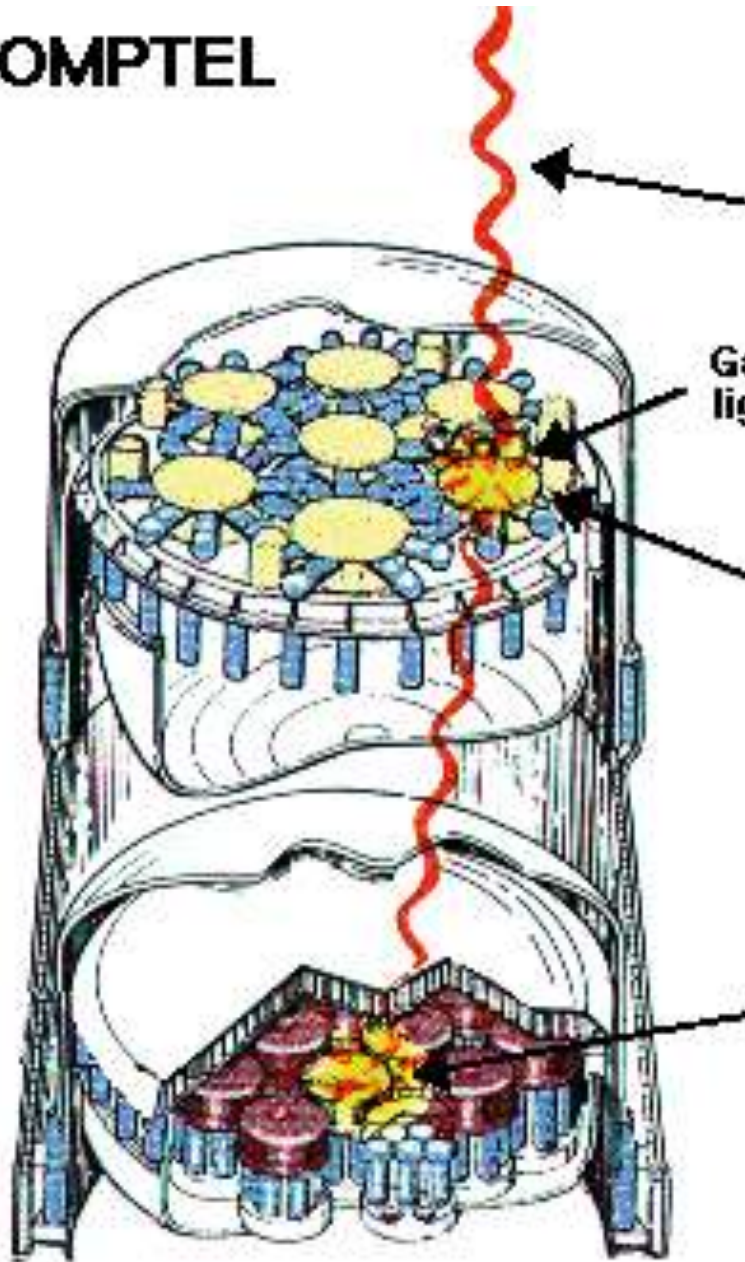
# Longer-lived PET isotopes

Radio-nuclide	Half-life (h)	Branching ratio $\beta^+$ (%)	Branching ratio $\gamma$ (%)	$h_{10}$ (mSv/h/GBq)
Sc-44	3.97	94.3	101	0.324
<b>Cu-64</b>	<b>12.7</b>	<b>17.6</b>	<b>0.5</b>	<b>0.03</b>
Y-86	14.7	31.9	320	0.515
<b>Zr-89</b>	<b>78.4</b>	<b>22.7</b>	<b>100</b>	<b>0.182</b>
<b>I-124</b>	<b>100.2</b>	<b>22.8</b>	<b>99</b>	<b>0.17</b>
Tb-152	17.5	17	142	



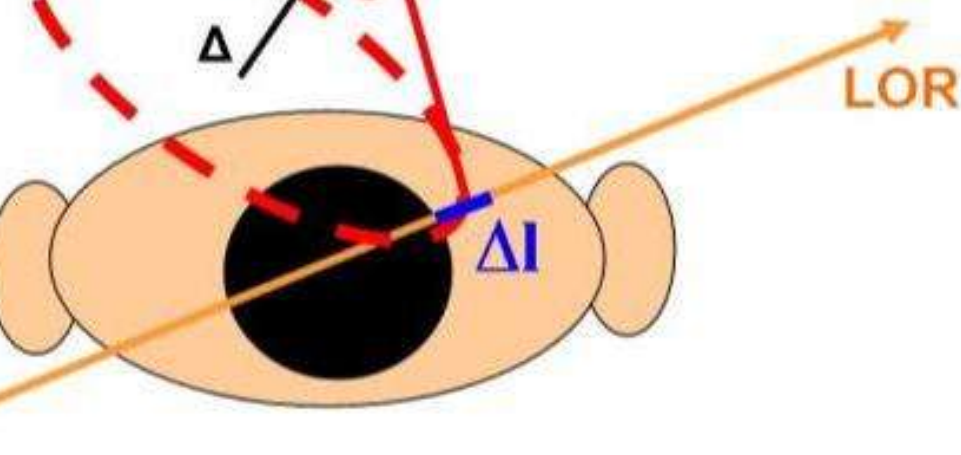
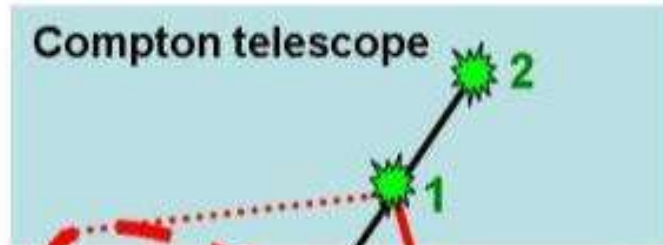
# Compton telescope

COMPTEL

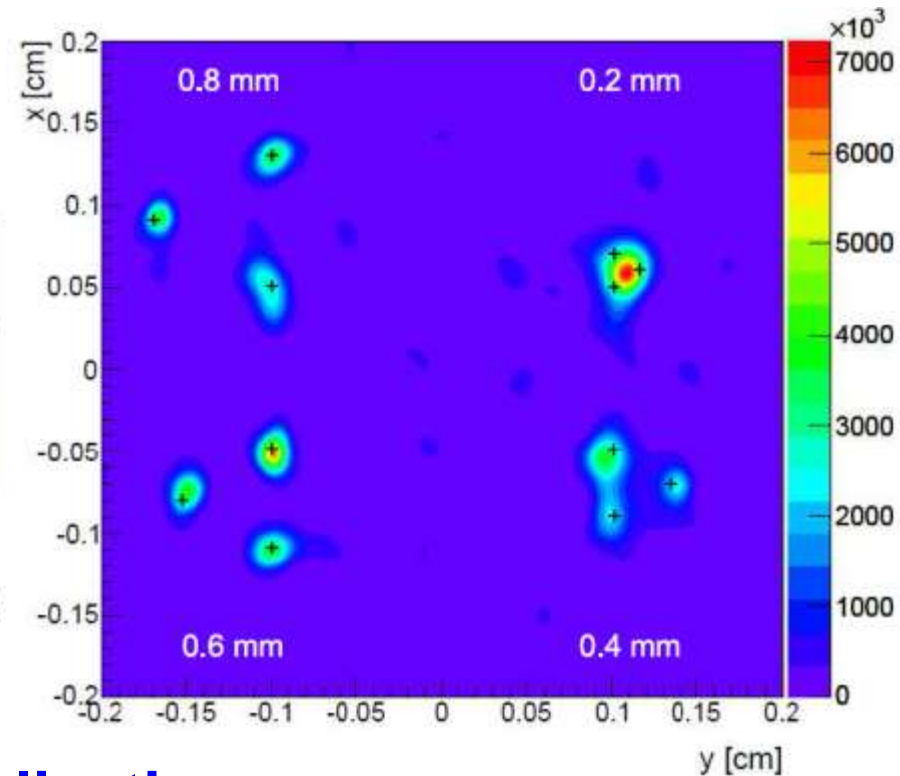
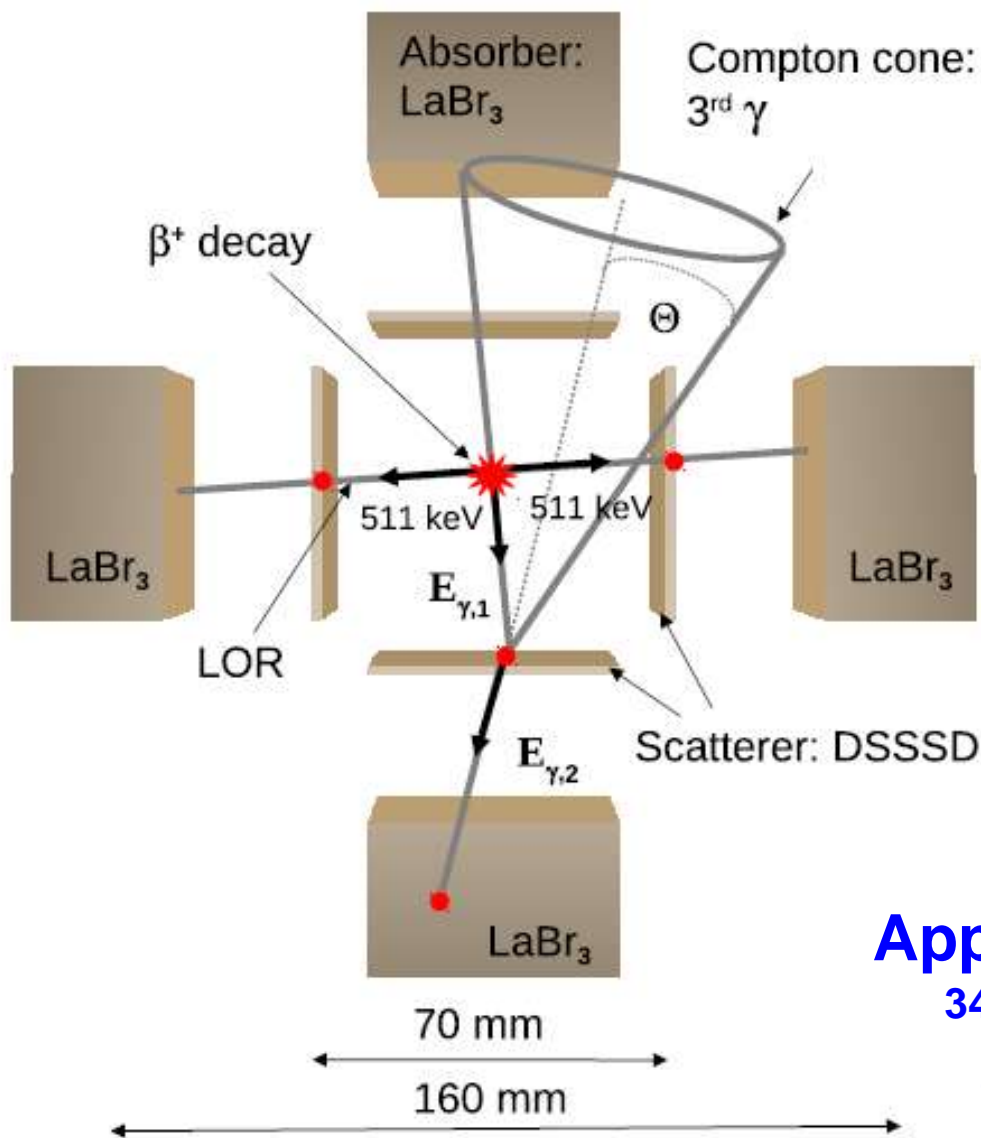


Gamma-ray

Gamma-ray scattered;  
light emitted.



# 3-photon-camera: PET-SPECT



## Applications:

$^{34\text{m}}\text{Cl}$ ,  $^{44}\text{Sc}$ ,  $^{44\text{m}}\text{Sc}$ ,  $^{52}\text{Mn}$ ,  $^{52\text{m}}\text{Mn}$ ,  
 $^{86}\text{Y}$ ,  $^{94\text{g}}\text{Tc}$ ,  $^{94\text{m}}\text{Tc}$ ,  $^{124}\text{I}$

*C. Lang et al. JINST 2014;9:P01080.*

# Cancer and efficiency of treatments

At time of diagnosis	Primary tumor	With metastases	Total
Diagnosed	58%	42%	100%
<b>Cured by:</b>			
Surgery	22%		
Radiation therapy	12%		
Surgery+radiation therapy	6%		
All other treatments and combinations incl. chemotherapy		5%	
<b>Fraction cured</b>	<b>69%</b>	<b>12%</b>	<b>45%</b>

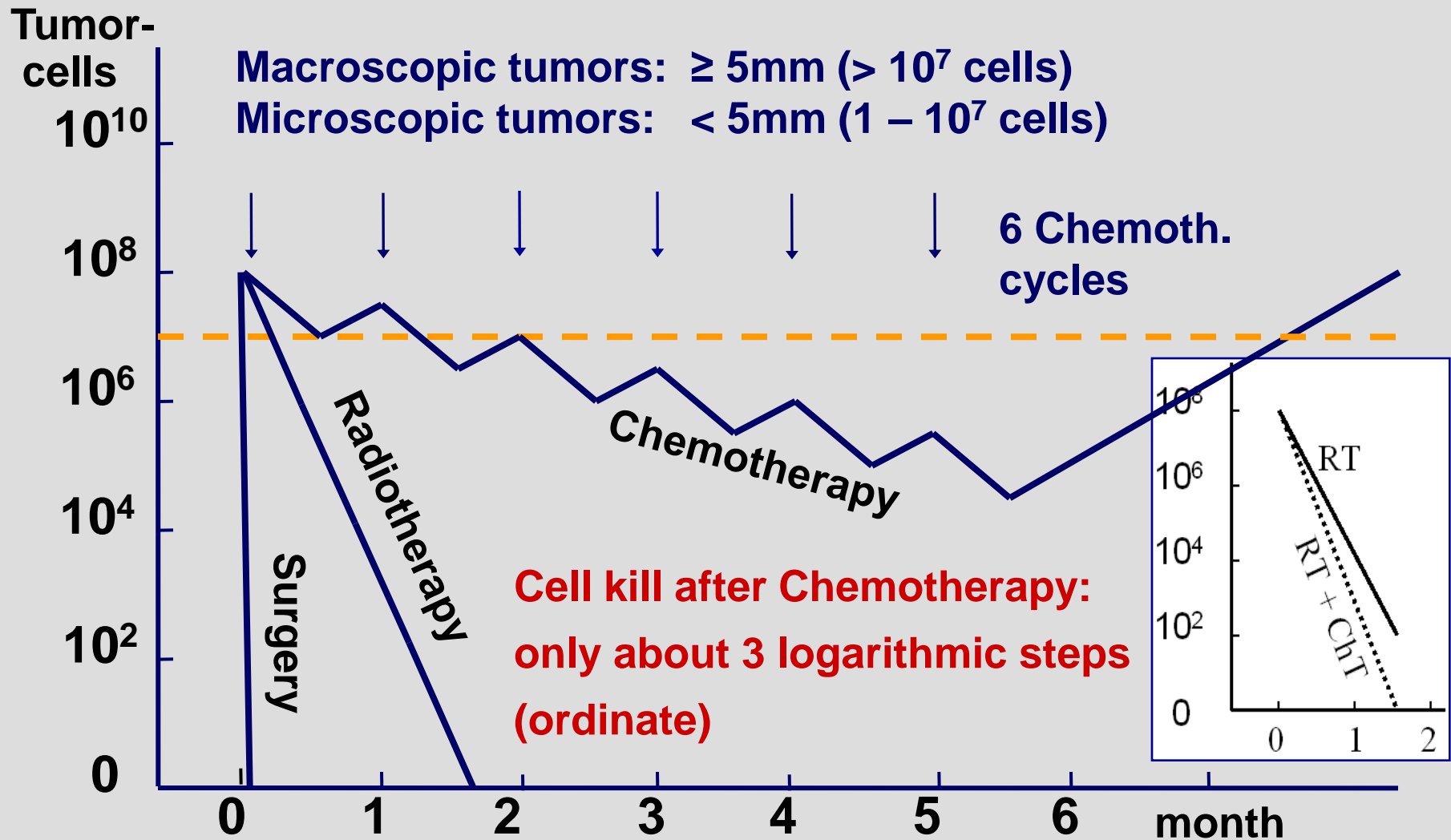
Over **one million deaths per year** from cancer in EU.

