Nuclear Technologies 3

Ulli Köster (koester@ill.fr)
Institut Laue-Langevin Grenoble
&
Université Grenoble Alpes

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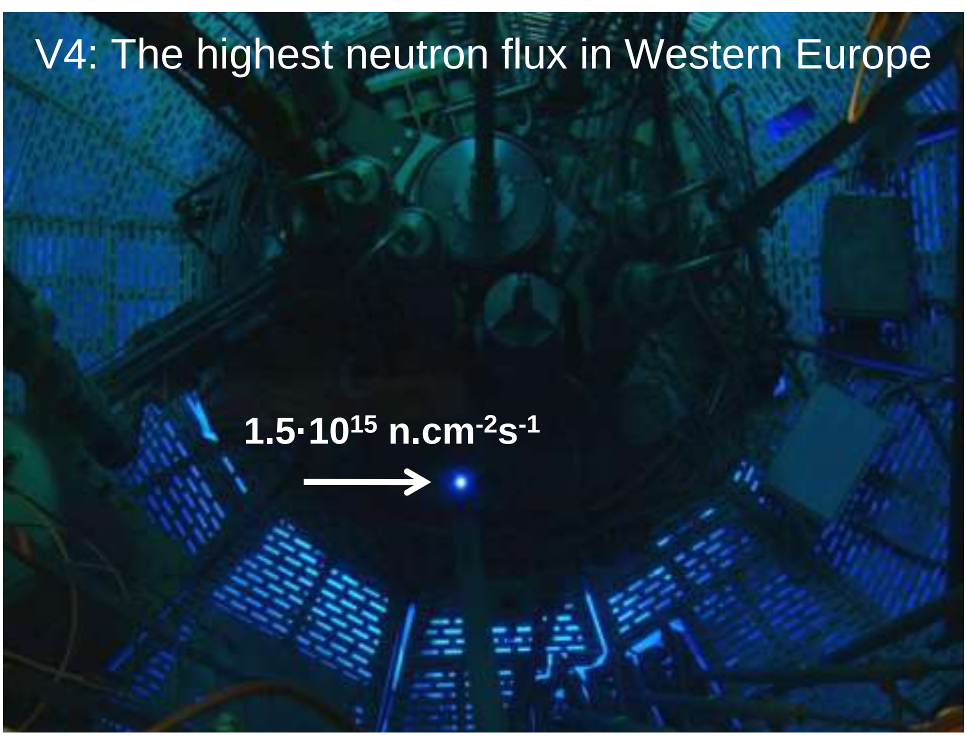
Institut Max von Laue – Paul Langevin

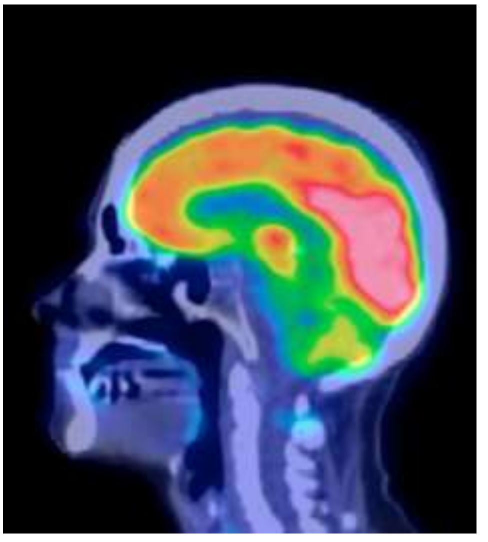
- founded 1967
- today governed by "associates" FR, DE, UK
  + member states: ES, CH, AT, IT, CZ, SE, BE, SK, DK, PL, SI
- over 40 instruments, mainly for neutron scattering,
  but also nuclear or particle physics
- user facility: >1400 scientific visitors from 40 countries per year

The LOHENGRIN fission fragment spectrometer



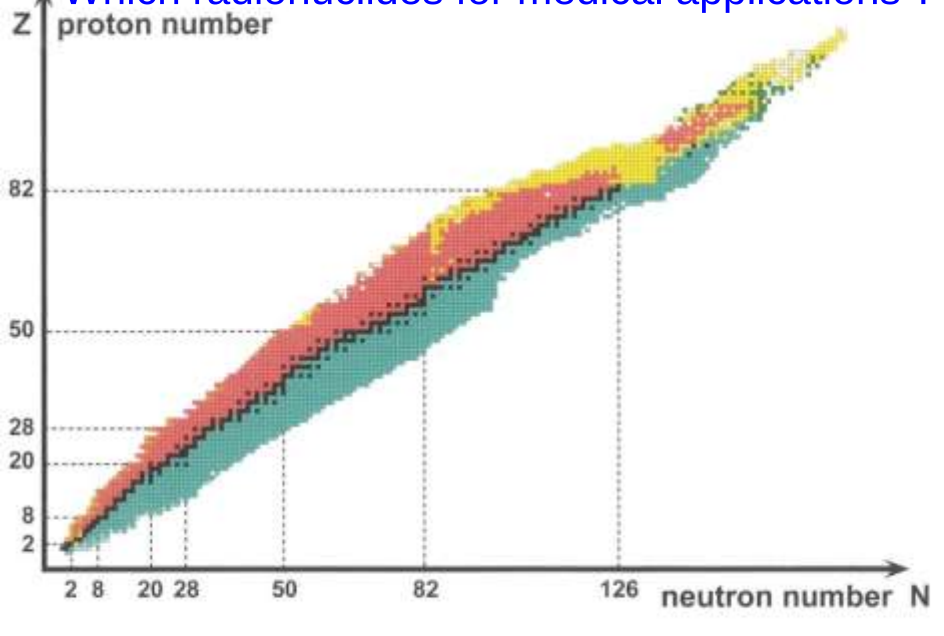
Structural imaging versus functional imaging
molecular imaging

Radiology

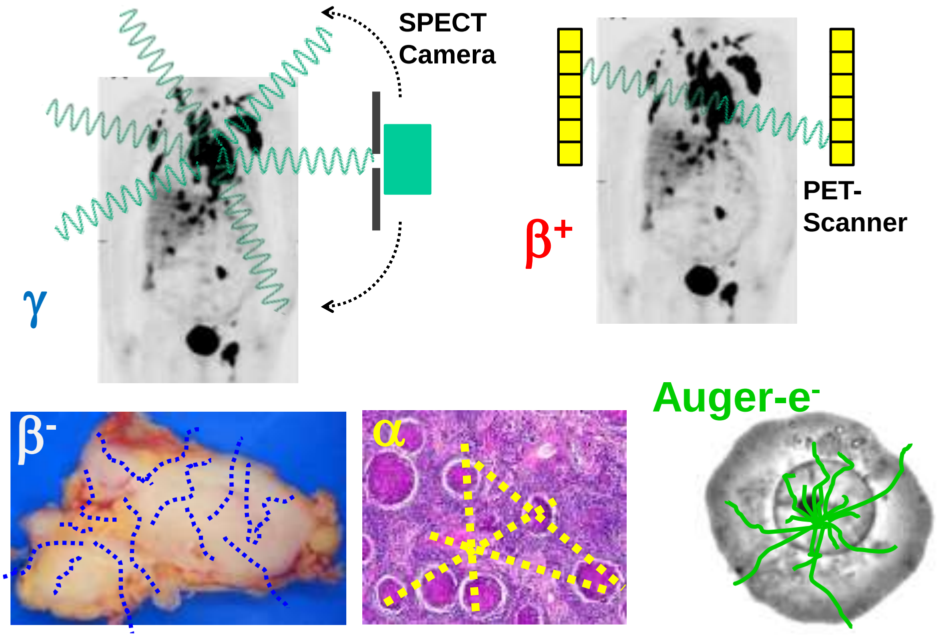


Nuclear Medicine

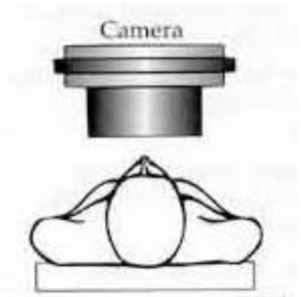
Question
Which radionuclides for medical applications ?