⇒ improve early diagnosis

⇒ improve systemic treatments



# Comparison of Therapies

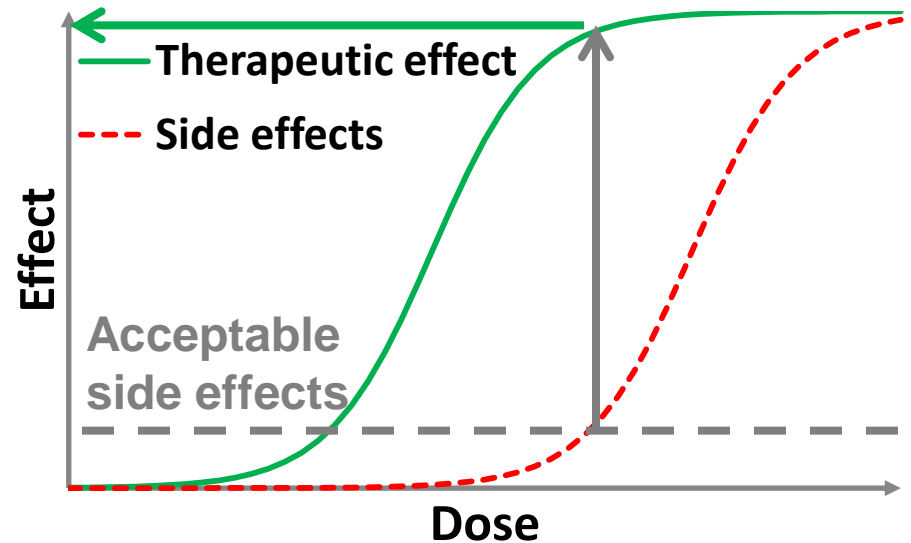
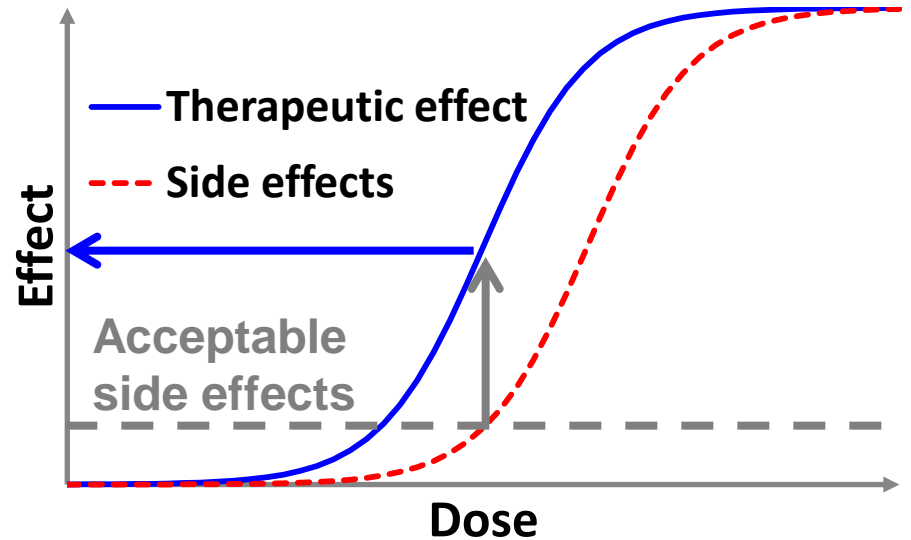


(Molls, TU München; according to Tannock: Lancet 1998, Nature 2006)

# Targeted therapies

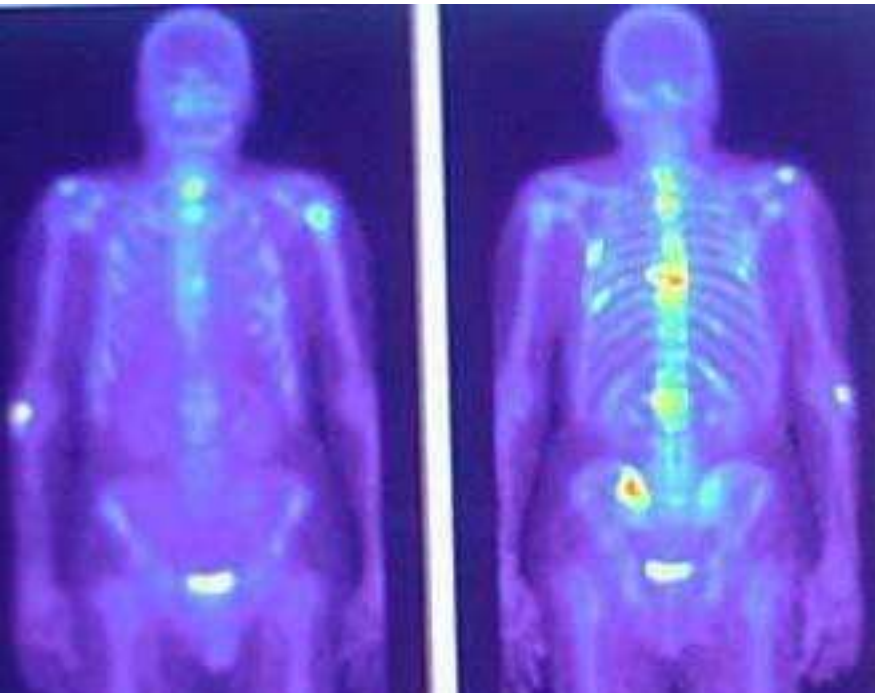


Paracelsus (1493-1541)  
“All things are poison, and  
nothing is without poison;  
only the dose permits something  
not to be poisonous.”



Selective targeting is essential  
to widen the therapeutic window!

# Metabolic targeting



## Thyroid cancer

$^{123}\text{I}^-$  for imaging

$^{131}\text{I}^-$  for therapy

## Bone metastases

1.5 million patients world-wide

$^{99\text{m}}\text{Tc}$ -MDP for SPECT imaging

$^{18}\text{F}$ - for PET imaging



## Therapy

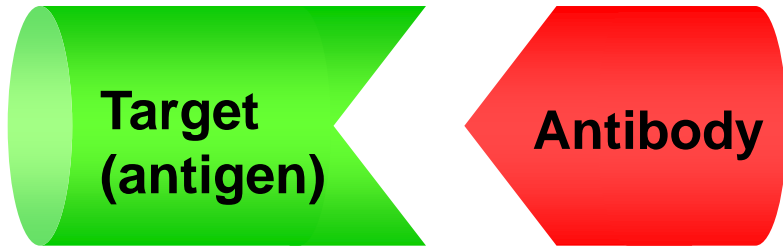
$^{153}\text{Sm}$ -EDTMP (Quadramet)

$^{89}\text{Sr}^{2+}$  (Metastron)

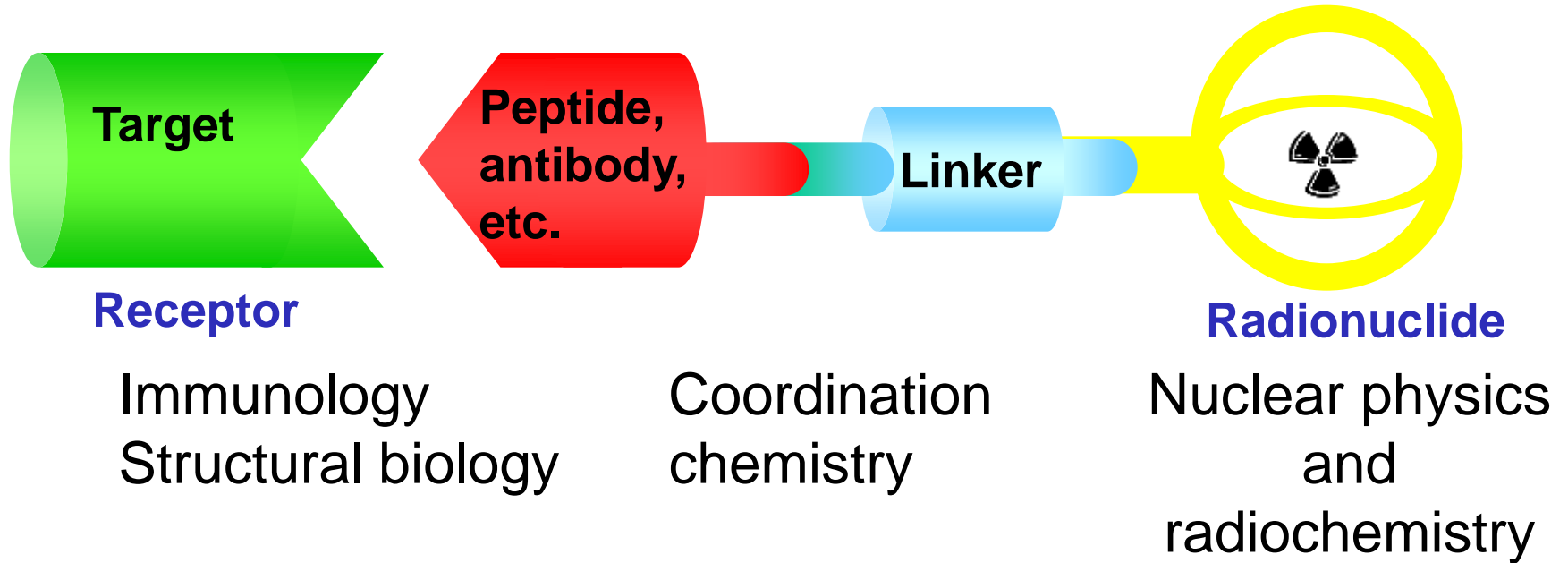
$^{223}\text{Ra}^{2+}$  (Xofigo/Alpharadin)



# Immunology approach

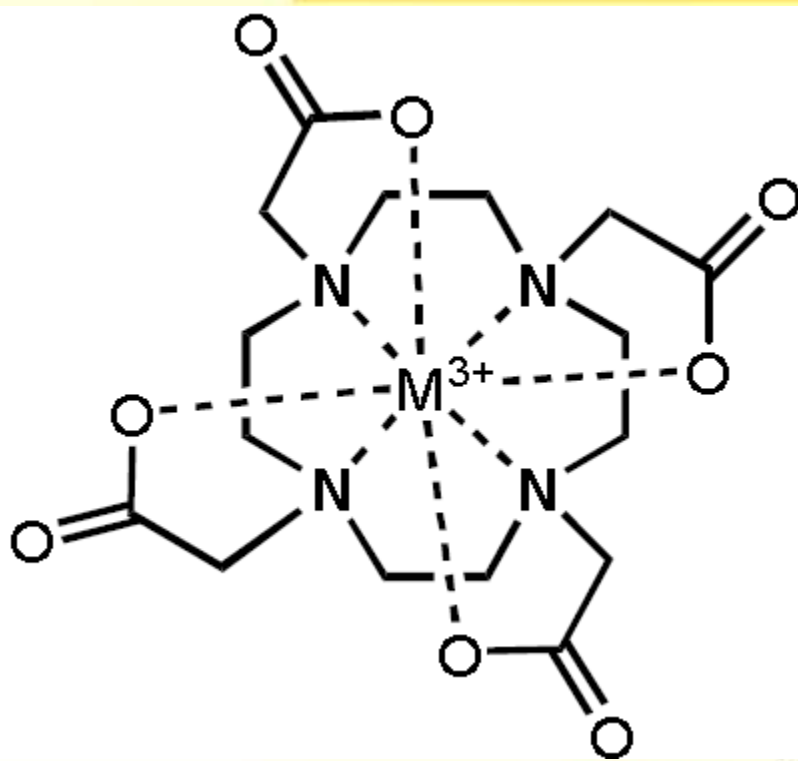


# Multidisciplinary collaboration to fight cancer

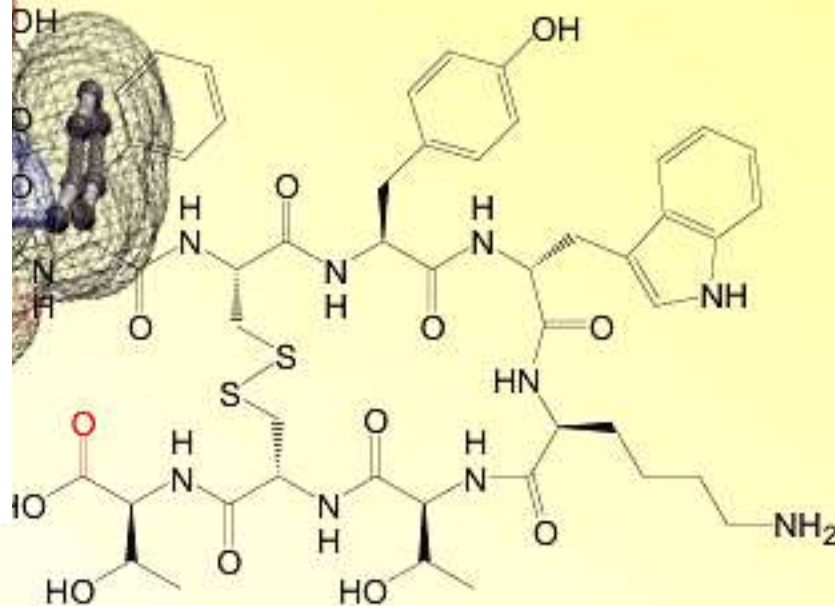


Nuclear medicine and medical physics

# Structural Formula of DOTA-TOC/TATE



DOTA-TATE



1,4,7,10-tetraazacyclododecantetraacetate

$^{111}\text{In}$

$^{90}\text{Y}$

$^{67}\text{Ga}$

$^{177}\text{Lu}$

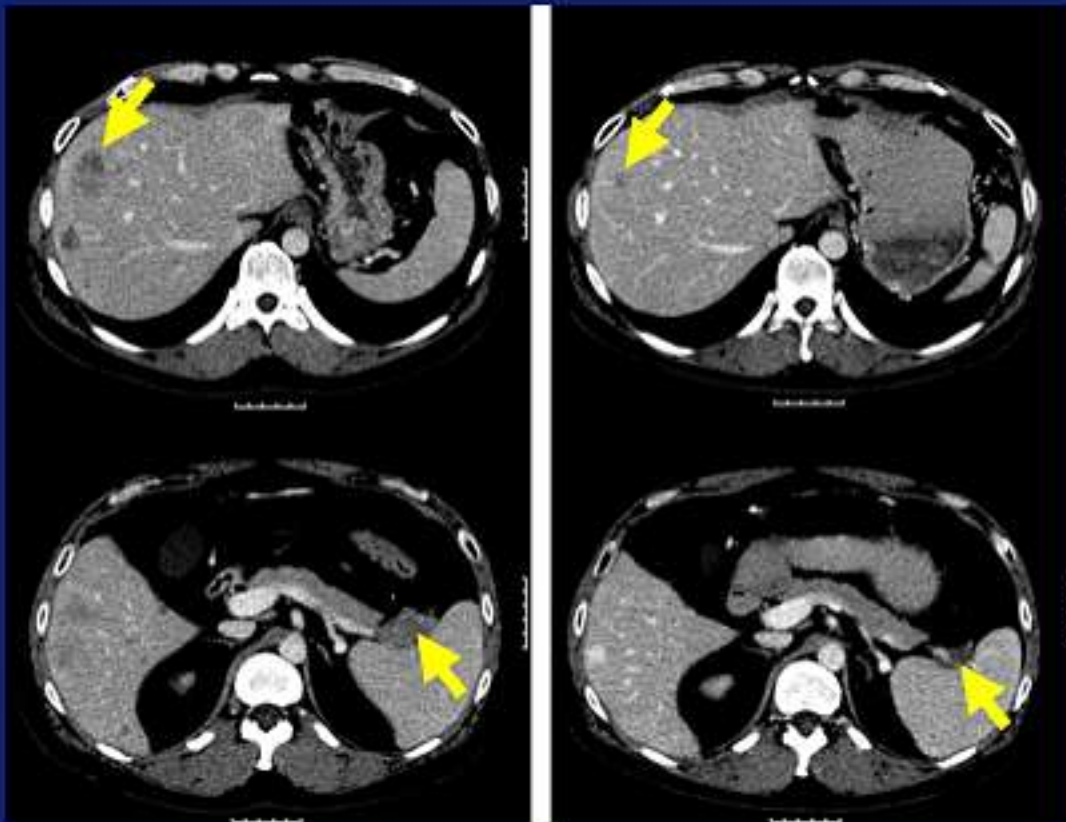
$^{68}\text{Ga}$

$^{213}\text{Bi}$

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

*Helmut Maecke, EANM-2007.*





Male

36 years of age

Small cell pancreatic  
neuroendocrine  
tumour

Liver metastases

Ki-67 index 10-15%  
(liver biopsy)

4 cycles with  $^{177}\text{Lu}$ -  
octreotate and  
capecitabine

Partial remission



1<sup>st</sup> therapy



4<sup>th</sup> therapy

*Roelf Valkema, EANM-2008.*

# Lymphoma therapy: RITUXIMAB+<sup>177</sup>Lu

E.B., 1941 (m): UPN 6

<sup>18</sup>FDG PET



1.9.2002

<sup>177</sup>Lu-Scan



13.9.2002

<sup>18</sup>FDG PET



15.11.2002

**Still  
in  
CR**

15.9.2009

*F. Forrer et al., J Nucl Med 2013;54:1045.*

# Radionuclides for RIT and PRRT

Radio-nuclide	Half-life (d)	E mean (keV)	E $\gamma$ (B.R.) (keV)	Range
<b>Y-90</b>	2.7	934 $\beta$	-	<b>12 mm</b>
<b>I-131</b>	8.0	182 $\beta$	364 (82%)	<b>3 mm</b>
<b>Lu-177</b>	6.7	134 $\beta$	208 (10%) 113 (6%)	<b>2 mm</b>

Established isotopes

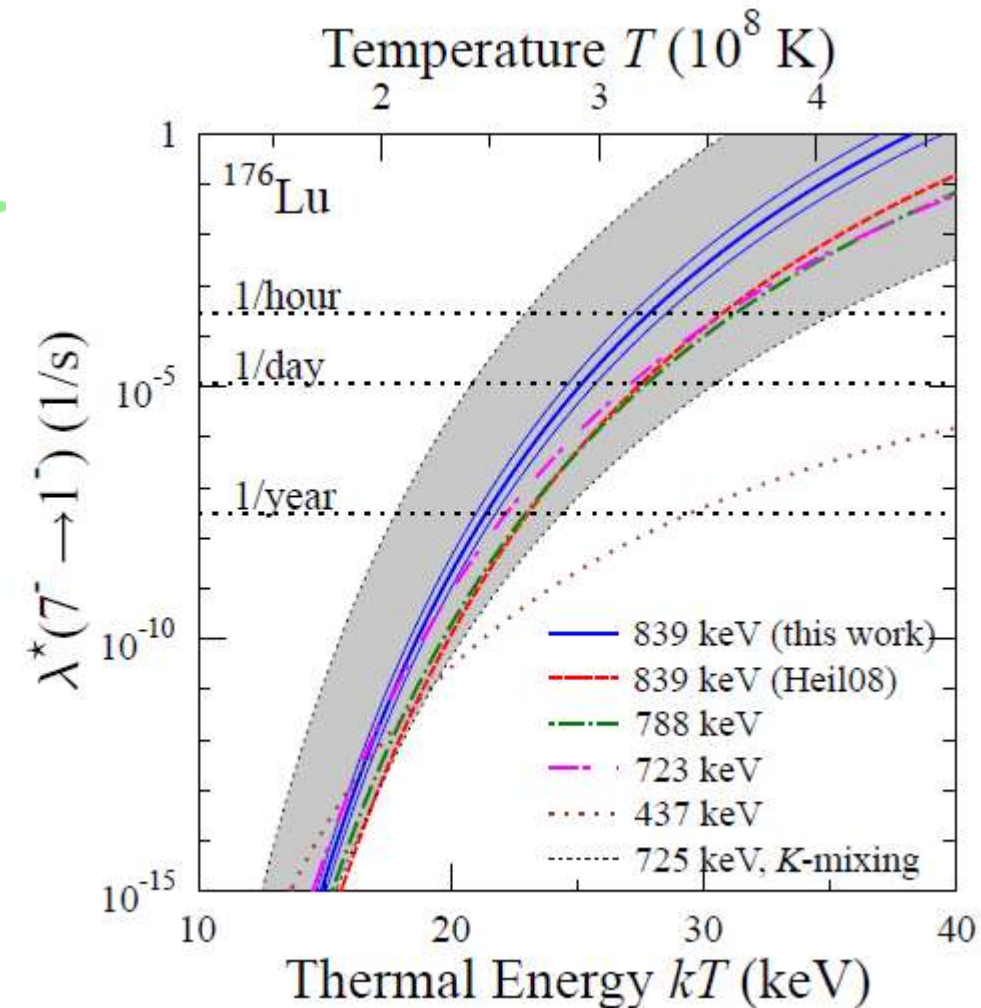
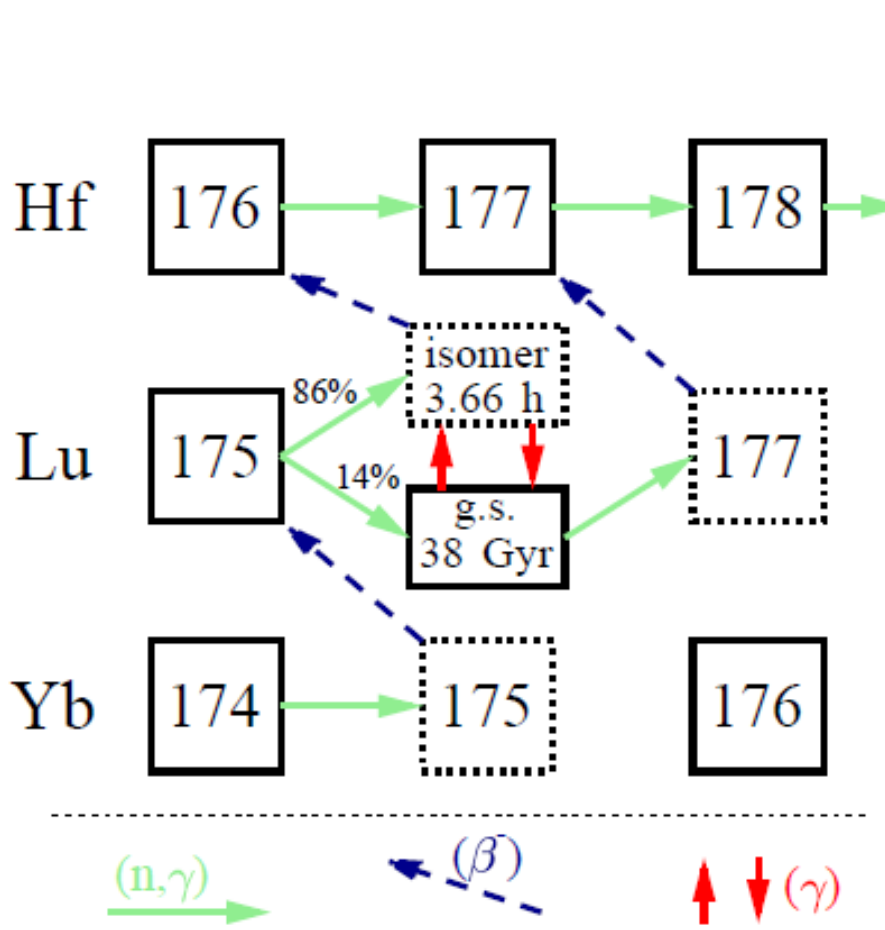
Emerging isotope



# Production of $^{177}\text{Lu}$

<p><b>Ta 175</b> 10.5 h</p> <p><math>\epsilon</math> <math>\gamma</math> 207; 349; 267; 82; 126; 1793...</p>	<p><b>Ta 176</b> 8.1 h</p> <p><math>\epsilon</math> <math>\beta^+</math>... <math>\gamma</math> 1159; 88; 1225...</p>	<p><b>Ta 177</b> 56.6 h</p> <p><math>\epsilon</math> <math>\beta^+</math> <math>\gamma</math> 113; 208... g</p>	<p><b>Ta 178</b> 9.25 m <math>\longleftrightarrow</math> 2.45 h</p> <p><math>\epsilon</math> <math>\beta^+</math> 0.9 <math>\gamma</math> 93; 1351; 1341... g <math>m_1</math></p>	<p><b>Ta 179</b> 665 d</p> <p><math>\epsilon</math> no <math>\gamma</math> g <math>\sigma</math> 930</p>	<p><b>Ta 180</b> 0.012</p> <p><math>&gt; 10^{15}</math> a   8.15 h</p> <p><math>\epsilon</math> <math>\beta^-</math> 0.7... <math>\gamma</math> 93; 104 g</p> <p><math>\sigma \sim 560</math></p>	<p><b>Ta 181</b> 99.988</p> <p><math>\sigma</math> 0.012 + 20 <math>\sigma_n, \alpha &lt; 10^{-5}</math></p>
<p><b>Hf 174</b> 0.16</p> <p><math>2.0 \cdot 10^{15}</math> a</p> <p><math>\alpha</math> 2.50 <math>\sigma</math> 600</p>	<p><b>Hf 175</b> 70.0 d</p> <p><math>\epsilon</math> <math>\gamma</math> 343...</p>	<p><b>Hf 176</b> 5.26</p> <p><math>\sigma</math> 23</p>	<p><b>Hf 177</b></p> <p>51 m   1.1 s   18.60</p> <p><math>\gamma</math> 277; 295; 327...   <math>\gamma</math> 208; 229; 379...   <math>\sigma</math> <math>10^{-7}</math> + 1 + 375</p>	<p><b>Hf 178</b></p> <p>31 a   4.0 s   27.28</p> <p><math>\gamma</math> 574; 495; 217...   <math>\gamma</math> 426; 326; 213; 89...   <math>\sigma</math> ? + 54 + 32</p>	<p><b>Hf 179</b></p> <p>25 d   18.7 s   13.62</p> <p><math>\gamma</math> 454; 363; 123; 146...   <math>\gamma</math> 214   <math>\sigma</math> 0.43 + 46</p>	<p><b>Hf 180</b></p> <p>5.5 h   35.08</p> <p><math>\gamma</math> 332; 443; 215; 57...   <math>\beta^-</math>...   <math>\sigma</math> 13 <math>\sigma_n, \alpha &lt; 1.3 \cdot 10^{-6}</math></p>
<p><b>Lu 173</b> 1.37 a</p> <p><math>\epsilon</math> <math>\gamma</math> 272; 79; 101... <math>e^-</math></p>	<p><b>Lu 174</b></p> <p>142 d   3.31 a</p> <p><math>\gamma</math> 45; 67... <math>e^-</math>; <math>\epsilon</math> <math>\gamma</math> (992; 273...)</p> <p><math>\epsilon</math> <math>\beta^+</math>... <math>\gamma</math> 1242; 76...</p>	<p><b>Lu 175</b> 97.41</p> <p><math>\sigma</math> 16 + 8</p>	<p><b>Lu 176</b> 2.59</p> <p>3.68 h   <math>3.8 \cdot 10^{10}</math> a</p> <p><math>\beta^-</math> 1.2; 1.3...; <math>\epsilon</math> <math>\gamma</math> 88... <math>e^-</math></p> <p><math>\beta^-</math> 0.6... <math>\gamma</math> 307; 202; 88... <math>\sigma</math> 2 + 2100</p>	<p><b>Lu 177</b></p> <p>160.1 d   6.71 d</p> <p><math>\beta^-</math> 0.2   <math>\beta^-</math> 0.5... <math>\gamma</math> 419; 208; 319; 122...   113... <math>m_1</math>   g <math>\sigma</math> 3.2   <math>\sigma</math> 1000</p> <p><math>\sigma</math> 3.2</p>	<p><b>Lu 178</b></p> <p>22.7 m   28.4 m</p> <p><math>\beta^-</math> 2.0... <math>\gamma</math> 93; 1341; <math>\gamma</math> 332...   1310; 1269...; g <math>m_1</math></p>	<p><b>Lu 179</b> 4.6 h</p> <p><math>\beta^-</math> 1.4... <math>\gamma</math> 214... g</p>
<p><b>Yb 172</b> 21.83</p> <p><math>\sigma \sim 1.3</math> <math>\sigma_n, \alpha &lt; 1E-6</math></p>	<p><b>Yb 173</b> 16.13</p> <p><math>\sigma</math> 16 <math>\sigma_n, \alpha &lt; 1E-6</math></p>	<p><b>Yb 174</b> 31.83</p> <p><math>\sigma</math> 63 <math>\sigma_n, \alpha &lt; 0.00002</math></p>	<p><b>Yb 175</b> 4.2 d</p> <p><math>\beta^-</math> 0.5... <math>\gamma</math> 396; 283; 114...</p>	<p><b>Yb 176</b></p> <p>12 s   12.76</p> <p><math>\gamma</math> 293 390; 190; 96...   <math>\sigma</math> 3.1 <math>\sigma_n, \alpha &lt; 1E-6</math></p>	<p><b>Yb 177</b></p> <p>6.5 s   1.9 h</p> <p><math>\beta^-</math> 1.4... <math>\gamma</math> 150; 1080; 122; 1241...   g <math>e^-</math></p>	<p><b>Yb 178</b> 74 m</p> <p><math>\beta^-</math> 0.6... <math>\gamma</math> 391; 348... g</p>
<p><b>Tm 171</b> 1.92 a</p> <p><math>\beta^-</math> 0.1... <math>\gamma</math> (67); <math>e^-</math> <math>\sigma \sim 160</math></p>	<p><b>Tm 172</b> 63.6 h</p> <p><math>\beta^-</math> 1.8; 1.9... <math>\gamma</math> 79; 1094; 1387; 1530; 1466; 1609...</p>	<p><b>Tm 173</b> 8.2 h</p> <p><math>\beta^-</math> 0.9; 1.3... <math>\gamma</math> 399; 461...</p>	<p><b>Tm 174</b></p> <p>2.29 s   5.4 m</p> <p><math>\gamma</math> 100; 152</p> <p><math>\beta^-</math> 1.2... <math>\gamma</math> 366; 992; 273; 177...</p>	<p><b>Tm 175</b> 15.2 m</p> <p><math>\beta^-</math> 0.9; 1.9... <math>\gamma</math> 515; 941; 364...</p>	<p><b>Tm 176</b> 1.9 m</p> <p><math>\beta^-</math> 2.0; 2.8... <math>\gamma</math> 190; 1069; 382...   g</p>	<p><b>Tm 177</b> 85 s</p> <p><math>\beta^-</math> <math>\gamma</math> 105; 518... g; m</p>

# $^{176}\text{Lu}$ : cosmochronometer or thermometer?



H. Beer et al., *Astrophys. J. Suppl.* 1981;46:295.  
 P. Mohr et al., 2009.  
 G. Gosselin et al., 2010.



# Production of $^{177}\text{Lu}$

<b>Ta 175</b> 10.5 h $\epsilon$ $\gamma$ 207; 349; 267; 82; 126; 1793...	<b>Ta 176</b> 8.1 h $\epsilon$ $\beta^+$ ... $\gamma$ 1159; 88; 1225...	<b>Ta 177</b> 56.6 h $\epsilon$ $\beta^+$ $\gamma$ 113; 208... g	<b>Ta 178</b> $\leftarrow$ 9.25 m $\rightarrow$ 2.45 h $\epsilon$ $\beta^+$ 0.9 $\gamma$ 93; 1351; 1341... $\epsilon$ $\gamma$ 332... g m <sub>1</sub>	<b>Ta 179</b> 665 d $\epsilon$ no $\gamma$ g $\sigma$ 930	<b>Ta 180</b> 0.012 $> 10^{15}$ a   8.15 h $\epsilon$ $\beta^-$ 0.7... $\gamma$ 93; 104 g $\sigma \sim 560$	<b>Ta 181</b> 99.988 $\sigma$ 0.012 + 20 $\sigma_n, \alpha < 10^{-5}$
<b>Hf 174</b> 0.16 $2.0 \cdot 10^{15}$ a $\alpha$ 2.50 $\sigma$ 600	<b>Hf 175</b> 70.0 d $\epsilon$ $\gamma$ 343...	<b>Hf 176</b> 5.26 $\sigma$ 23	<b>Hf 177</b> 51 m   1.1 s   18.60 $\epsilon$ $\gamma$ 277; 295; 327... $\gamma$ 208; 229; 379... $\sigma$ $10^{-7}$ + 1 + 375	<b>Hf 178</b> 31 a   4.0 s   27.28 $\epsilon$ $\gamma$ 574; 495; 217... $\sigma$ 45 $\gamma$ 426; 326; 213; 89... $\sigma$ ? + 54 + 32	<b>Hf 179</b> 25 d   18.7 s   13.62 $\epsilon$ $\gamma$ 454; 363; 123; 146... $\gamma$ 214 $\sigma$ 0.43 + 46	<b>Hf 180</b> 5.5 h   35.08 $\epsilon$ $\gamma$ 332; 443; 215; 57... $\beta^-$ ... m $\sigma_n, \alpha < 1.3 \cdot 10^{-5}$
<b>Lu 173</b> 1.37 a $\epsilon$ $\gamma$ 272; 79; 101... $e^-$	<b>Lu 174</b> 142 d   3.31 a $\epsilon$ $\gamma$ 45; 67... $e^-$ ; $\epsilon$ $\gamma$ (992; 273...) $\epsilon$ $\beta^+$ ... $\gamma$ 1242; 76...	<b>Lu 175</b> 97.41 $\sigma$ 16 + 8	<b>Lu 176</b> 2.59 3.68 h   $3.8 \cdot 10^{10}$ a $\beta^-$ 1.2; 1.3...; $\epsilon$ $\gamma$ 88... $e^-$ $\sigma$ 2 + 2100	<b>Lu 177</b> 160.1 d   6.71 d $\beta^-$ 0.2   $\beta^-$ 0.5... $\gamma$ 93; 208; 113... g $\sigma$ 1000 $\sigma$ 3.2	<b>Lu 178</b> 22.7 m   28.4 m $\beta^-$ 2.0... $\gamma$ 93; 1341; 1310; 1269...; g m <sub>1</sub>	<b>Lu 179</b> 4.6 h $\beta^-$ 1.4... $\gamma$ 214... g
<b>Yb 172</b> 21.83 $\sigma \sim 1.3$ $\sigma_n, \alpha < 1E-6$	<b>Yb 173</b> 16.13 $\sigma$ 16 $\sigma_n, \alpha < 1E-6$	<b>Yb 174</b> 31.83 $\sigma$ 63 $\sigma_n, \alpha < 0.00002$	<b>Yb 175</b> 4.2 d $\beta^-$ 0.5... $\gamma$ 396; 283; 114...	<b>Yb 176</b> 12 s   12.76 $\epsilon$ $\gamma$ 293 390; 190; 96... $\sigma$ 3.1 $\sigma_n, \alpha < 1E-6$	<b>Yb 177</b> 6.5 s   1.9 h $\beta^-$ 1.4... $\gamma$ 150; 1080; 122; 1241... g $e^-$	<b>Yb 178</b> 74 m $\beta^-$ 0.6... $\gamma$ 391; 348;... g
<b>Tm 171</b> 1.92 a	<b>Tm 172</b> 63.6 h	<b>Tm 173</b> 8.2 h	<b>Tm 174</b> 2.29 s   5.4 m	<b>Tm 175</b> 15.2 m	<b>Tm 176</b> 1.9 m	<b>Tm 177</b> 85 s

**Waste problem for hospitals!**

*R. Henkelmann et al., Eur. J. Nucl. Med. Mol. Imag. 36 (2009) S260.*



# Production of $^{177}\text{Lu}$

<b>Ta 175</b> 10.5 h $\epsilon$ $\gamma$ 207; 349; 267; 82; 126; 1793...	<b>Ta 176</b> 8.1 h $\epsilon$ $\beta^+$ ... $\gamma$ 1159; 88; 1225...	<b>Ta 177</b> 56.6 h $\epsilon$ $\beta^+$ $\gamma$ 113; 208... g	<b>Ta 178</b> $\leftarrow$ 9.25 m $\rightarrow$ 2.45 h $\epsilon$ $\beta^+$ 0.9 $\gamma$ 93; 1351; 1341... $\epsilon$ $\gamma$ 332... g m <sub>1</sub>	<b>Ta 179</b> 665 d $\epsilon$ no $\gamma$ g $\sigma$ 930	<b>Ta 180</b> 0.012 $> 10^{15}$ a $\sigma \sim 560$ $\epsilon$ $\beta^-$ 0.7... $\gamma$ 93; 104 g	<b>Ta 181</b> 99.988 $\sigma$ 0.012 + 20 $\sigma_n, \alpha < 10^{-5}$
<b>Hf 174</b> 0.16 $2.0 \cdot 10^{15}$ a $\alpha$ 2.50 $\sigma$ 600	<b>Hf 175</b> 70.0 d $\epsilon$ $\gamma$ 343...	<b>Hf 176</b> 5.26 $\sigma$ 23	<b>Hf 177</b> 51 m   1.1 s   18.60 $\epsilon$ $\gamma$ 277; 295; 327... $\gamma$ 208; 229; 379... $\sigma$ $10^{-7}$ + 1 + 375	<b>Hf 178</b> 31 a   4.0 s   27.28 $\epsilon$ $\gamma$ 574; 495; 217... $\gamma$ 426; 326; 213; 89... $\sigma$ 45 $\sigma$ ? + 54 + 32	<b>Hf 179</b> 25 d   18.7 s   13.62 $\epsilon$ $\gamma$ 454; 363; 123; 146... $\gamma$ 214 $\sigma$ 0.43 + 46	<b>Hf 180</b> 5.5 h   35.08 $\epsilon$ $\gamma$ 332; 443; 215; 57... $\beta^-$ ... m $\sigma_n, \alpha < 1.3 \cdot 10^{-5}$
<b>Lu 173</b> 1.37 a $\epsilon$ $\gamma$ 272; 79; 101... $e^-$	<b>Lu 174</b> 142 d   3.31 a $\epsilon$ $\gamma$ 45; 67... $e^-$ ; $\epsilon$ $\gamma$ (992; 273...) $\epsilon$ $\beta^+$ ... $\gamma$ 1242; 76...	<b>Lu 175</b> 97.41 $\sigma$ 16 + 8	<b>Lu 176</b> 2.59 3.68 h   $3.8 \cdot 10^{10}$ a $\beta^-$ 1.2; 1.3...; $\epsilon$ $\gamma$ 88... $e^-$ $\sigma$ 2 + 2100	<b>Lu 177</b> 160.1 d   6.71 d $\beta^-$ 0.2... $\beta^-$ 0.5... $\gamma$ 93; 208; 113... g $\sigma$ 3.2   $\sigma$ 1000	<b>Lu 178</b> 22.7 m   28.4 m $\beta^-$ 2.0... $\gamma$ 93; 1341; 1310; 1269...; g m <sub>1</sub>	<b>Lu 179</b> 4.6 h $\beta^-$ 1.4... $\gamma$ 214... g
<b>Yb 172</b> 21.83 $\sigma \sim 1.3$ $\sigma_n, \alpha < 1E-6$	<b>Yb 173</b> 16.13 $\sigma$ 16 $\sigma_n, \alpha < 1E-6$	<b>Yb 174</b> 31.83 $\sigma$ 63 $\sigma_n, \alpha < 0.00002$	<b>Yb 175</b> 4.2 d $\beta^-$ 0.5... $\gamma$ 396; 283; 114...	<b>Yb 176</b> 12 s   12.76 $\epsilon$ $\gamma$ 293 390; 190; 96... $\sigma$ 3.1 $\sigma_n, \alpha < 1E-6$	<b>Yb 177</b> 6.5 s   1.9 h $\beta^-$ 1.4... $\gamma$ 150; 1080; 122; 1241... g $e^-$	<b>Yb 178</b> 74 m $\beta^-$ 0.6... $\gamma$ 391; 348;... g
<b>Tm 171</b> 1.92 a	<b>Tm 172</b> 63.6 h	<b>Tm 173</b> 8.2 h	<b>Tm 174</b> 2.29 s   5.4 m	<b>Tm 175</b> 15.2 m	<b>Tm 176</b> 1.9 m	<b>Tm 177</b> 85 s