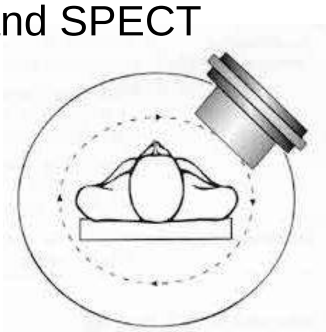
The Nuclear Medicine Alphabet



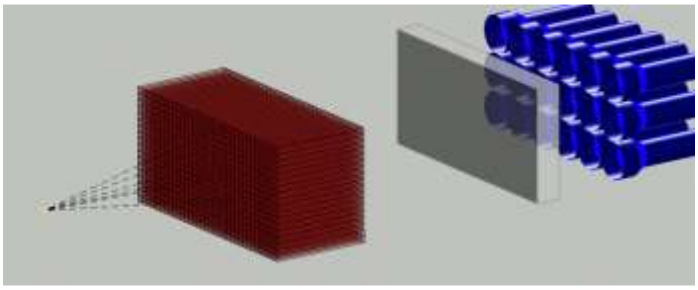
Scintigraphy and SPECT



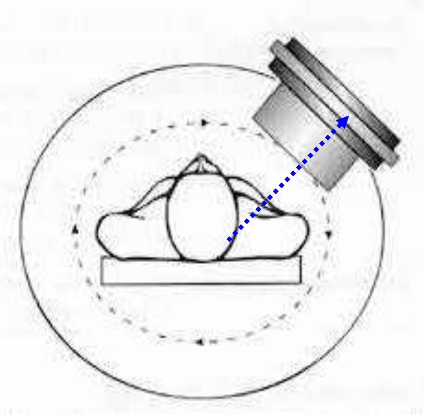
2D: planar scan (Gamma camera)



3D: SPECT: Single Photon Emission Computed Tomography



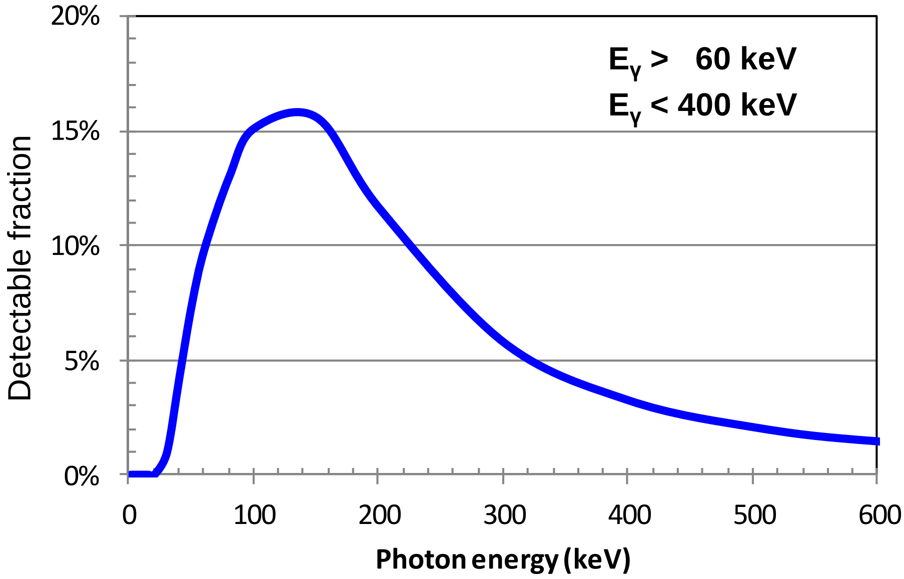
Question: Ideal gamma ray energy for scintigraphy/SPECT?



$$N = N_0 \, e^{-\int_0^d \mu(x)dx}$$

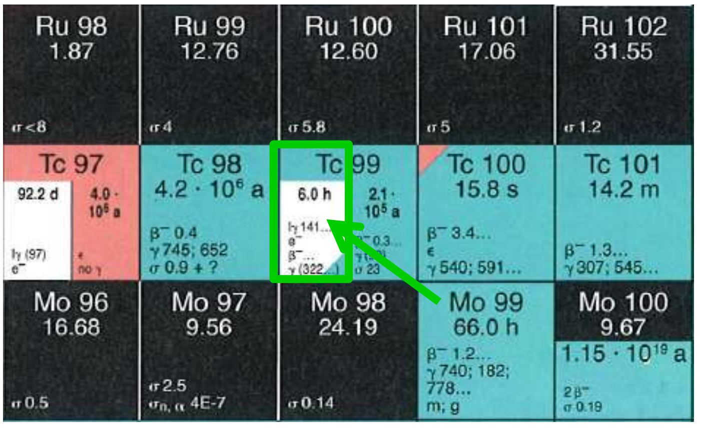
10 cm soft tissue
0.2 cm aluminium (detector encapsulation)
1 cm NaI

Ideal gamma ray energy for scintigraphy/SPECT



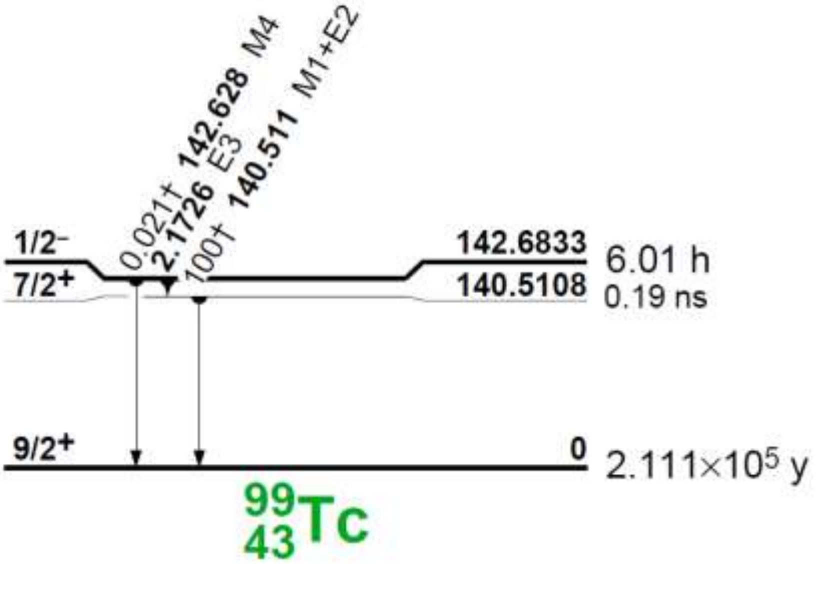
10 cm soft tissue, 0.2 cm aluminium (detector encapsulation), 1 cm NaI

^{99m}Tc: ideal for SPECT and gamma cameras



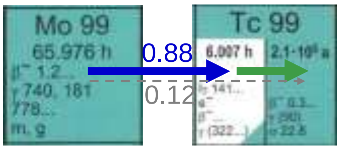
- IT with 89% 140.5 keV gamma ray, $T_{1/2}$ = 6 h
- decays to quasi-stable daughter
- ^{99m}Tc fed in 88% of β^- decays of ^{99}Mo, $T_{1/2}$ = 66 h
- produces nearly carrier-free product

Q: Why is the ^{99m}Tc isomeric half-life so long ?



The Bateman equations

^{99}**Mo** $\rightarrow$ ^{99m}Tc



^{99}Mo $\rightarrow$ ^{99m}**Tc** $\rightarrow$ ^{99g}Tc

$dN_1/dt = -\lambda_1 N_1$

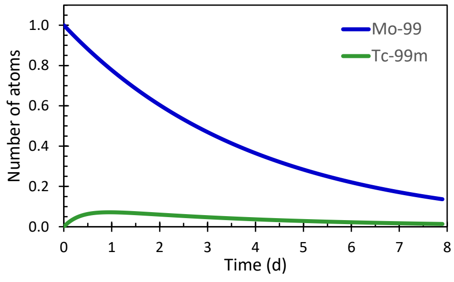
$N_1(t) = N_1(0)\exp(-\lambda_1 t)$

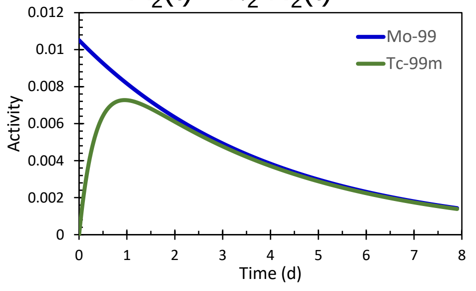
$A_1 = \lambda_1 N_1 = \lambda_1 N_1(0)\exp(-\lambda_1 t)$

$dN_2/dt = \lambda_1 N_1 - \lambda_2 N_2$

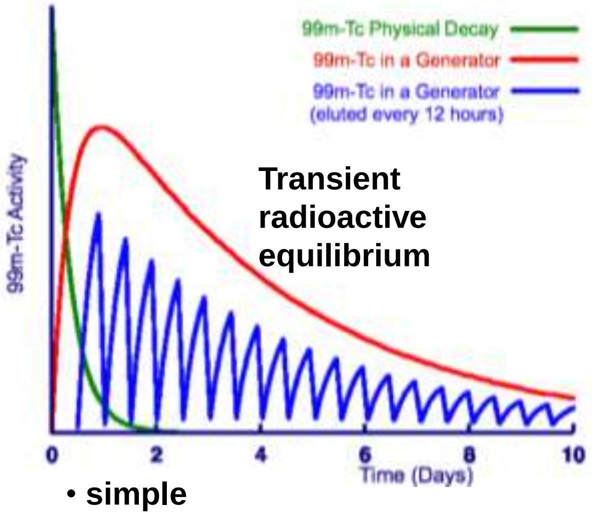
$$N_2(t) = N_2(0)\exp(-\lambda_2 t) + \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1(0)\left[\exp(-\lambda_1 t) - \exp(-\lambda_2 t)\right] * 0.88$$

$A_2(t) = \lambda_2 N_2(t)$



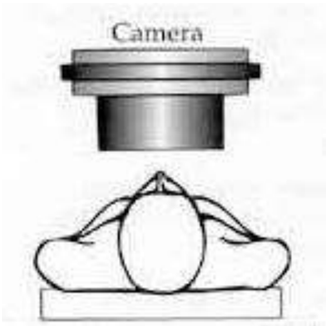


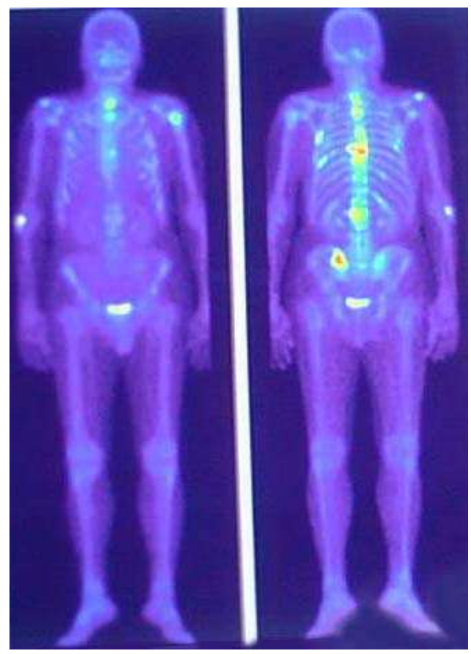
^{99}Mo/^{99m}Tc generator



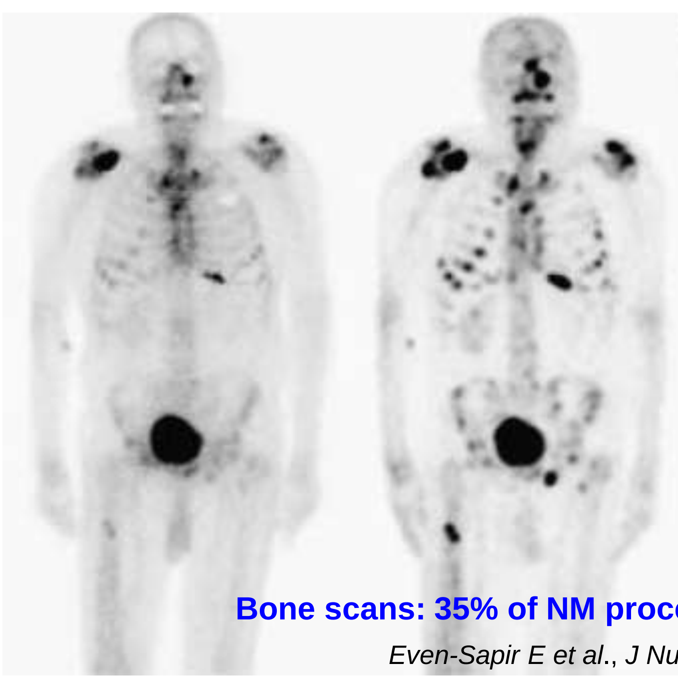
- **simple**
- **reliable**
- **portable**
- **self-shielded**

Bone metastases





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

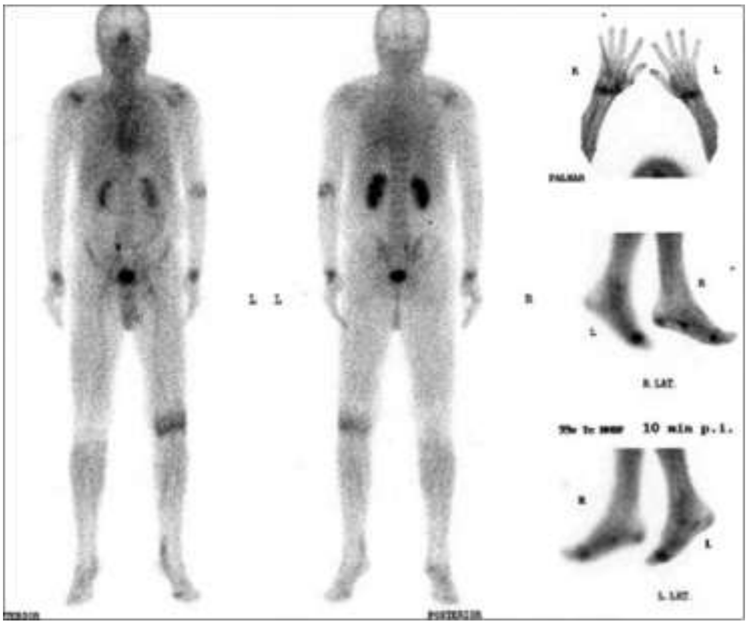


Bone scans: 35% of NM procedures in Europe

Even-Sapir E et al., *J Nucl Med* 2006; 47: 287.

^{99m}Tc-MDP planar **^{99m}Tc-MDP SPECT**

Rheumathoid arthritis

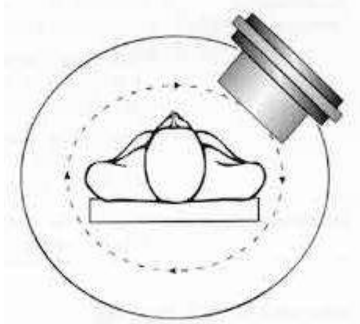


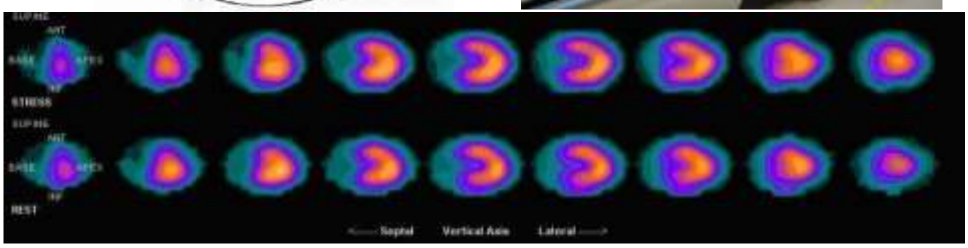
L. Knut, World J Nucl Med. 2015; 14:10.