**Waste problem for hospitals!**

R. Henkelmann et al., *Eur. J. Nucl. Med. Mol. Imag.* 36 (2009) S260.

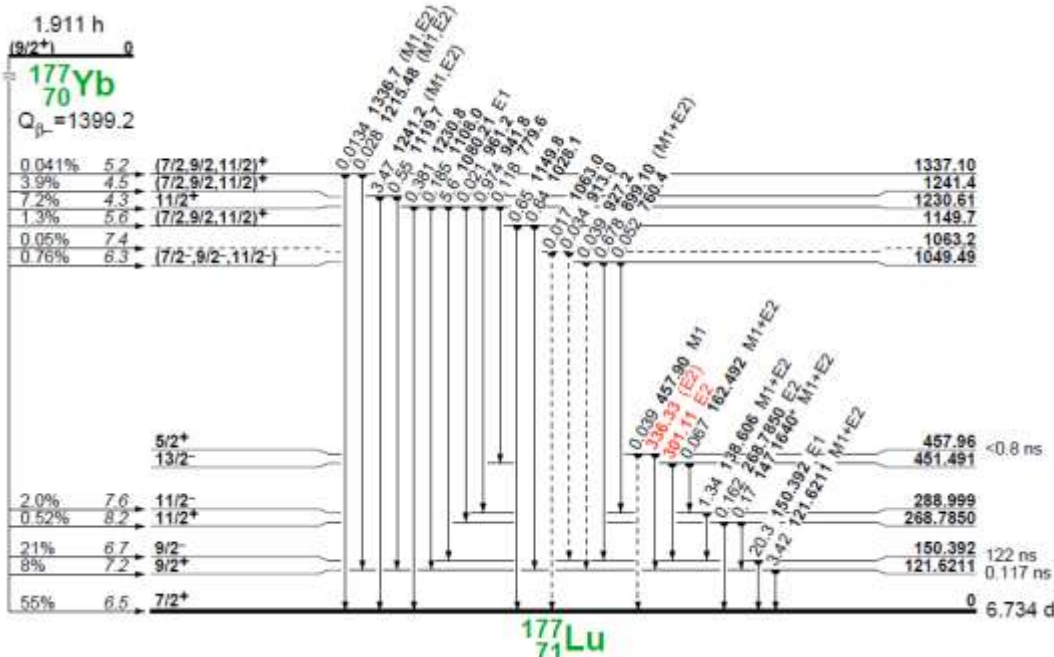


# Question

How to get  $^{177g}\text{Lu}$  without  $^{177m}\text{Lu}$  contamination ?

<b>Hf 176</b> 5.26  $\sigma$ 23	<b>Hf 177</b> 51 m   1.1 s   18.60			<b>Hf 178</b> 31 a   4.0 s   27.28			<b>Hf 179</b> 25 d   18.7 s   13.62		
	$t_{1/2}$ 277; 295; 327...	$t_{1/2}$ 208; 229; 379...	$\sigma$ $10^{-7}$ + 1 + 375	$t_{1/2}$ 574; 495; 217... $\sigma$ 45	$t_{1/2}$ 426; 326; 213; 89...	$\sigma$ ? + 54 + 32	$t_{1/2}$ 454; 363; 123; 146...	$t_{1/2}$ 214 ...	$\sigma$ 0.43 + 46
<b>Lu 175</b> 97.41  $\sigma$ 16 + 8	<b>Lu 176</b> 2.59		<b>Lu 177</b> 160.1 d   6.71 d		<b>Lu 178</b> 22.7 m   28.4 m				
	<b>3.68 h</b> $\beta^-$ 1.2; 1.3...; $\epsilon$ $\gamma$ 88... $e^-$	<b><math>3.8 \cdot 10^{10}</math> a</b> $\beta^-$ 0.6... $\gamma$ 307; 202; 88... $\sigma$ 2 + 2100	$\beta^-$ 0.2 $t_{1/2}$ 414; 319; 122... $m_1$ $\sigma$ 3.2	$\beta^-$ 0.5... $\gamma$ 208; 113... $g$ $\sigma$ 1000	$\beta^-$ 1.2... $\gamma$ 332... $m_1$	$\beta^-$ 2.0... $\gamma$ 93; 1341; 1310; 1269...; $g$			
<b>Yb 174</b> 31.83  $\sigma$ 63 $\sigma_n, \alpha < 0.00002$	<b>Yb 175</b> 4.2 d		<b>Yb 176</b> 12 s   12.76		<b>Yb 177</b> 6.5 s   1.9 h				
	$\beta^-$ 0.5... $\gamma$ 396; 283; 114...		$t_{1/2}$ 293 390; 190; 96...	$\sigma$ 3.1 $\sigma_{n, \alpha} < 1E-6$	$t_{1/2}$ 104; 228 $e^-$	$\beta^-$ 1.4... $\gamma$ 150; 1080; 122; 1241... $g$			

# Alternative production route to $^{177}\text{Lu}$



<b>Ta 179</b> 665 d $\epsilon$ no $\gamma$ g $\sigma$ 930	<b>Ta 180</b> 0.012 $> 10^{15}$ a $\sigma \sim 560$ $\epsilon$ $\beta^- 0.7...$ $\gamma$ 93; 104 g	<b>Ta 181</b> 99.988 $\sigma$ 0.012 + 20 $\sigma_n, \alpha < 10^{-5}$				
<b>Hf 178</b> 31 a $\gamma$ 574; 495; 217... $\sigma$ 45	<b>Hf 179</b> 27.28 $\gamma$ 454; 363; 123; $\sigma$ 45 $\sigma$ ? $\sigma$ +54 $\sigma$ +32	<b>Hf 180</b> 5.5 h $\gamma$ 332; 443; 215; 57... $\beta^-$ ... m $\sigma$ 13 $\sigma_n, \alpha < 1.3 \cdot 10^{-5}$				
<b>Lu 177</b> 160.1 d $\beta^- 0.2$ $\gamma$ 414; 319; 122... m $\sigma$ 3.2	<b>Lu 178</b> 6.71 d $\beta^- 0.5...$ $\gamma$ 208; 113... g $\sigma$ 1000	<b>Lu 179</b> 4.6 h $\beta^- 1.4...$ $\gamma$ 214... g				
<b>Yb 172</b> 21.83 $\sigma \sim 1.3$ $\sigma_n, \alpha < 1E-6$	<b>Yb 173</b> 16.13 $\sigma$ 16 $\sigma_n, \alpha < 1E-6$	<b>Yb 174</b> 31.83 $\sigma$ 63 $\sigma_n, \alpha < 0.00002$	<b>Yb 175</b> 4.2 d $\beta^- 0.5...$ $\gamma$ 396; 283; 114...	<b>Yb 176</b> 12 s $\gamma$ 293; 390; 190; 96... $\sigma$ 3.1	<b>Yb 177</b> 6.5 s $\beta^- 1.2...$ $\gamma$ 332... m $\sigma$ 1000 $\sigma$ 3.2	<b>Yb 178</b> 74 m $\beta^- 1.4...$ $\gamma$ 150; 1080; 122; 1241 g
<b>Tm 171</b> 1.92 a $\beta^- 0.1...$ $\gamma$ (67); $e^-$ $\sigma \sim 160$	<b>Tm 172</b> 63.6 h $\beta^- 1.8; 1.9...$ $\gamma$ 79; 1094; 1387; 1530; 1466; 1609...	<b>Tm 177</b> 85 s $\beta^-$ $\gamma$ 105; 518... g; m				

- Free of long-lived isomer
- Non-carrier-added quality
- “Needs” high-flux reactor

## Question

How long does it take to separate lutetium from ytterbium?



# Answer: The history of lutetium separation

1878 Separation of Yb  
by Jean-Charles Galissard de Marignac

1907 Separation of Lu from Yb  
Georges Urbain  
Carl Auer von Welsbach  
Charles James

1995- Large-scale separation of Lu  
for production of LSO and LYSO crystals  
by Mark Andreaco (CTI) and  
George Schweitzer (Univ. Tennessee)

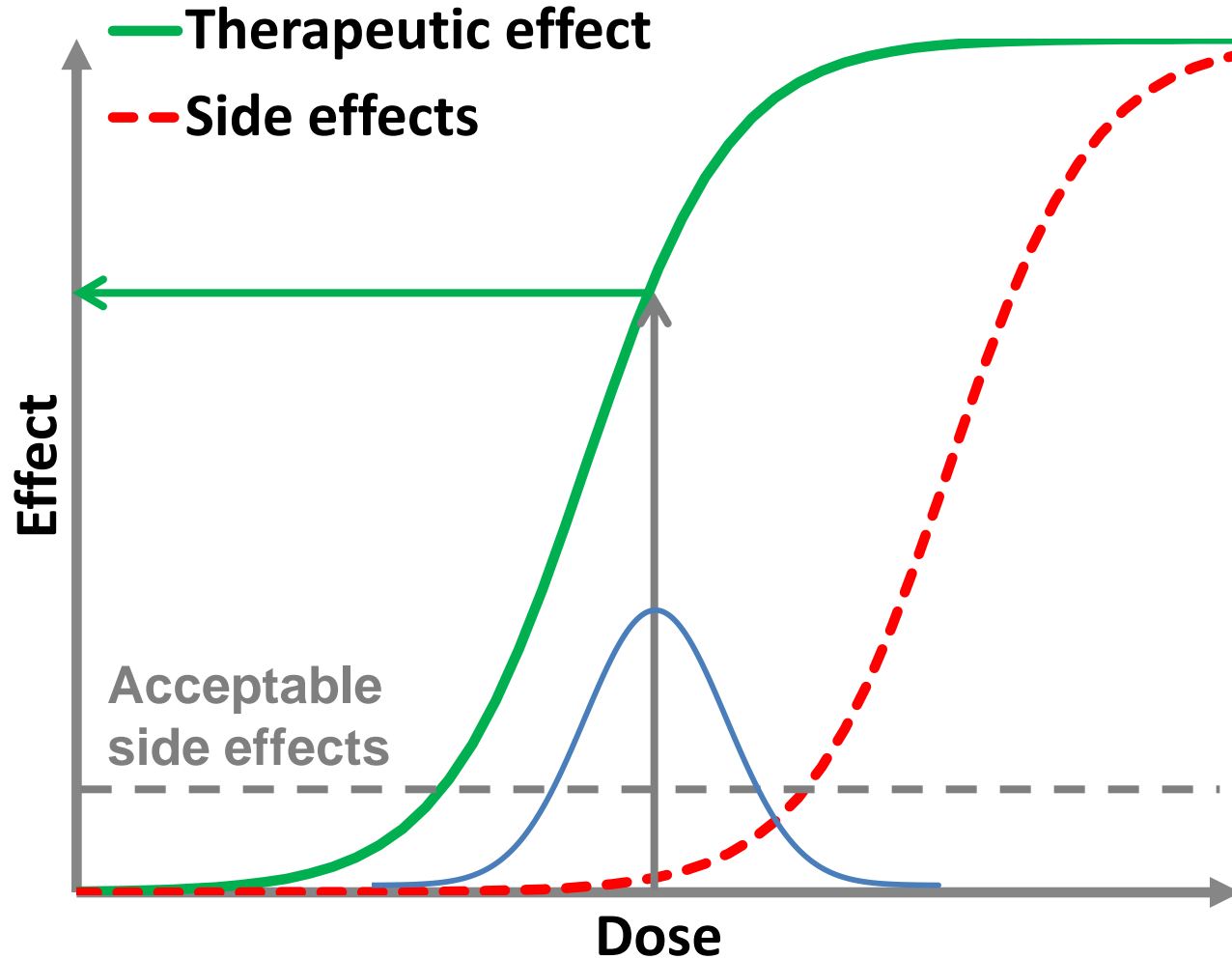
2007 Rapid large-scale separation  
of n.c.a.  $^{177}\text{Lu}$  from irradiated Yb  
by ITG Garching



The rising star  
for therapy



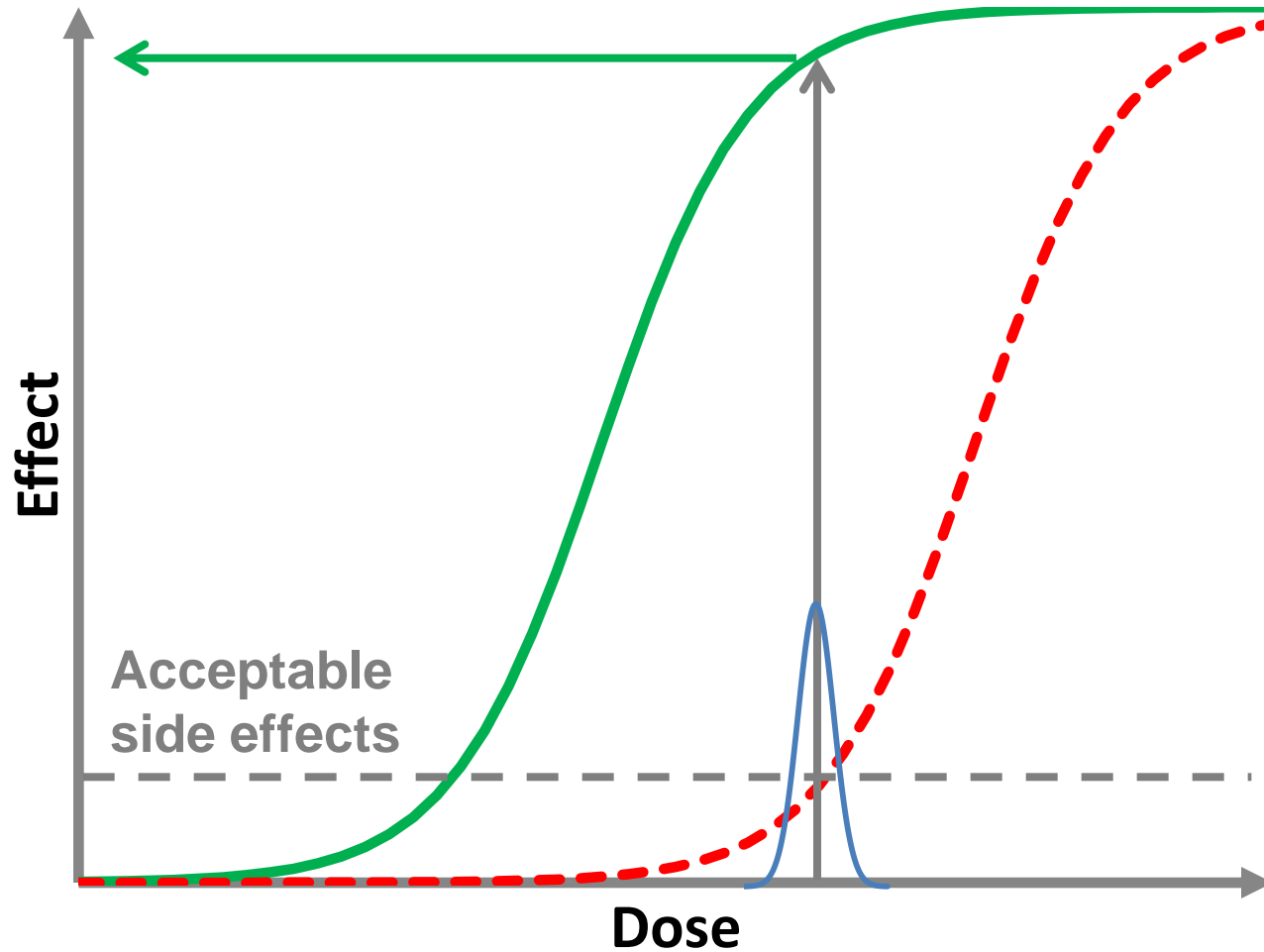
# Theranostics



Accurate dosimetry is essential for optimum use of the therapeutic window.



# Theranostics



Accurate dosimetry is essential for optimum use of the therapeutic window.

# Matched pairs for theranostics

<b>Sc 43</b> 3.89 h $\beta^+$ 1.2... $\gamma$ 373...	<b>Sc 44</b> 58.61 h    3.92 h $\gamma$ 271 $\gamma$ (1002, 1261, 1157) $\beta^+$ 1.5... $\gamma$ 1157...	<b>Sc 45</b> 100 $\sigma$ 10 + 17	<b>Sc 46</b> 18.75 s    83.79 d $\beta^-$ 0.4, 1.5 $\gamma$ 1121, 889... $\sigma$ 8.0 $\gamma$ 142	<b>Sc 47</b> 3.35 d $\beta^-$ 0.4, 0.6 $\gamma$ 159	<b>Sc 48</b> 43.67 h $\beta^-$ 0.7... $\gamma$ 984, 1312, 1038...	<b>Sc 49</b> 57.2 m $\beta^-$ 2.0 $\gamma$ (1762, 1623)
<b>Ca 42</b> 0.647 $\sigma$ 0.65	<b>Ca 43</b> 0.135 $\sigma$ 6	<b>Ca 44</b> 2.086 $\sigma$ 0.8	<b>Ca 45</b> 163 d $\beta^-$ 0.3... $\gamma$ (12), $e^-$ $\sigma$ ~15	<b>Ca 46</b> 0.004 $\sigma$ 0.70	<b>Ca 47</b> 4.54 d $\beta^-$ 0.7, 2.0... $\gamma$ 1297, 808, 489...	<b>Ca 48</b> 0.187 $1.9 \cdot 10^{19}$ a $2\beta^-, \beta^-$ $\sigma$ 1.09

$^{44}\text{Sc}$  for diagnostics

$^{47}\text{Sc}$  for therapy

# Question

Why is  $^{46}\text{Ca}$  so rare ?

$$^{46}\text{Ca}/\text{Ca} = 4\text{E-}5$$

Ca 40	Ca 41	Ca 42	Ca 43	Ca 44	Ca 45	Ca 46	Ca 47	Ca 48
96.941	$1.03 \cdot 10^5$ a	0.647	0.135	2.086	163 d	0.004	4.54 d	0.187
$\sigma$ 0.41 $\sigma_{n,\alpha}$ 0.00013	$\epsilon$ , no $\gamma$ $\sigma$ -4 $\sigma_{n,\alpha}$ 0.18 $\sigma_{n,p}$ 0.007	$\sigma$ 0.65	$\sigma$ 6	$\sigma$ 0.8	$\beta^-$ 0.3... $\gamma$ (12), $e^-$ $\sigma$ ~15	$\sigma$ 0.70	$\beta^-$ 0.7, 2.0... $\gamma$ 1297, 808 489...	$1.9 \cdot 10^{19}$ a $2\beta^-, \beta^-$ $\sigma$ 1.09

# Answer by B<sup>2</sup>FH and Olivier

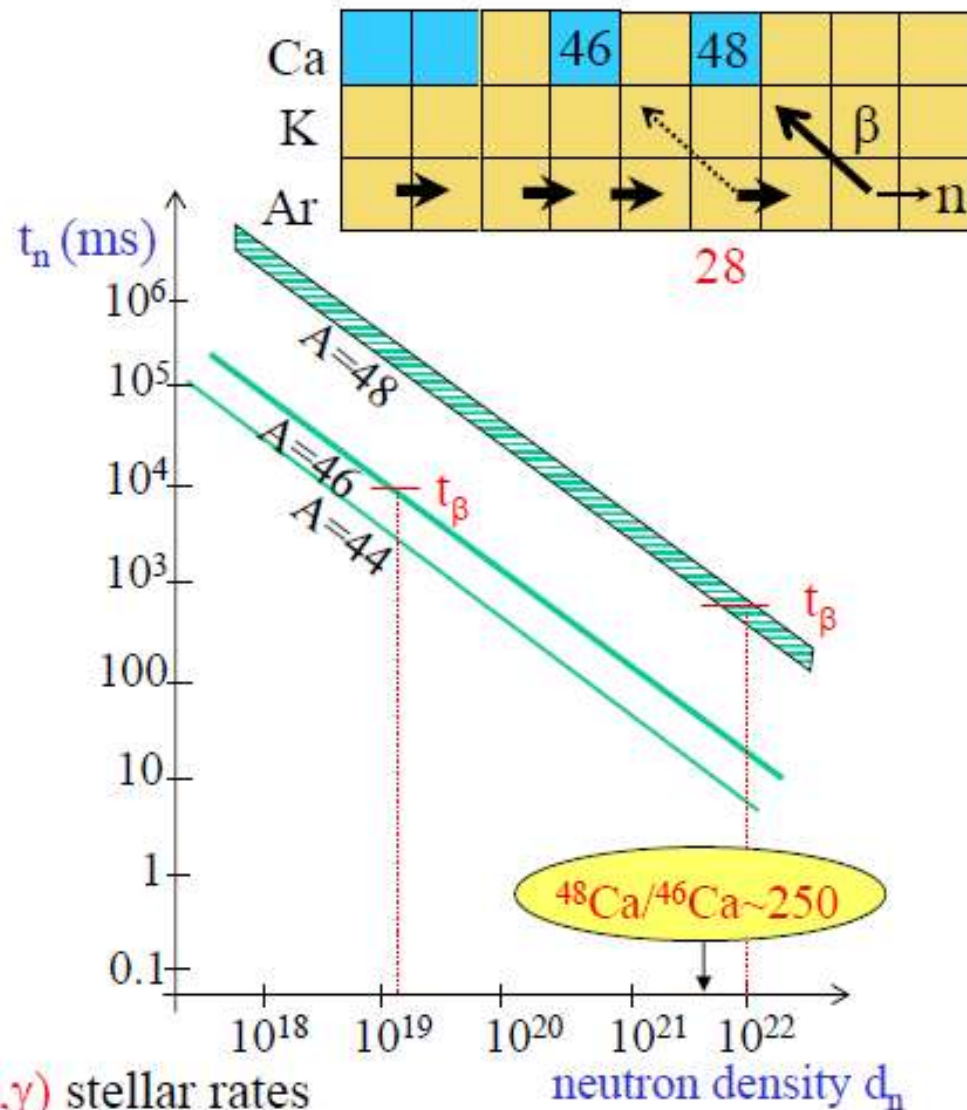
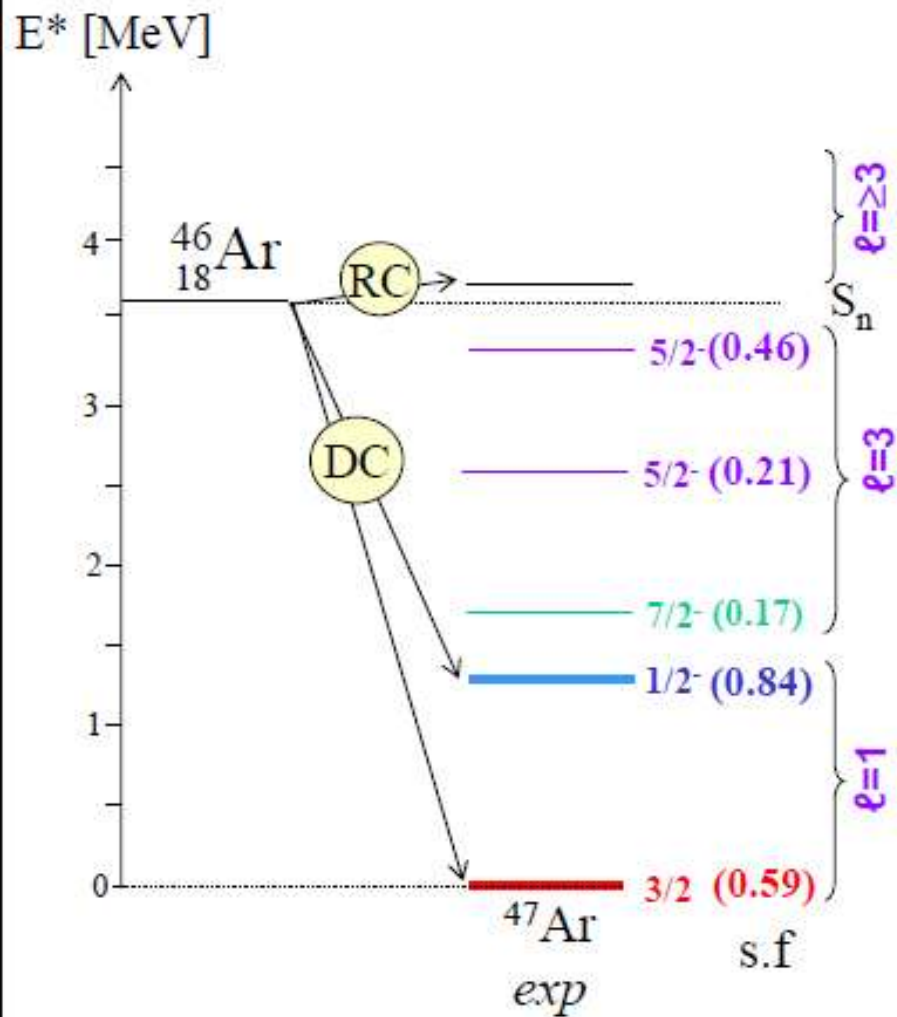
this region. Only for S<sup>36</sup>, Ca<sup>46</sup>, and Ca<sup>48</sup> in this region is there no other method of production than the *r* process.

<b>Sc 43</b> 3.89 h  β <sup>+</sup> 1.2... γ 373...	<b>Sc 44</b> 58.61 h 3.92 h ly 271 c γ (1002 1261 1157) β <sup>+</sup> 1.5... γ 1157...	<b>Sc 45</b> 100 σ 10 + 17	<b>Sc 46</b> 18.75 s 83.79 d ly 142 β <sup>-</sup> 0.4, 1.5 γ 1121 899... σ 8.0	<b>Sc 47</b> 3.35 d β <sup>-</sup> 0.4, 0.6 γ 159	<b>Sc 48</b> 43.67 h β <sup>-</sup> 0.7... γ 984, 1312 1038...	<b>Sc 49</b> 57.2 m β <sup>-</sup> 2.0 γ (1762, 1623)	<b>Sc 50</b> 1.7 m β <sup>-</sup> 3.7, 4.2... γ 1554, 1121 524...	<b>Sc 51</b> 12.4 s β <sup>-</sup> 4.3, 5.0... γ 1437, 2144 1568...
<b>Ca 42</b> 0.647 σ 0.65	<b>Ca 43</b> 0.135 σ 6	<b>Ca 44</b> 2.086 σ 0.8	<b>Ca 45</b> 163 d β <sup>-</sup> 0.3... γ (12), e <sup>-</sup> σ -15	<b>Ca 46</b> 0.004 σ 0.70	<b>Ca 47</b> 4.54 d β <sup>-</sup> 0.7, 2.0... γ 1297, 808 489...	<b>Ca 48</b> 0.187 1.9·10 <sup>19</sup> a 2β <sup>-</sup> , β <sup>-</sup> σ 1.09	<b>Ca 49</b> 8.72 m β <sup>-</sup> 2.2, 2.9... γ 3084, 4072...	<b>Ca 50</b> 13.9 s β <sup>-</sup> 3.1 γ 257, 1519, 72 1591
<b>K 41</b> 6.7302 σ 1.46	<b>K 42</b> 12.36 h β <sup>-</sup> 3.5... γ 1525...	<b>K 43</b> 22.2 h β <sup>-</sup> 0.8, 1.8... γ 373, 618...	<b>K 44</b> 22.13 m β <sup>-</sup> 5.7... γ 1157, 2151...	<b>K 45</b> 17.8 m β <sup>-</sup> 2.3, 4.2... γ 174, 1706...	<b>K 46</b> 115 s β <sup>-</sup> 6.4... γ 1347, 3700...	<b>K 47</b> 17.5 s β <sup>-</sup> 4.1... γ 2013, 586 565	<b>K 48</b> 6.8 s β <sup>-</sup> 5.3, 8.4... γ 3832, 780... βn 0.23...	<b>K 49</b> 1.26 s β <sup>-</sup> 4.0, 10.5... βn 1.38, 1.51 0.44... γ 4272, 2249...
<b>Ar 40</b> 99.6035 σ 0.64	<b>Ar 41</b> 1.83 h β <sup>-</sup> 1.2, 2.5... γ 1294... σ 0.5	<b>Ar 42</b> 33 a β <sup>-</sup> -0.6 no γ	<b>Ar 43</b> 5.37 m β <sup>-</sup> γ 975, 738 1440...	<b>Ar 44</b> 11.87 m β <sup>-</sup> γ 183, 1703 1886...	<b>Ar 45</b> 21.5 s β <sup>-</sup> 3.2, 5.8... γ 1020, 3707 61...	<b>Ar 46</b> 7.8 s β <sup>-</sup> γ 1944...	<b>Ar 47</b> 1.23 s β <sup>-</sup> 9.8... γ 360, 1660 1742...	<b>Ar 48</b> 475 ms β <sup>-</sup>
<b>Cl 39</b> 56 m β <sup>-</sup> 1.9, 3.4... γ 1287, 250 1517...	<b>Cl 40</b> 1.35 m β <sup>+</sup> 3.2, 7.5... γ 1461, 2840 2622...	<b>Cl 41</b> 38.4 s β <sup>-</sup> 3.8... γ 167, 515...	<b>Cl 42</b> 6.9 s β <sup>-</sup> γ 1207...	<b>Cl 43</b> 3.13 s β <sup>-</sup> 6.1, 7.8... γ 762, 1032 679...	<b>Cl 44</b> 0.56 s β <sup>-</sup> γ 1158, 853 2796, 2010... βn	<b>Cl 45</b> 413 ms β <sup>-</sup> γ 542 - 2751 βn	<b>Cl 46</b> 223 ms β <sup>-</sup> βn	<b>Cl 47</b> 101 ms β <sup>-</sup> βn?





# Neutron capture rates on $^{44,46,48}\text{Ar}$



(d,p) access to  $E^*$ , s.f., spins  $\rightarrow$  derive (n, $\gamma$ ) stellar rates

Direct capture (E1) with  $l_n = 0$  on  $p$  states dominates

Speed up neutron-captures at the N=28 closed shell

collab. with T.Rauscher

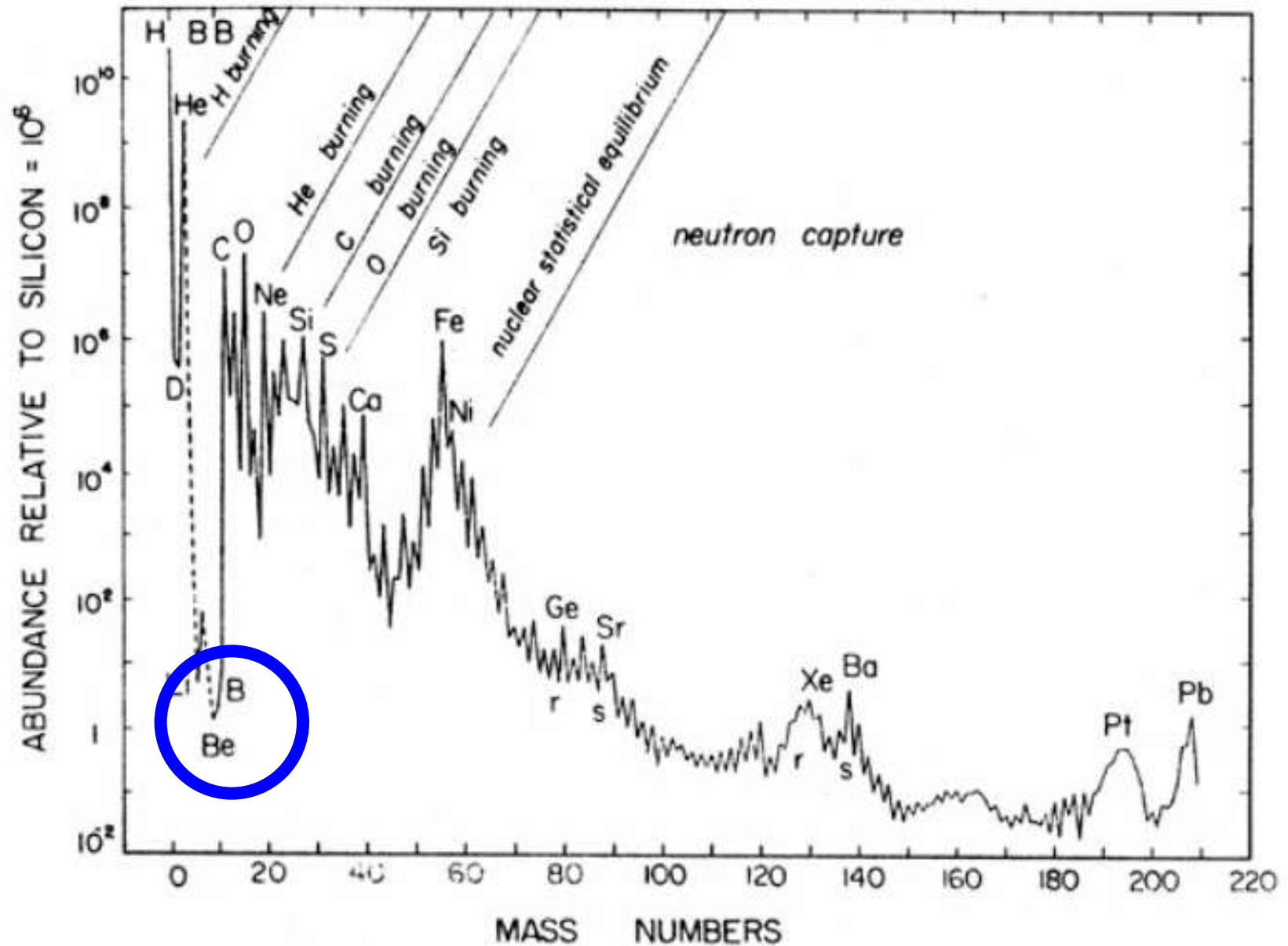
# Terbium: a unique element for nuclear medicine



<b>Dy 150</b> 7.2 m	<b>Dy 151</b> 17 m	<b>Dy 152</b> 2.4 h	<b>Dy 153</b> 6.29 h	<b>Dy 154</b> 3.0 · 10 <sup>6</sup> a	<b>Dy 155</b> 10.0 h	<b>Dy 156</b> 0.056	<b>Dy 157</b> 8.1 h	<b>Dy 158</b> 0.095	<b>Dy 159</b> 144.4 d	<b>Dy 160</b> 2.329	<b>Dy 161</b> 18.889	<b>Dy 162</b> 25.475
<b>Tb 149</b> 4.2 m	<b>Tb 150</b> 8.8 m	<b>Tb 151</b> 25 a	<b>Tb 152</b> 4.2 m	<b>Tb 153</b> 2.34 d	<b>Tb 154</b> 23 h	<b>Tb 155</b> 5.32 d	<b>Tb 156</b> 5.4 h	<b>Tb 157</b> 99 a	<b>Tb 158</b> 10.5 a	<b>Tb 159</b> 100	<b>Tb 160</b> 72.3 d	<b>Tb 161</b> 6.90 d
<b>Gd 148</b> 74.6 a	<b>Gd 149</b> 9.28 d	<b>Gd 150</b> 1.8 · 10 <sup>6</sup> a	<b>Gd 151</b> 120 d	<b>Gd 152</b> 0.20	<b>Gd 153</b> 239.47 d	<b>Gd 154</b> 2.18	<b>Gd 155</b> 14.80	<b>Gd 156</b> 20.47	<b>Gd 157</b> 15.65	<b>Gd 158</b> 24.84	<b>Gd 159</b> 18.48 h	<b>Gd 160</b> 21.86