Veterinary scintigraphy

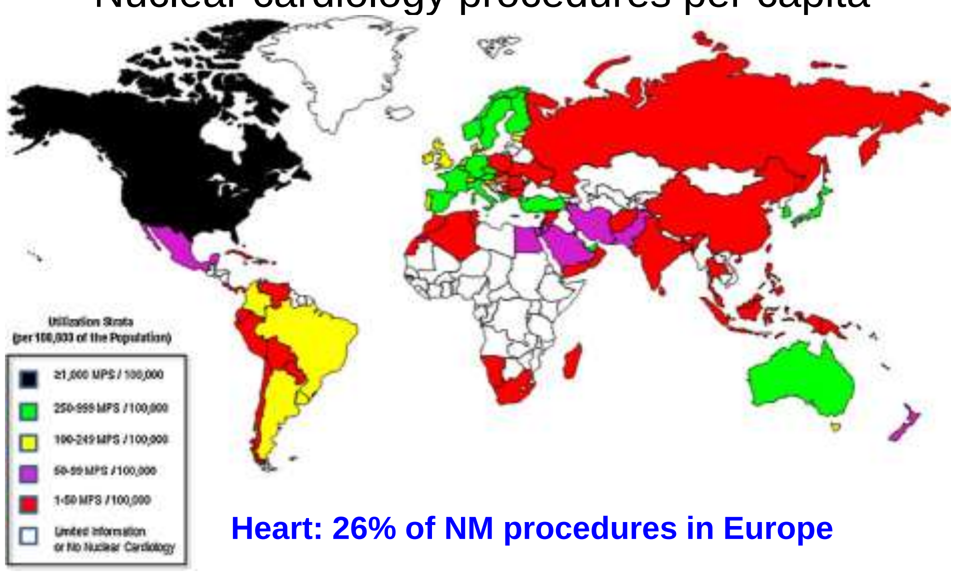
Ischemic heart disease

- diagnose by ECG and cardiac stress test with SPECT
- treatment by medication, angioplasty or bypass surgery





Nuclear cardiology procedures per capita

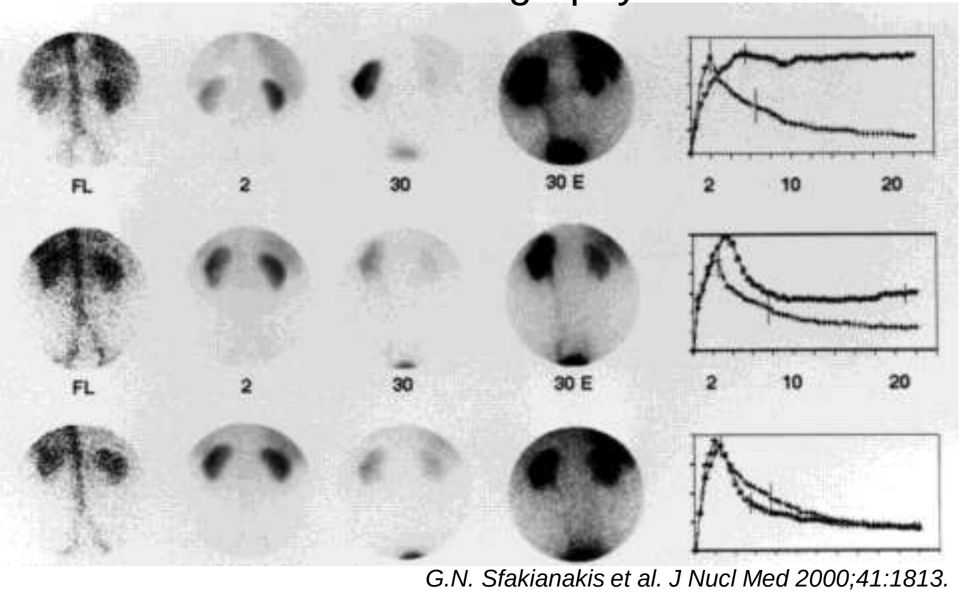


Heart: 26% of NM procedures in Europe

2007: 8.54M myocardial perfusion SPECT procedures reimbursed in the USA

J.V. Vitola et al., J Nucl Cardiol 2009;16:956.

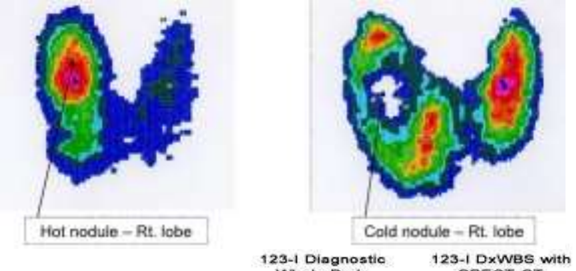
Scintirenography

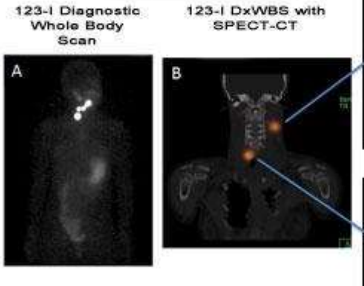


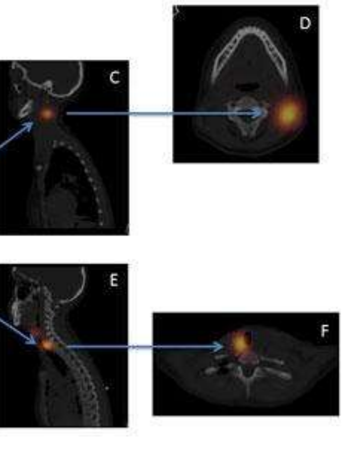
G.N. Sfakianakis et al. J Nucl Med 2000;41:1813.

Kidney: 13% of NM procedures in Europe

Thyroid scintigraphy





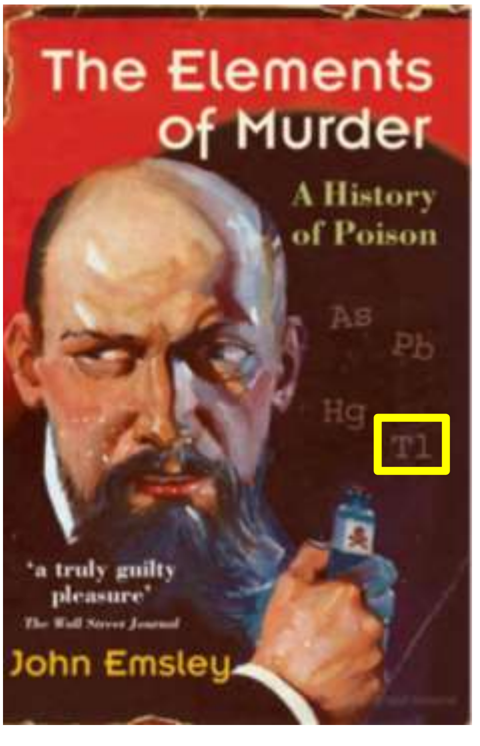


$^{123}I^-$, $^{131}I^-$ or $^{99m}TcO_4^-$

Thyroid: 12% of NM procedures in Europe

SPECT isotopes

Radio-nuclide	Half-life (h)	E_γ (keV)	I_γ (%)	Decay type
Ga-67	78	93 185	42 21	EC
Kr-81m	0.004	190	64	IT
Tc-99m	6	141	89	IT
In-111	67	171 245	91 94	EC
I-123	13	159	83	EC
Xe-133	126	81	38	β^-
Tl-201	73	70 167	59 10	EC
I-131	192	364	82	β^-
Lu-177	161	113 208	6 10	β^-



Thallium for patients ?