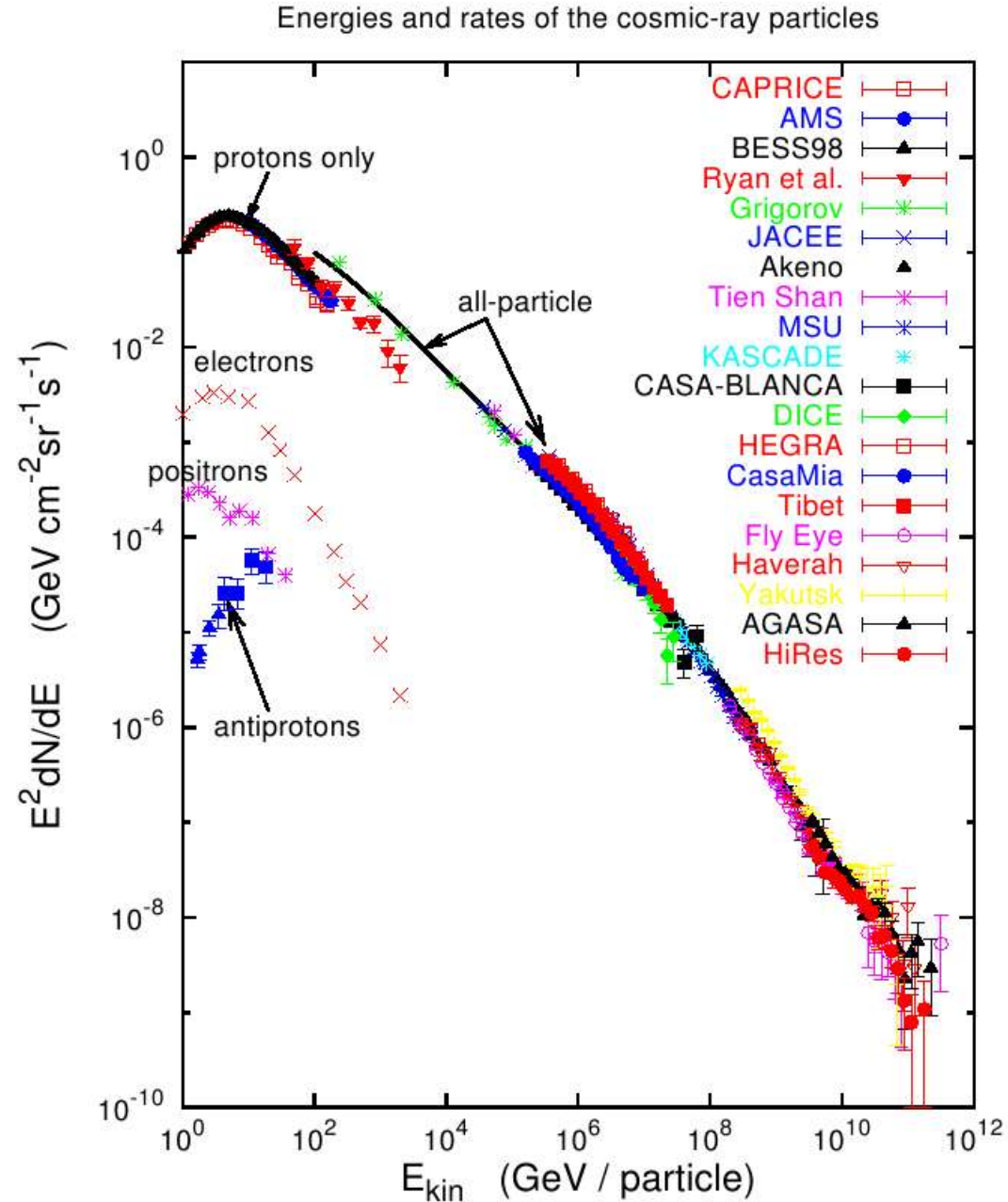
# Question: How is Be and B produced ?



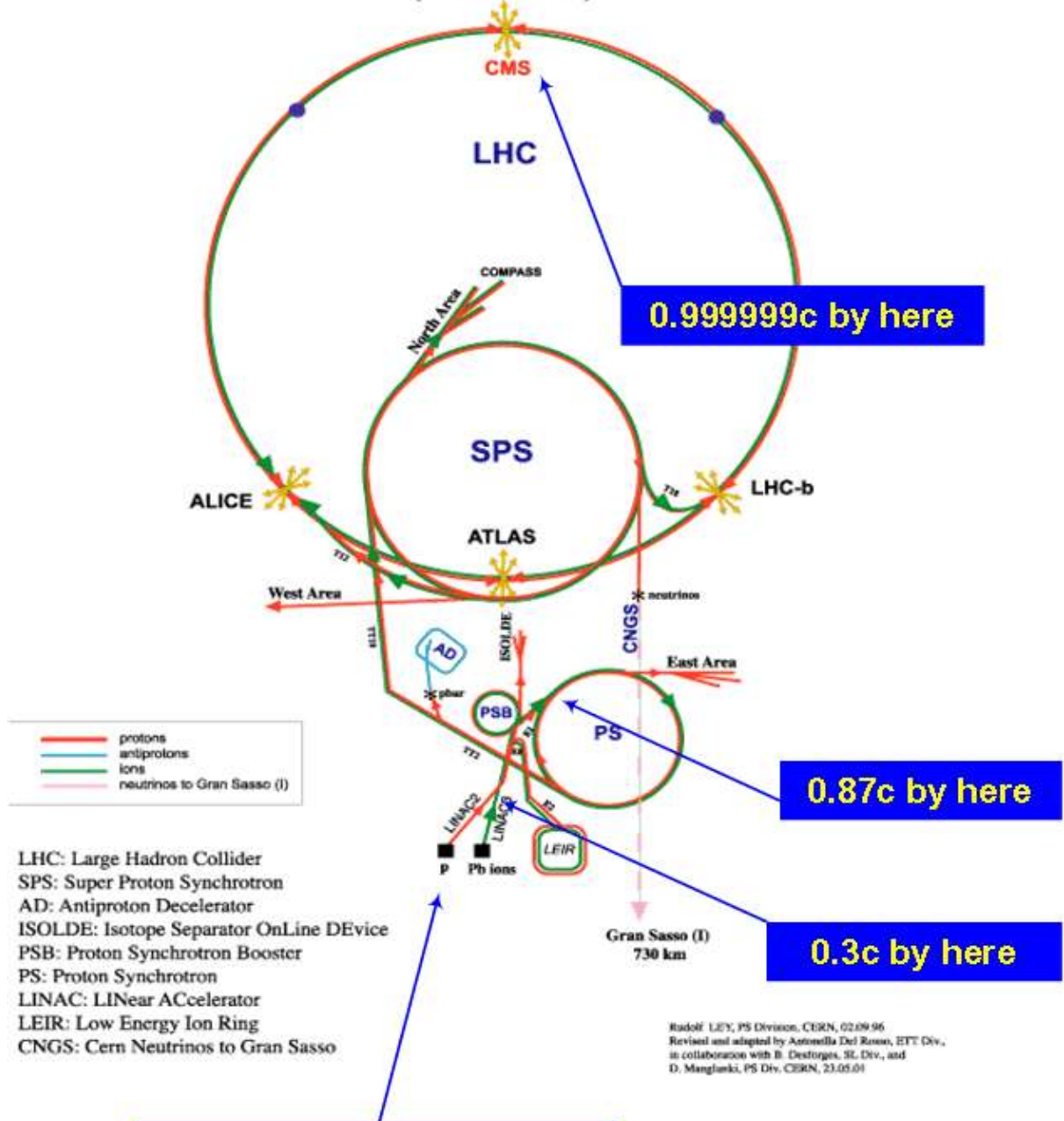


# Answer: spallation production

$^{12}\text{C}(p, X)$   
 $^{16}\text{O}(p, X)$   
etc.



# CERN Accelerators (not to scale)



— protons  
— antiprotons  
— ions  
— neutrinos to Gran Sasso (I)

LHC: Large Hadron Collider  
 SPS: Super Proton Synchrotron  
 AD: Antiproton Decelerator  
 ISOLDE: Isotope Separator OnLine DEvice  
 PSB: Proton Synchrotron Booster  
 PS: Proton Synchrotron  
 LINAC: LINEar ACcelerator  
 LEIR: Low Energy Ion Ring  
 CNGS: Cern Neutrinos to Gran Sasso

**0.999999c by here**

**0.87c by here**

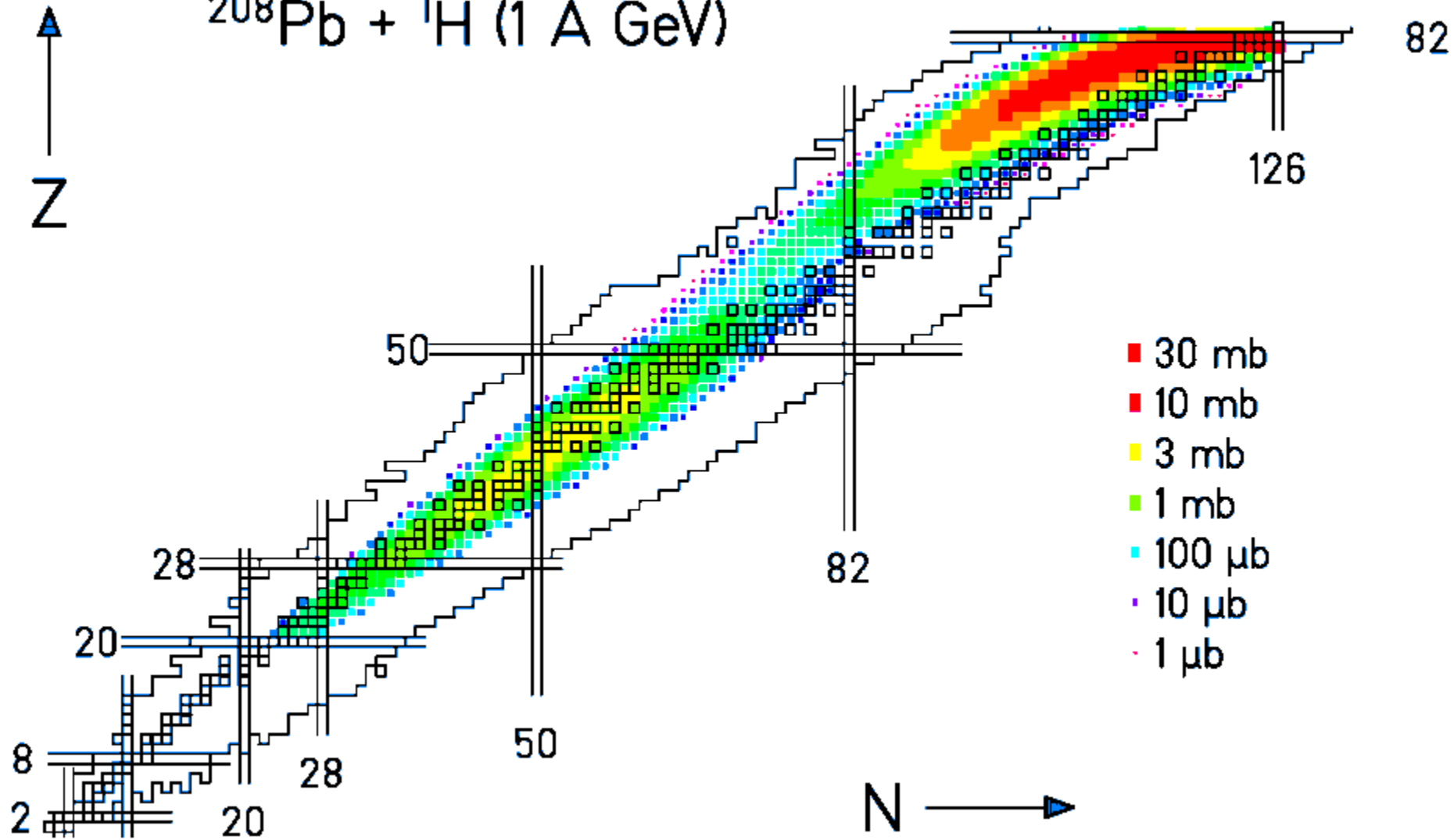
**0.3c by here**

**Start the protons out here**

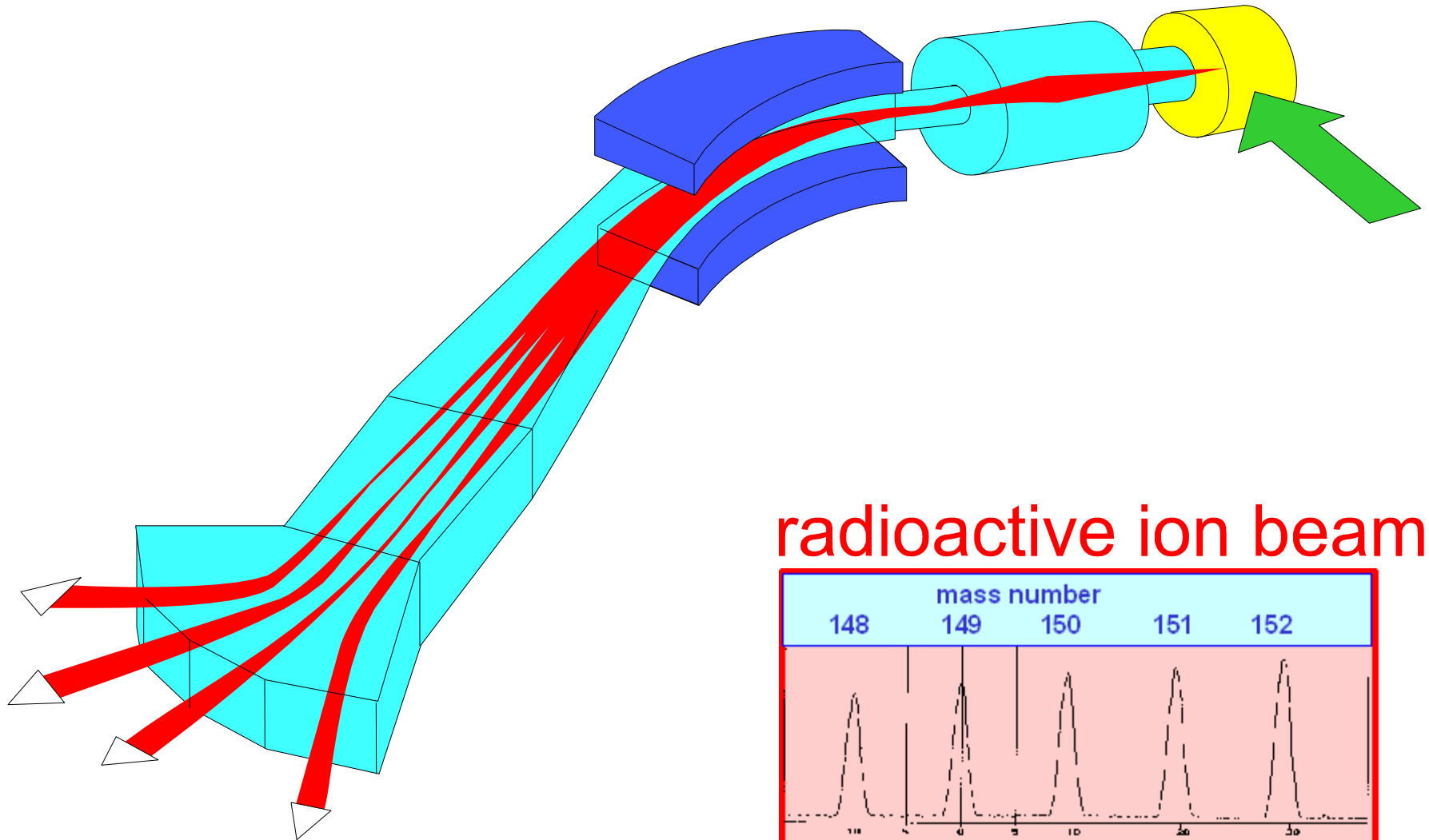
Rudolf LEY, PS Division, CERN, 02.09.96  
 Revised and adapted by Antonella Del Rossa, ETI Div.,  
 in collaboration with B. Destorques, ST, Div., and  
 D. Manghanti, PS Div, CERN, 23.05.01

# High energy proton induced reactions

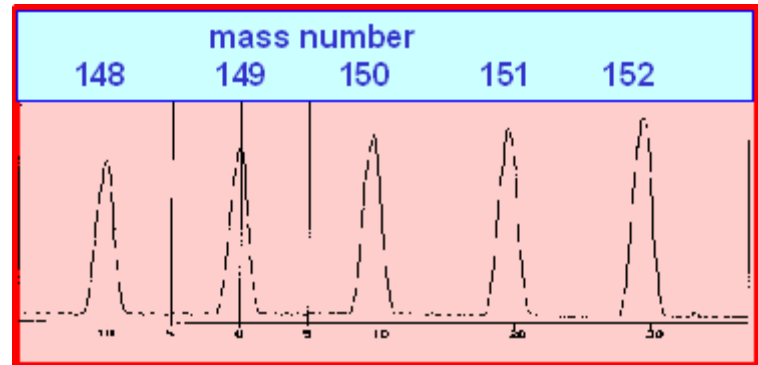
$^{208}\text{Pb} + ^1\text{H}$  (1 A GeV)



# Production of $^{149}\text{Tb}$ , $^{152}\text{Tb}$ and $^{155}\text{Tb}$ at ISOLDE

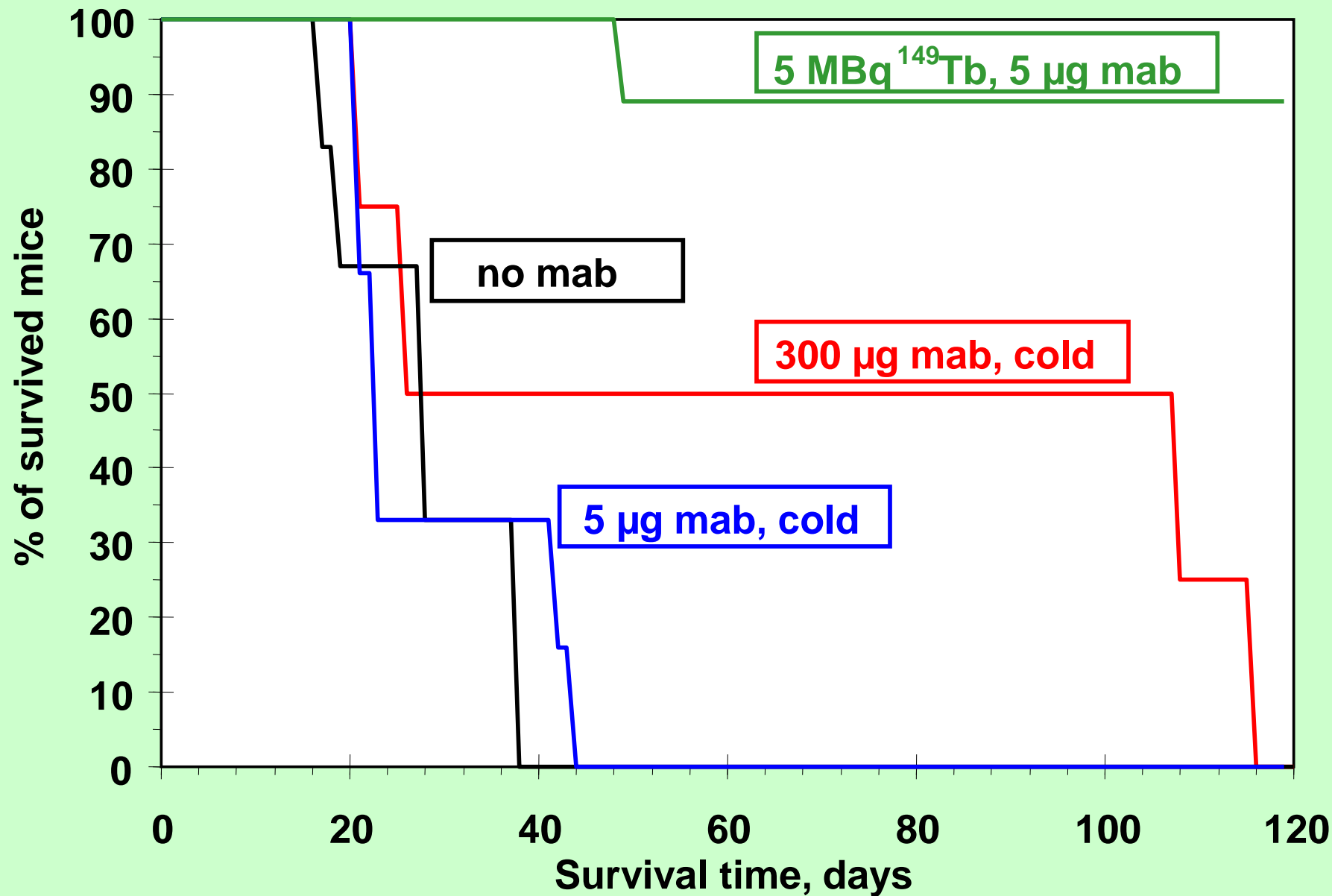


radioactive ion beams





# Preclinical study with lymphoma mouse model

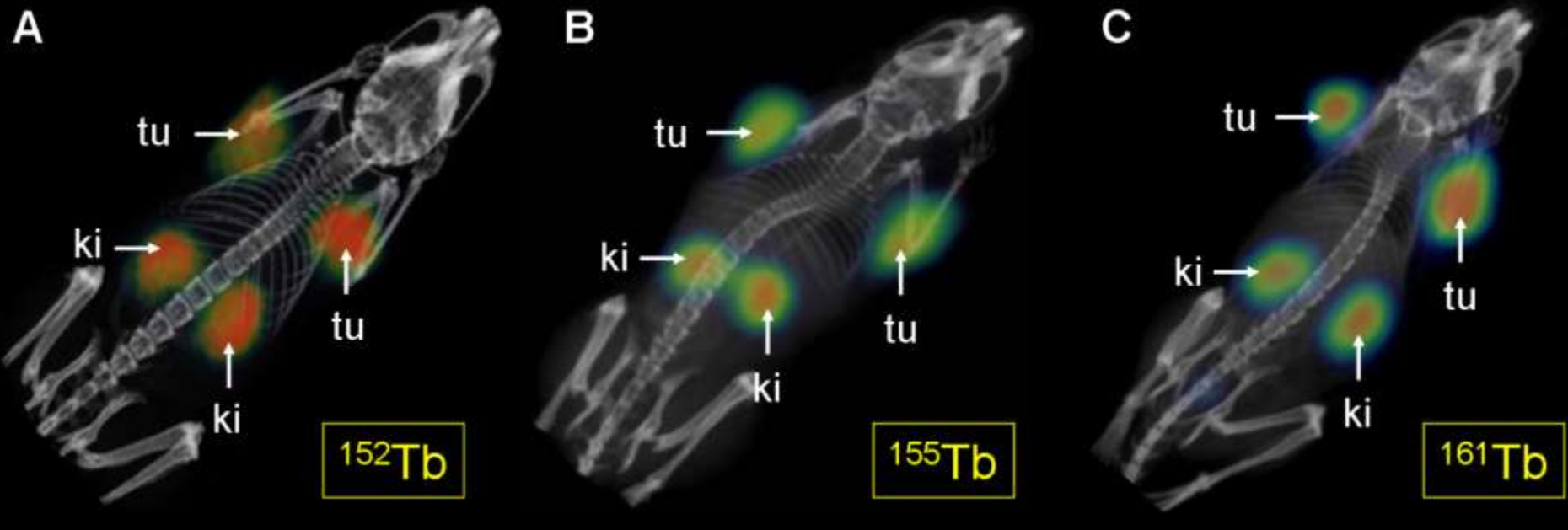


# Theranostics with terbium isotopes

*PET*

*SPECT*

*SPECT*



ISOLDE



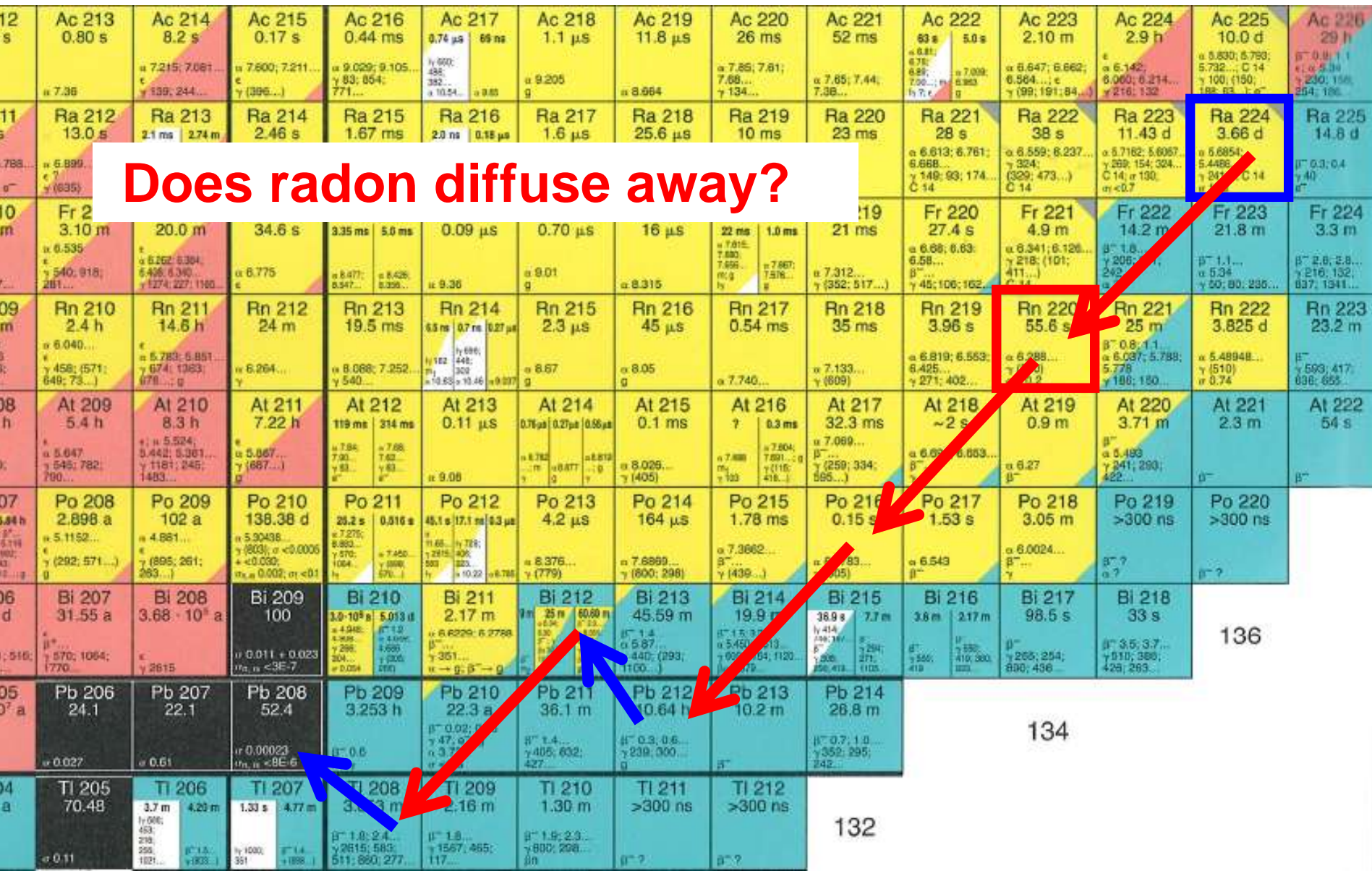
ISOLDE

PAUL SCHERRER INSTITUT  
PSI

ILL  
NEUTRONS  
FOR SCIENCE

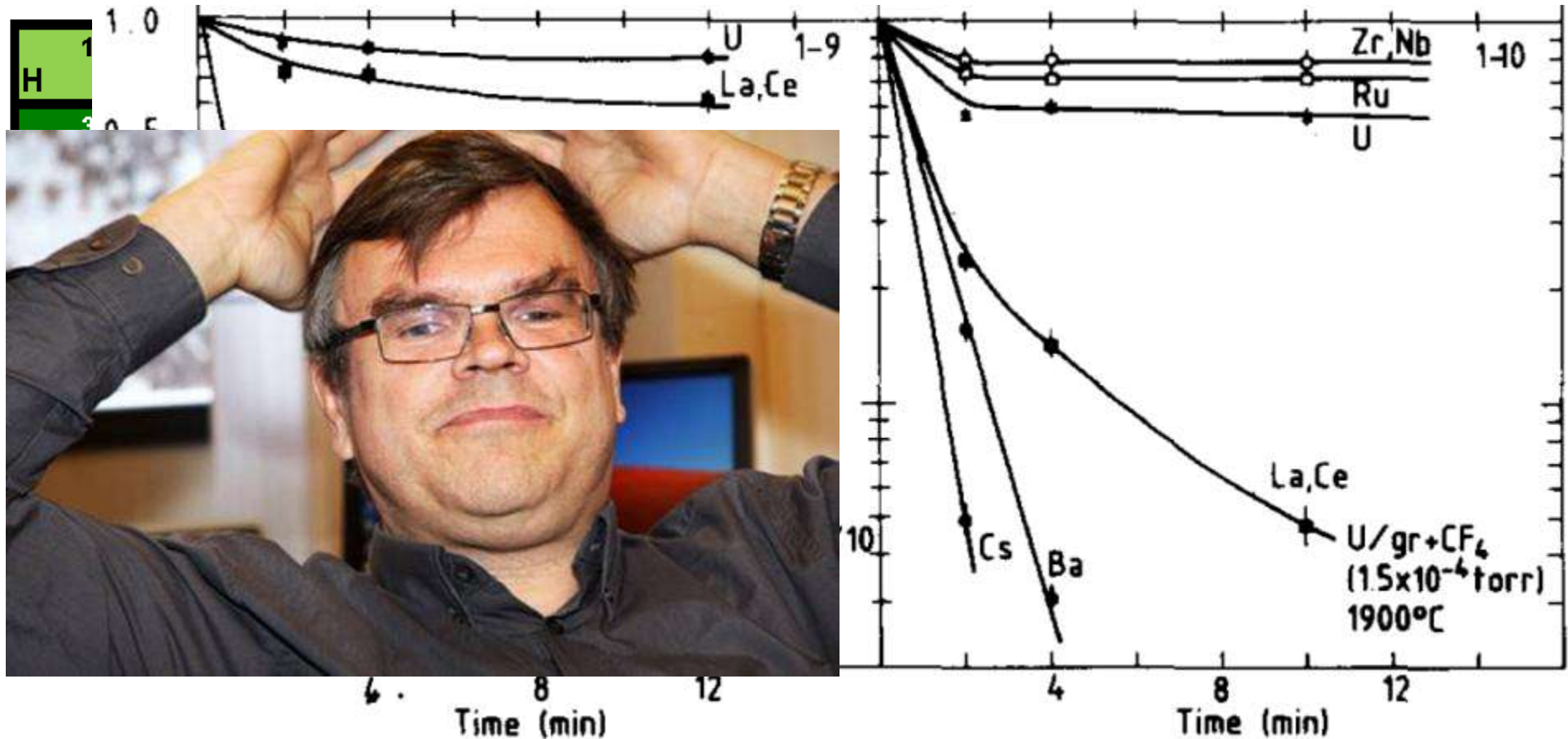
Radio-nuclide	Half-life	Daughters	Half-life	Cumulative $\alpha$ /decay	$E_{\alpha}$ mean (MeV)	Range ( $\mu\text{m}$ )
Tb-149	4.1 h			0.17	3.97	25
<i>Pb-212</i>	<i>10.6 h</i>	Bi-212 Po-212	1.01 h 0.3 $\mu\text{s}$	1	7.74	65
Bi-212	1.01 h	Po-212	0.3 $\mu\text{s}$	1	7.74	65
<i>Bi-213</i>	<i>0.76 h</i>	Po-213	4 $\mu\text{s}$	1	8.34	75
At-211	7.2 h	Po-211	0.5 s	1	6.78	55
Ra-223	11.4 d	Rn-219 Po-215 <i>Pb-211</i> Bi-211	4 s 1.8 ms <i>0.6 h</i> 130 s	4	6.59	>50
Ra-224	3.66 d	Rn-220 Po-216 <i>Pb-212</i> Bi-212	56 s 0.15 s <i>10.6 h</i> 1.01 h	4	6.62	>50
Ac-225	10.0 d	Fr-221 At-217 <i>Bi-213</i> Po-213	294 s 32 ms <i>0.76 h</i> 4 $\mu\text{s}$	4	6.88	>50

# Isotopes for targeted alpha therapy





# Radioisotopes available at ISOLDE-CERN



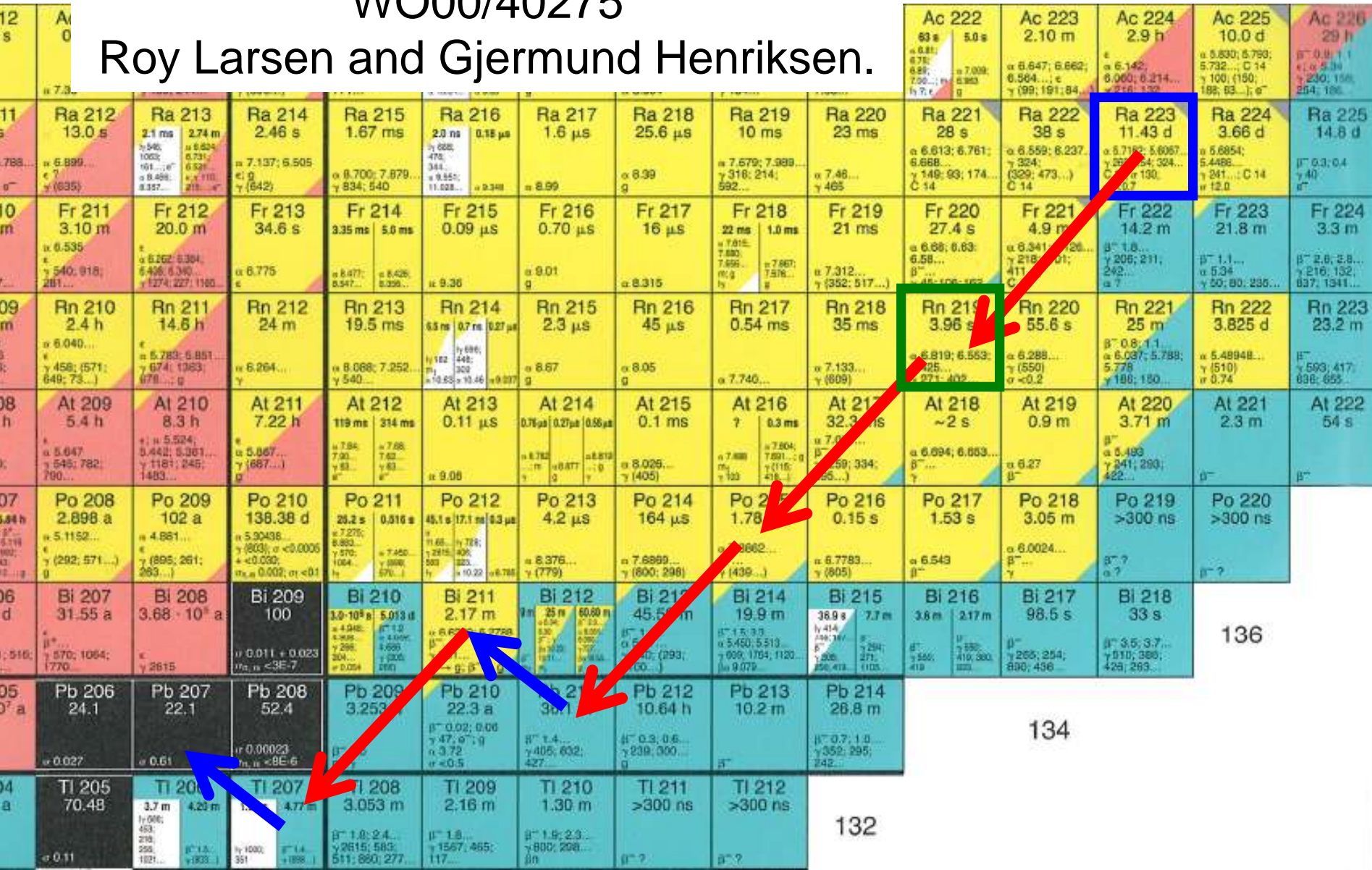
90	91	92	93	94	95	96	97	98	99	100	101	102	103
Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Diffusion and release measurements to develop new beams  
 e.g. *P. Hoff et al., NIM 221 (1984) 313.*

# Isotopes for targeted alpha therapy

WO00/40275

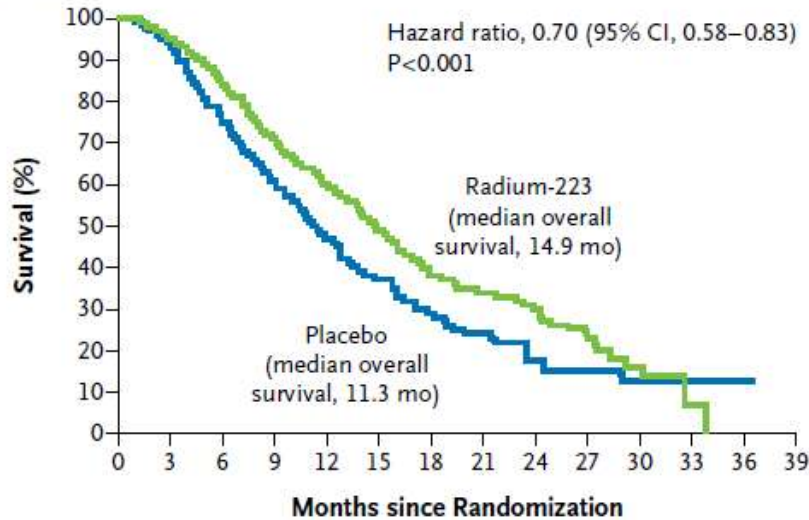
Roy Larsen and Gjermund Henriksen.