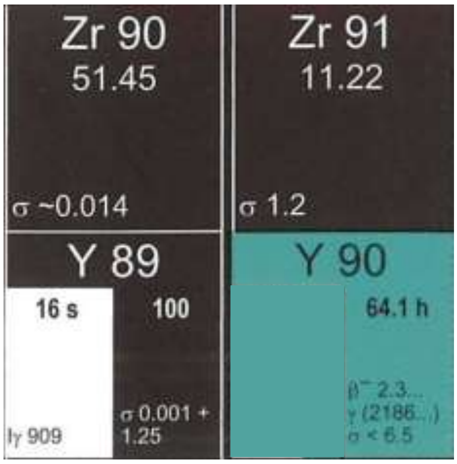
- MBq to GBq activities correspond to ng to µg
- no chemical toxicity at this level
- provided stable isotopes are absent ("carrier-free") or relatively low abundant ("non-carrier-added")
- high specific activity or high molar activity is frequently a decisive quality criterion for nuclear medicine applications!

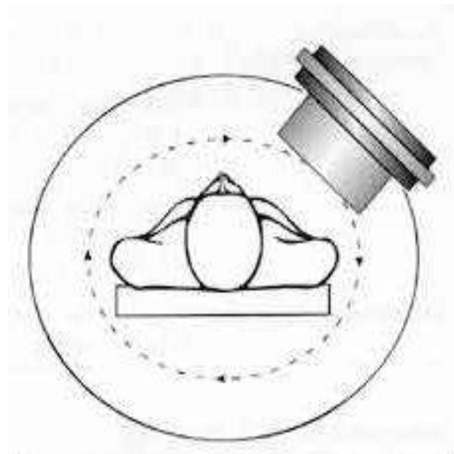
$A/m = \lambda N_A/M = N_A \ln(2)/(M \cdot T_{1/2})$

specific activity (Bq/g)

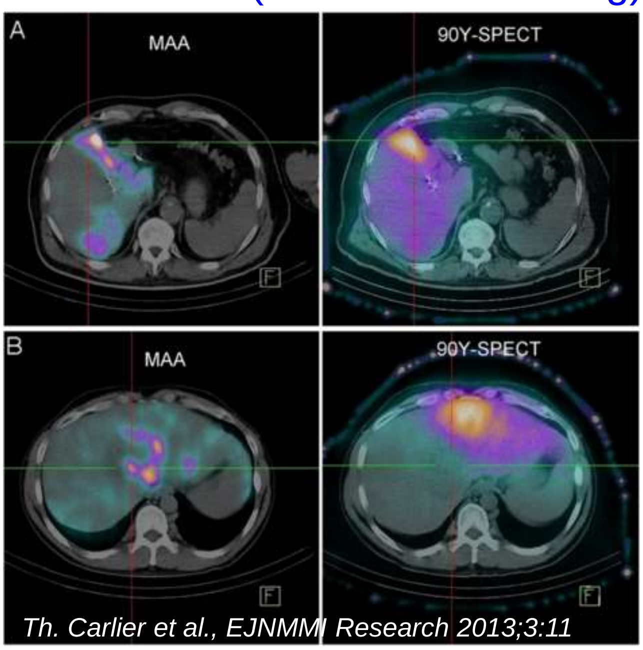
Question

Can one make SPECT images with a pure β^- emitter ?



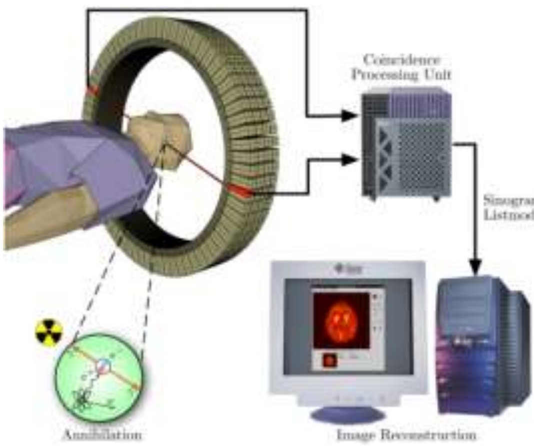


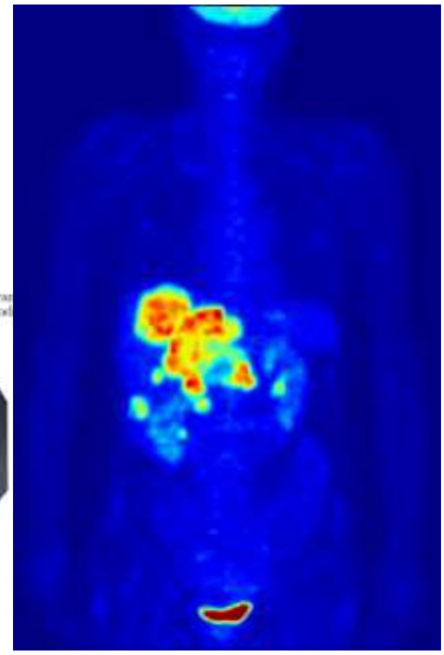
Answer: YES (via Bremsstrahlung)



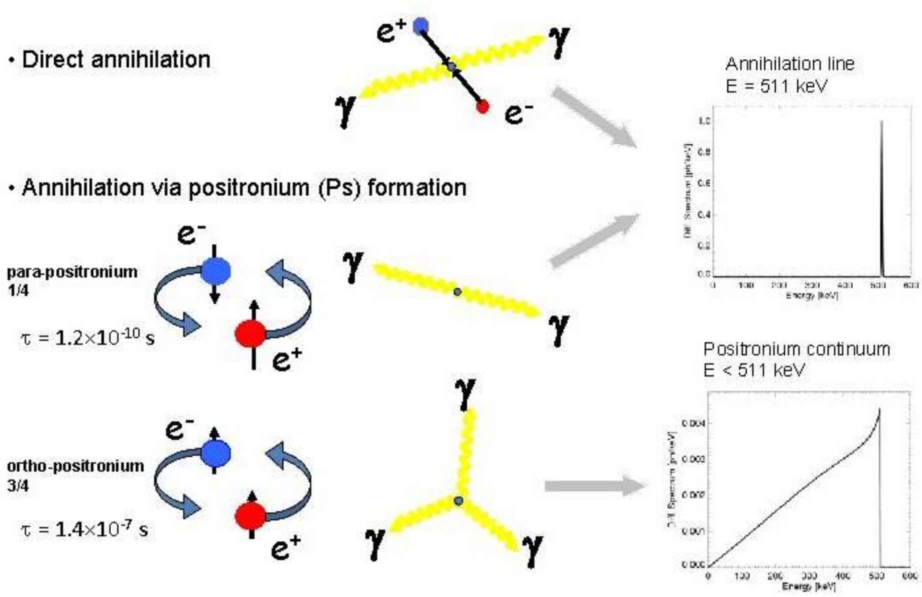
Th. Carlier et al., EJNMMI Research 2013;3:11

Positron Emission Tomography





Electron Positron Annihilation



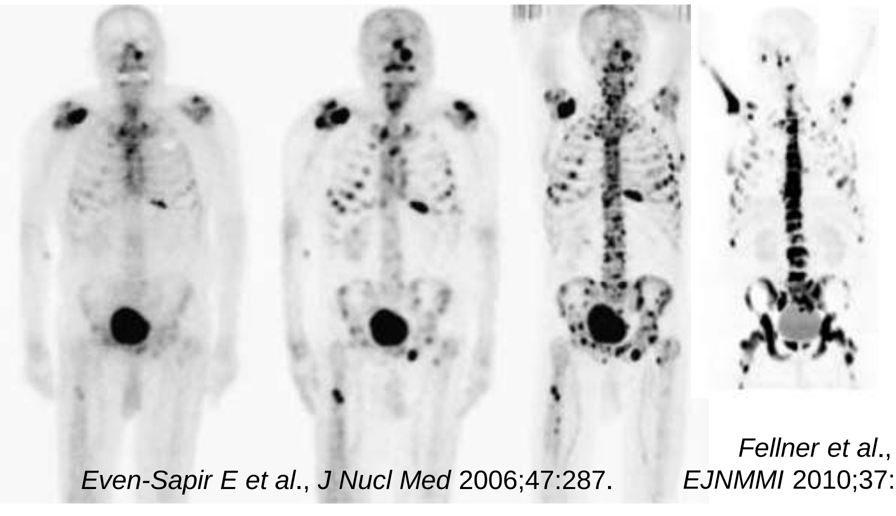
See also: https://doi.org/10.1038/s41467-021-25905-9

PET isotopes

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

^{18}F-Fluorodeoxyglucose (FDG)

Bone scans for bone metastasis screening



Even-Sapir E et al., *J Nucl Med* 2006;47:287.

Fellner et al., *EJNMMI* 2010;37:834.

^{99m}Tc-MDP planar **^{99m}Tc-MDP SPECT** **^{18}F$^-$ PET** **^{68}Ga-BPAMD PET**

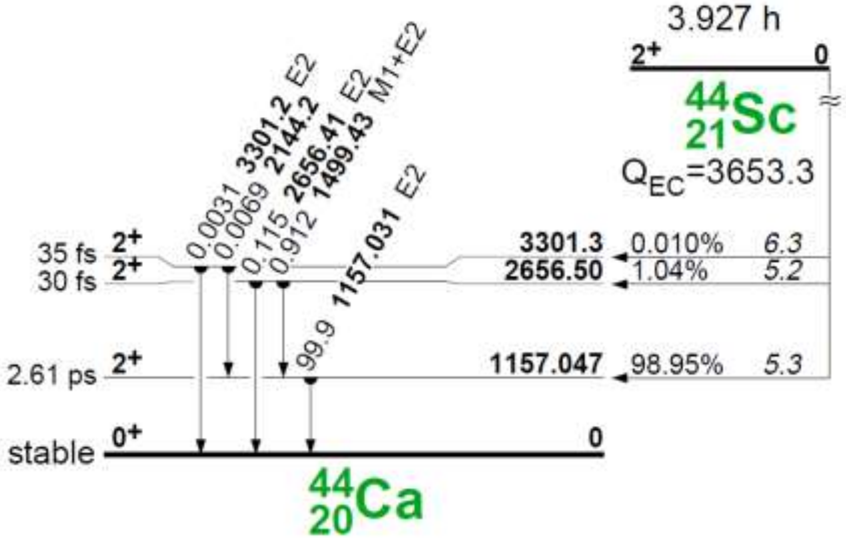
PET isotopes

Radio-nuclide	Half-life (h)	Intensity β^+ (%)	E mean (MeV)	Range (mm)
C-11	**0.34**	**99.8**	**0.39**	**1.3**
N-13	**0.17**	**99.8**	**0.49**	**1.8**
O-15	**0.03**		**0.74**	**3.2**
F-18	**1.83**		**0.25**	**0.7**
Ga-68	**1.13**		**0.83**	**3.8**
Rb-82	**0.02**		**3.38**	**20**

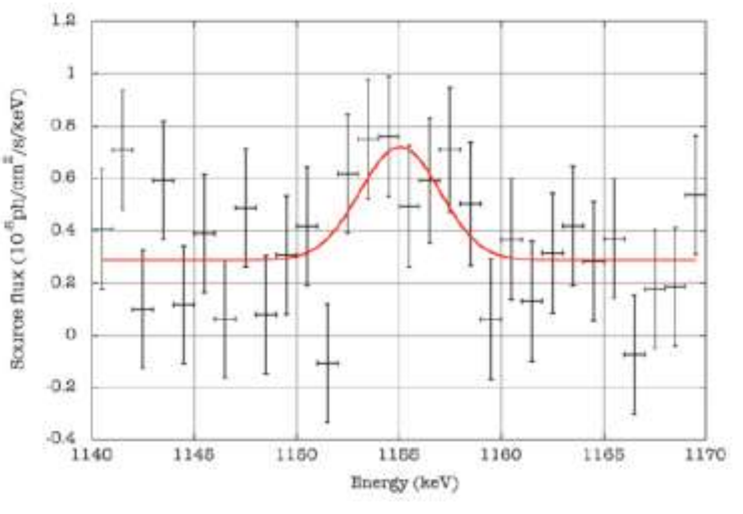
Mother isotope:
271 d
25 d

Longer-lived PET isotopes

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



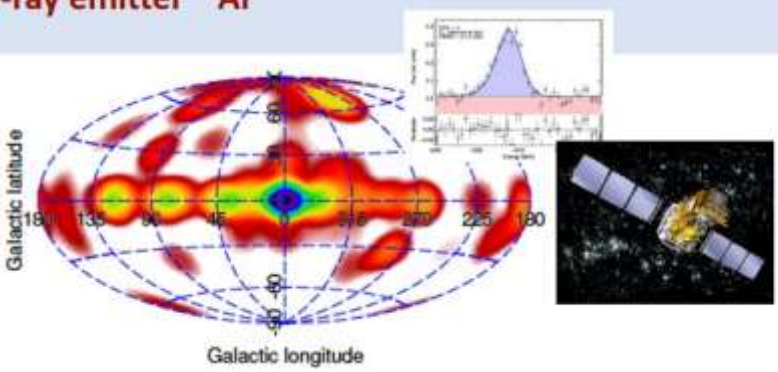
^{44}Sc in the universe



M. Leising, R. Diehl, PoS 2009.

Q: How to determine the source direction ?

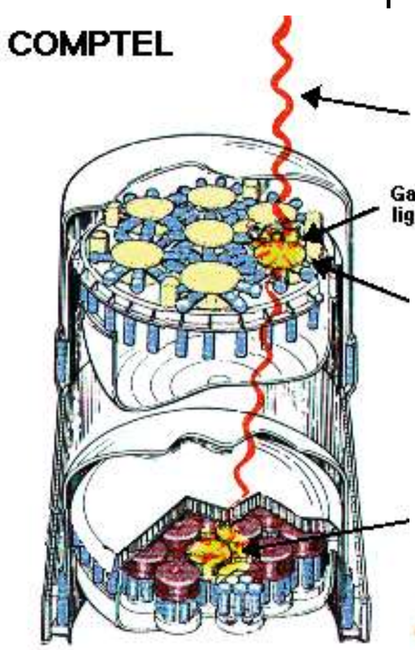
Cosmic γ-ray emitter ^{26}Al

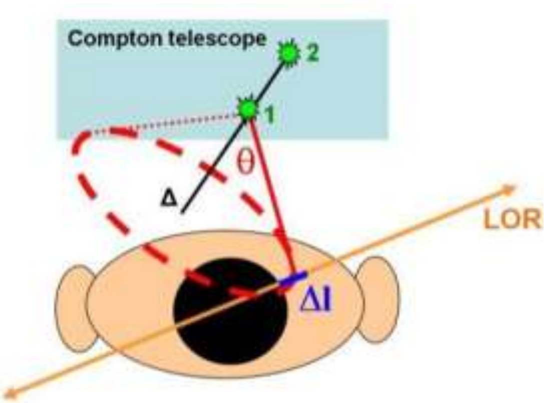


Main Origin of ^{26}Al in massive stars (Diehl et al, Nature 439 (2006))

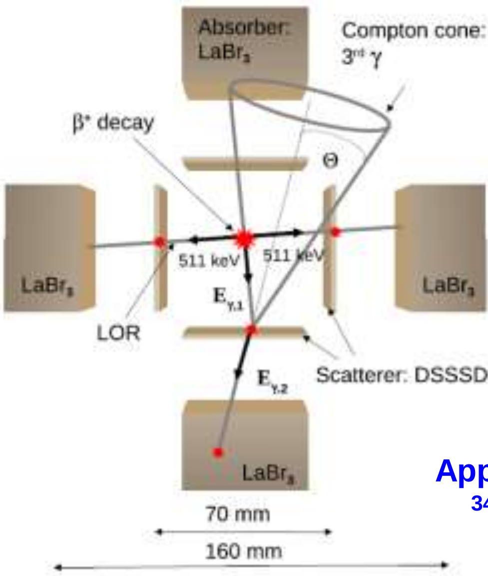
Claudia Lederer-Woods, 25 Jan 2024

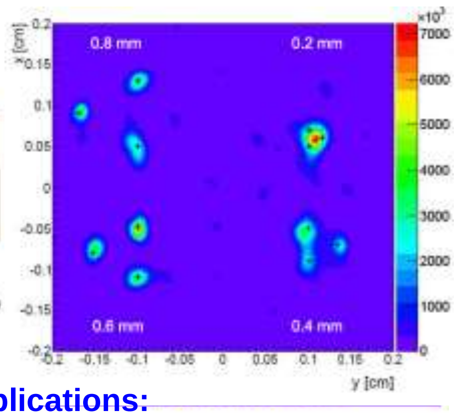
Compton telescope





3-photon-camera: PET-SPECT





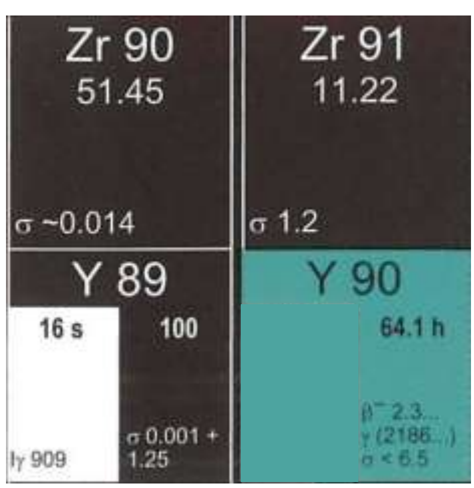
Applications:

^{34m}Cl, ^{44}Sc, ^{44m}Sc, ^{52}Mn, ^{52m}Mn, ^{86}Y, ^{94g}Tc, ^{94m}Tc, ^{124}I, ^{10}C, ^{14}O

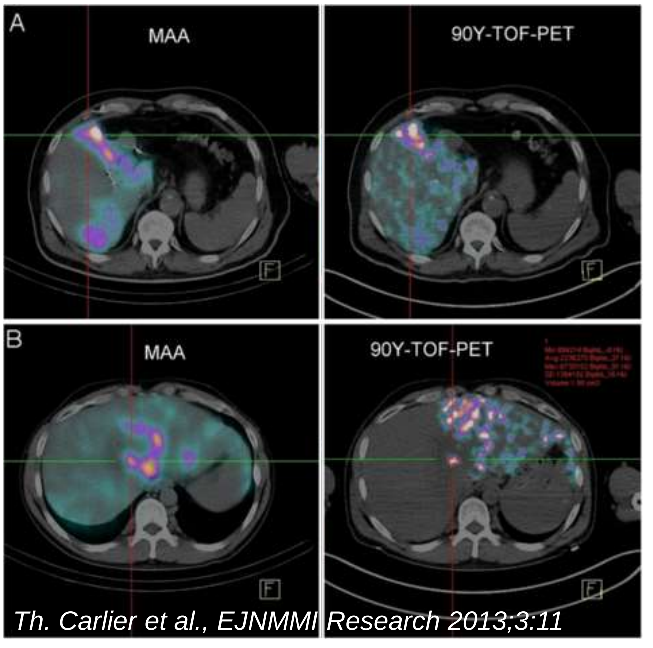
C. Lang et al. JINST 2014;9:P01080.

Question

Can one make PET images with a β$^-$ (beta-minus) emitter?

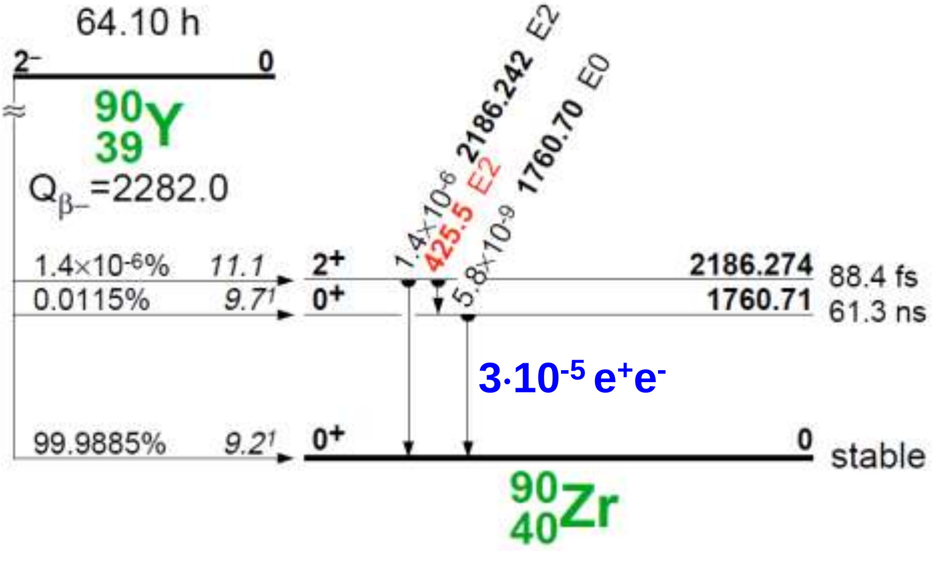


Answer: YES (with ^{90}Y)



Th. Carlier et al., EJNMMI Research 2013;3:11

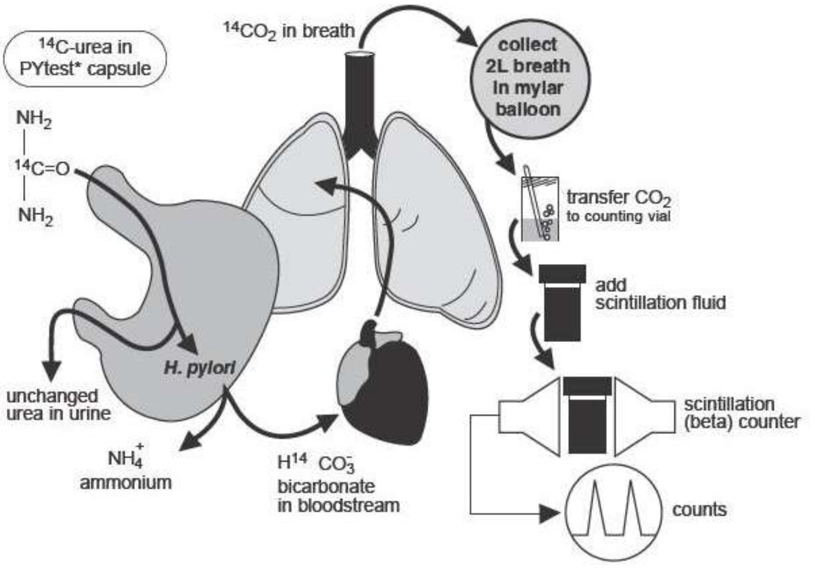
PET with a β^- emitter !



Radiotracer diagnostics without imaging

Helicobacter pylori: chronic stomach inflation (ulcers, pain)
cause of 60-90% of all stomach cancers

111 kBq



Question

Why 111 kBq?

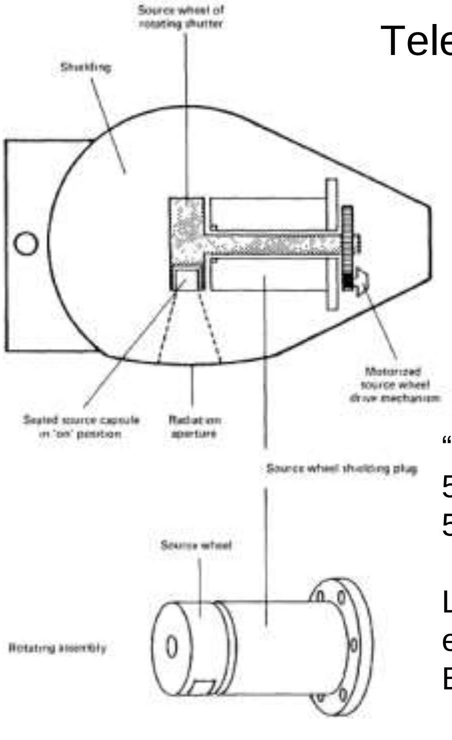
1 Ci = 37 GBq
1 mCi = 37 MBq
1 μCi = 37 kBq