# $^{223}\text{Ra}$ : Alpharadin/Xofigo

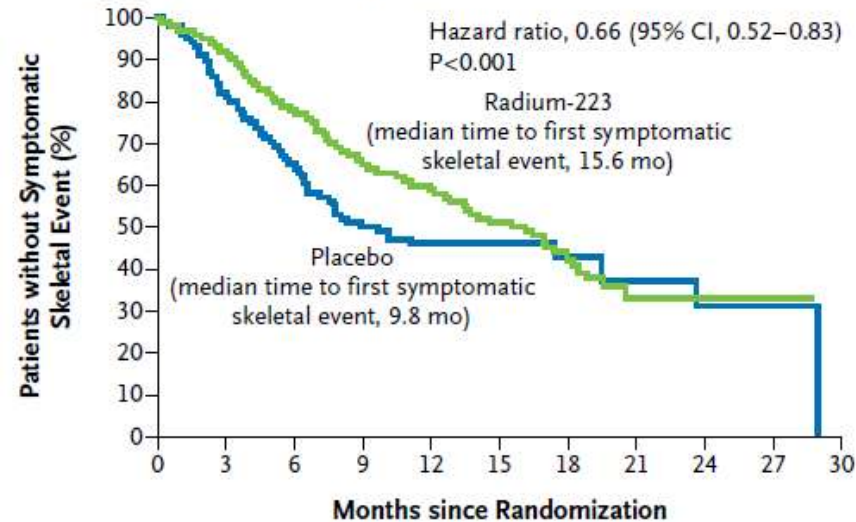
**A Overall Survival**



**No. at Risk**

Radium-223	614	578	504	369	274	178	105	60	41	18	7	1	0	0
Placebo	307	288	228	157	103	67	39	24	14	7	4	2	1	0

**B Time to First Symptomatic Skeletal Event**



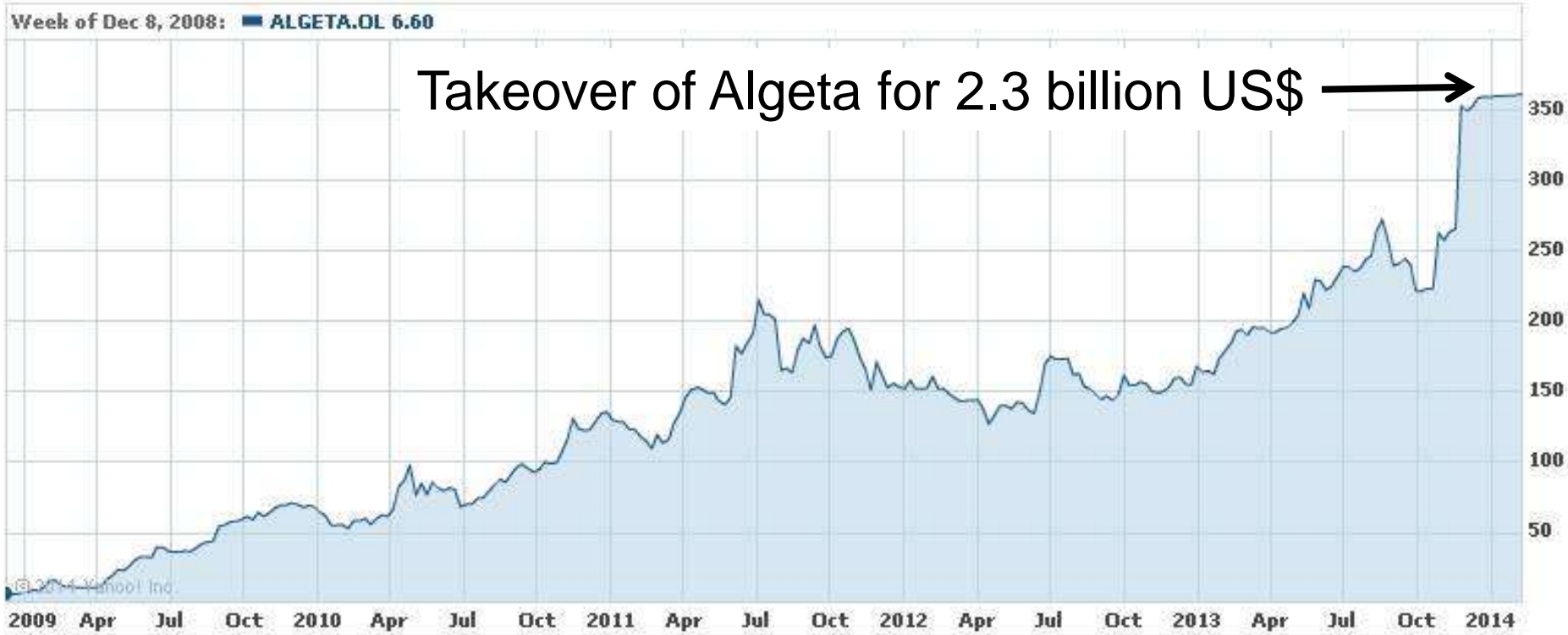
**No. at Risk**

Radium-223	614	496	342	199	129	63	31	8	8	1	0
Placebo	307	211	117	56	36	20	9	7	4	1	0

C. Parker, S. Nilsson, D. Heinrich, S.I. Helle, J.M. O'Sullivan, S.D. Fosså, A. Chodacki, P. Wiechno, J. Logue, M. Seke, A. Widmark, D.C. Johannessen, P. Hoskin, D. Bottomley, N.D. James, A. Solberg, I. Syndikus, J. Kliment, S. Wedel, S. Boehmer, M. Dall'Oglio, L. Franzén, R. Coleman, N.J. Vogelzang, C.G. O'Bryan-Tear, K. Staudacher, J. Garcia-Vargas, M. Shan, Ø.S. Bruland, and O. Sartor, for the ALSYMPCA Investigators\*

*The* **NEW ENGLAND**  
**JOURNAL of MEDICINE**

# Prospects of targeted alpha therapies ?



SANOFI



**AREVA Med**  
*<sup>212</sup>Pb for Powerful Targeted Therapies*



Bayer HealthCare



# Targeted radionuclide therapies in the clinic

**Thyroid:**  $^{131}\text{I}$

**Brain:**  $^{90}\text{Y}$ -mab,  $^{131}\text{I}$ -mab (I/II),  $^{211}\text{At}$ -mab (I),  $^{213}\text{Bi}$ -pept.(I)

**Lymphoma:**  
**Zevalin®** ( $^{90}\text{Y}$ -mab)  
**Bexxar®** ( $^{131}\text{I}$ -mab)  
 $^{131}\text{I}/^{177}\text{Lu}$ -mabs (I/II)

**Leukemia, myeloma:**  
 $^{90}\text{Y}$ -mab,  $^{213}\text{Bi}$ -mab (II)  
 $^{225}\text{Ac}$ -mab

**Bone metastases:**  
**Metastron®** ( $^{90}\text{SrCl}_2$ )  
**Quadramet®** ( $^{153}\text{Sm-EDTMP}$ )  
**Zofigo®** ( $^{223}\text{RaCl}_2$ )

**Medullary Thyroid:**  
 $^{131}\text{I}$ -mab (II)  
 $^{90}\text{Y}$ -pept.

**Neuroblastoma:**  
 $^{131}\text{I}$ -MIBG

**Breast:**  
 $^{90}\text{Y}$ -mab,  $^{90}\text{Y}$ -pept.  
 $^{212}\text{Pb}$ -mab (I)

**Neuroendocrine (GEP-NET):**  
 $^{177}\text{Lu}$ -peptides (III)  
 $^{90}\text{Y}$ -peptides

**Lung (SCLC):**  
 $^{177}\text{Lu}$ -mab (II)

**Liver (HCC):**  
**Theraspheres® & SIRspheres®** ( $^{90}\text{Y}$ )

**Pancreas:**  
 $^{90}\text{Y}$ -mab (II)

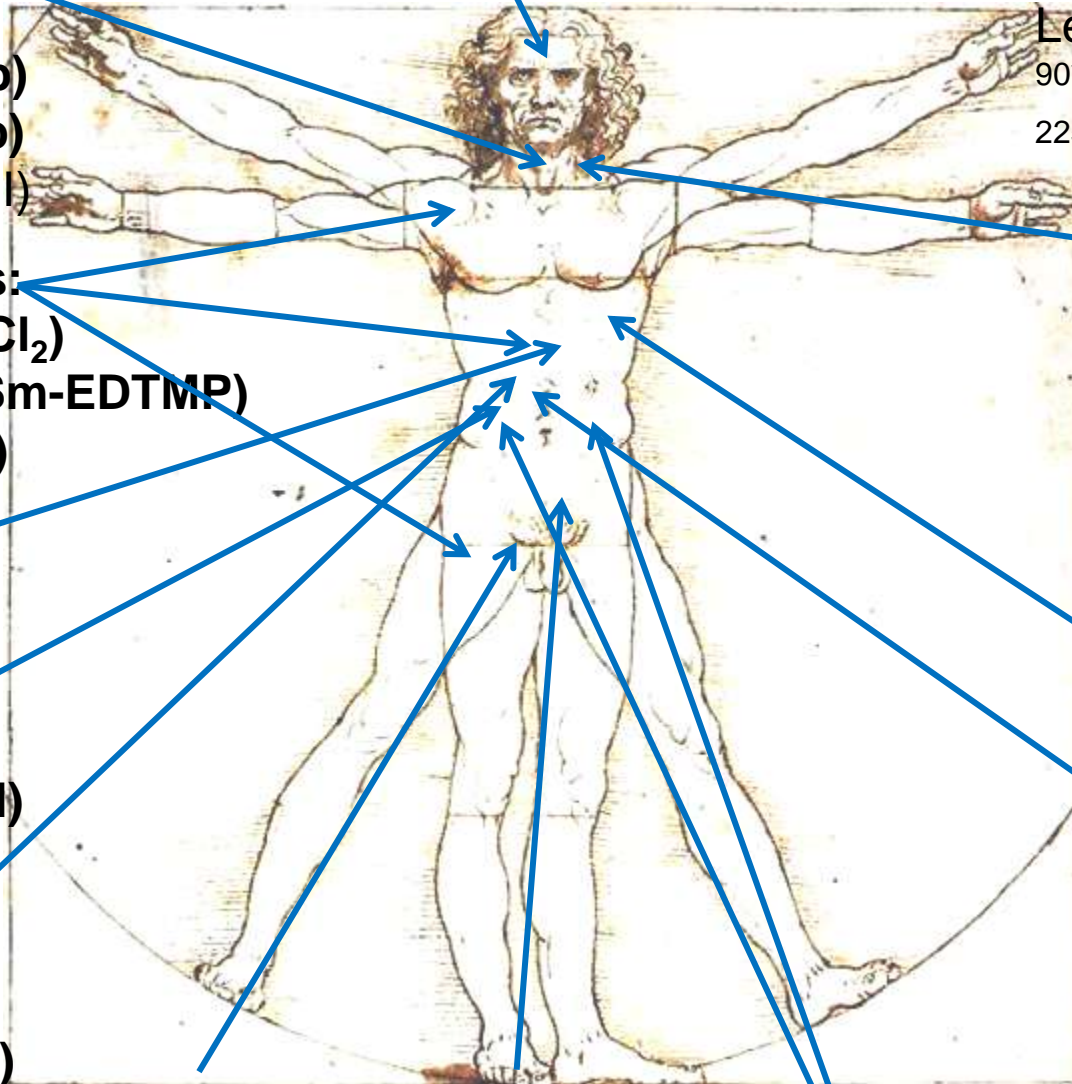
$^{188}\text{Re}$ -Lipiodol (II)  
 $^{166}\text{Ho}$ -microspheres

**Colon & rectum:**  
 $^{131}\text{I}$ -mab (II)

**Prostate:**  
 $^{177}\text{Lu}$ -mab (II)

**Kidneys (RCC):**  
 $^{90}\text{Y}/^{177}\text{Lu}$ -mab (I)

**Melanoma:**  
 $^{213}\text{Bi}$ -mab(I)



# Radionuclides for RIT and PRRT

Radio-nuclide	Half-life	E mean (keV)	E <sub>γ</sub> (B.R.) (keV)	Range
<b>Y-90</b>	64 h	934 β	-	<b>12 mm</b>
<b>I-131</b>	8 days	182 β	364 (82%)	<b>3 mm</b>
<b>Lu-177</b>	7 days	134 β	208 (10%) 113 (6%)	<b>2 mm</b>
<b>Tb-161</b>	7 days	154 β 5, 17, 40 e <sup>-</sup>	75 (10%)	<b>2 mm</b> <b>1-30 μm</b>
<b>Tb-149</b>	4.1 h	3967 α	165,..	<b>25 μm</b>
<b>Ge-71</b>	11 days	8 e <sup>-</sup>	-	<b>1.7 μm</b>
<b>Er-165</b>	10.3 h	5.3 e <sup>-</sup>	-	<b>0.6 μm</b>

**cross-fire**

**Estab-  
lished  
isotopes**

**Emerging  
isotopes**

**R&D  
isotopes:  
supply-  
limited!**

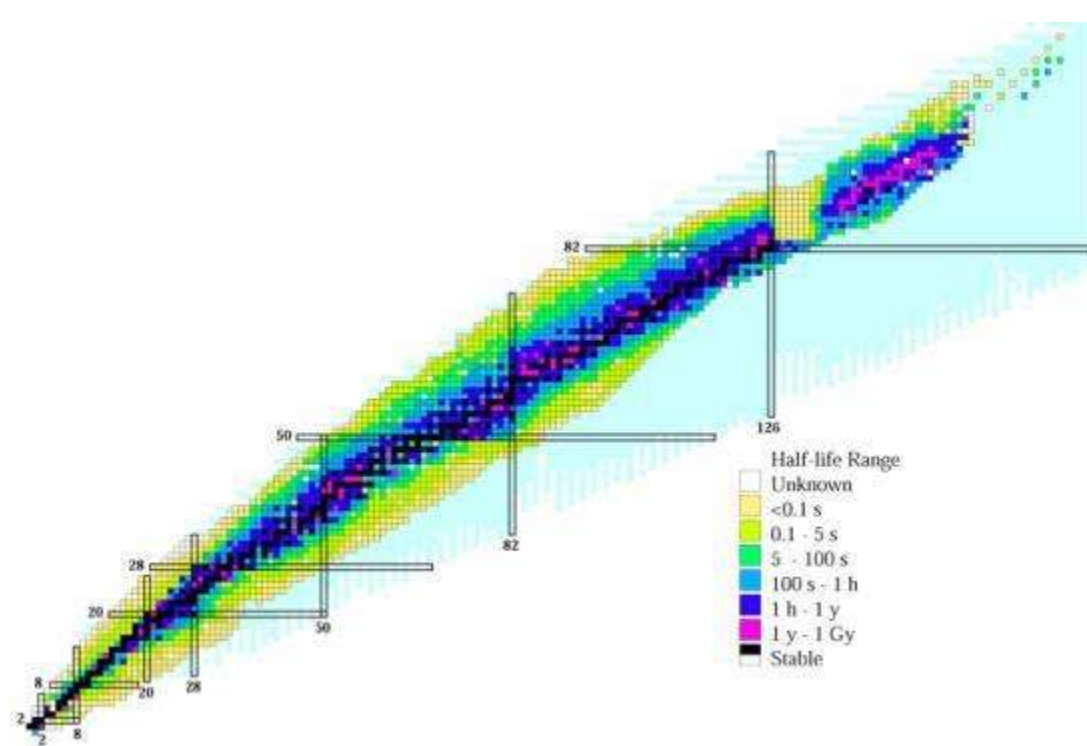
**localized**

**Modern, better targeted bioconjugates require shorter-range radiation ⇒ need for **adequate (R&D) radioisotope supply.****



Paracelsus (1493-1541)  
“Many have said of Alchemy,  
that it is for the making of gold  
and silver. For me such is not  
the aim, but to consider only  
what virtue and power may lie  
in medicines.”

(Edwardes)



500 years later:  
“Many have said of nuclear physics,  
that it is for the making of gold and  
silver (and other elements’) isotopes.  
For us such is not the only aim, but  
also to consider what virtue and  
power may lie in it for medicine.”