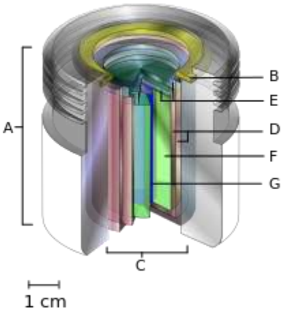
3 μCi = 111 kBq

From diagnostics

to therapy

Teletherapy units

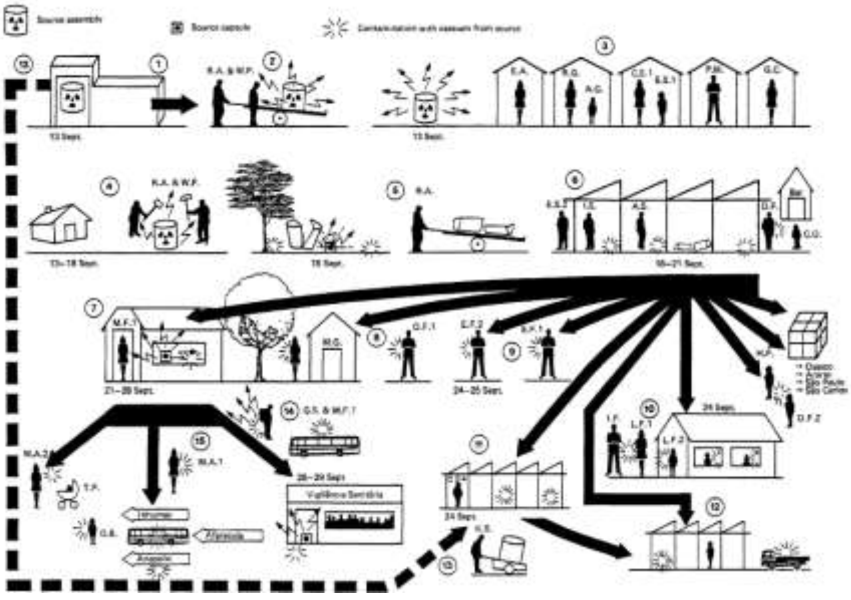




“Cobalt-bomb” or “Cesium-bomb”
50 – 100 TBq of ^{60}Co or ^{137}Cs
5 – 10 Gy/h at 1 m

Less operation and maintenance effort with respect to LINACs, BUT long-term legacy!

Civilian radiation accidents



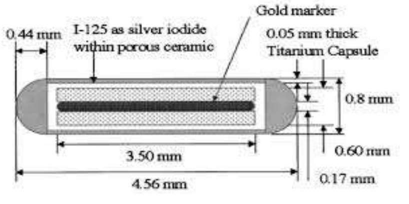
Goiania, Ciudad Juarez, Samut Prakan, etc.

10. *A hole is made to remove a radiation hot spot giving a dose rate of 0.5 $Sv \cdot h^{-1}$.*

Brachytherapy

High Dose Rate (HDR) brachytherapy
short-term insertion of ^{60}Co, ^{137}Cs, ^{169}Yb or ^{192}Ir sources

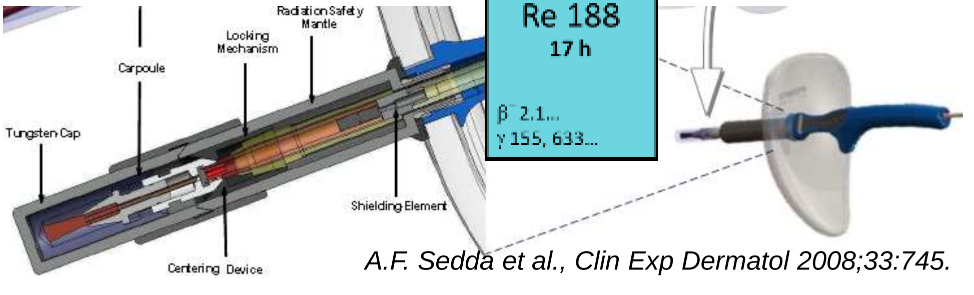
Low Dose Rate (LDR) brachytherapy
long-term insertion of ^{32}P, ^{103}Pd, ^{125}I, ^{131}Cs, etc. sources ("seeds")



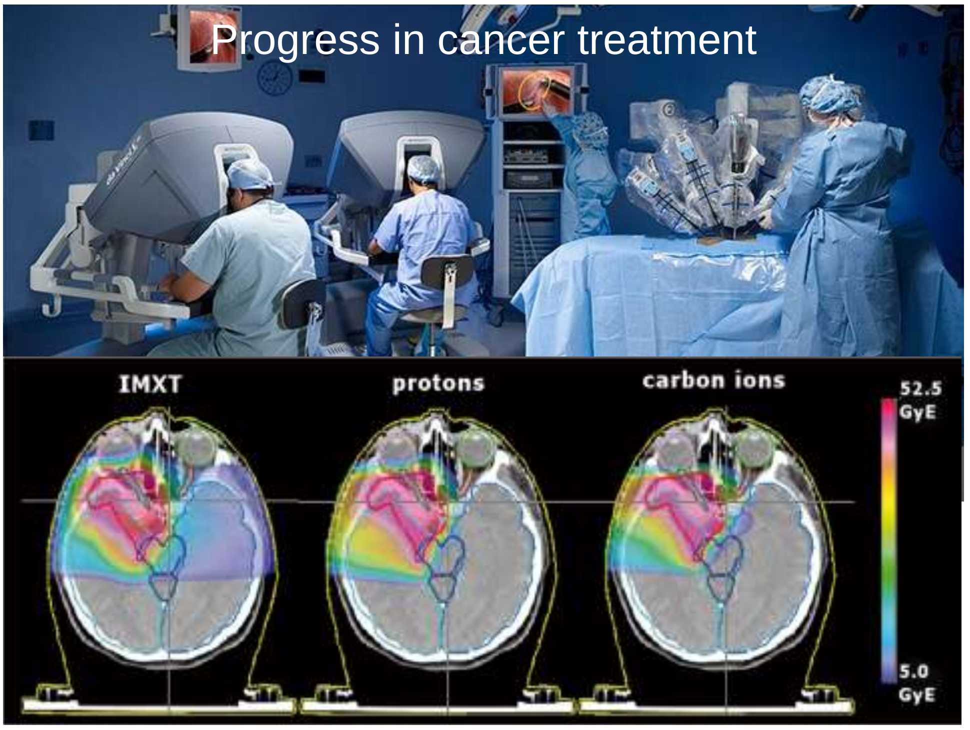
OncoBeta Rhenium skin cancer therapy

non-melanoma skin cancer:

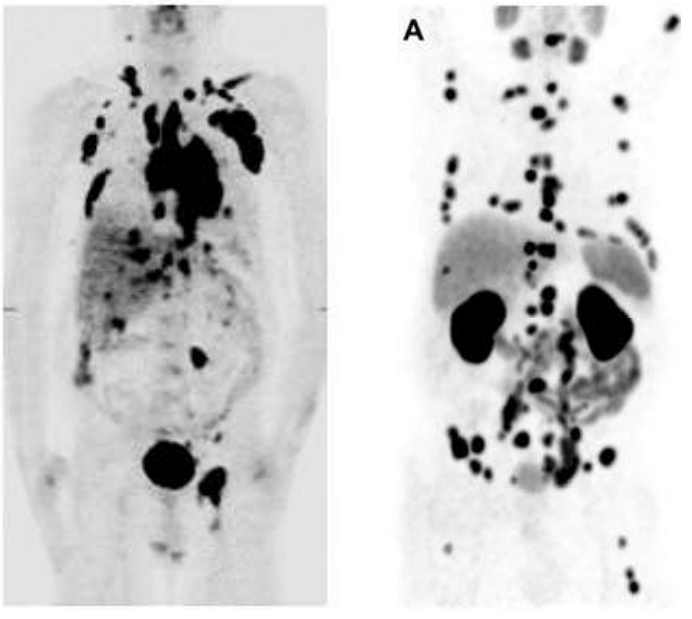
- basal cell carcinoma and squamish cell carcinoma
- in the Alps 20-30% lifetime risk to develop skin cancer



A.F. Sedda et al., Clin Exp Dermatol 2008;33:745.

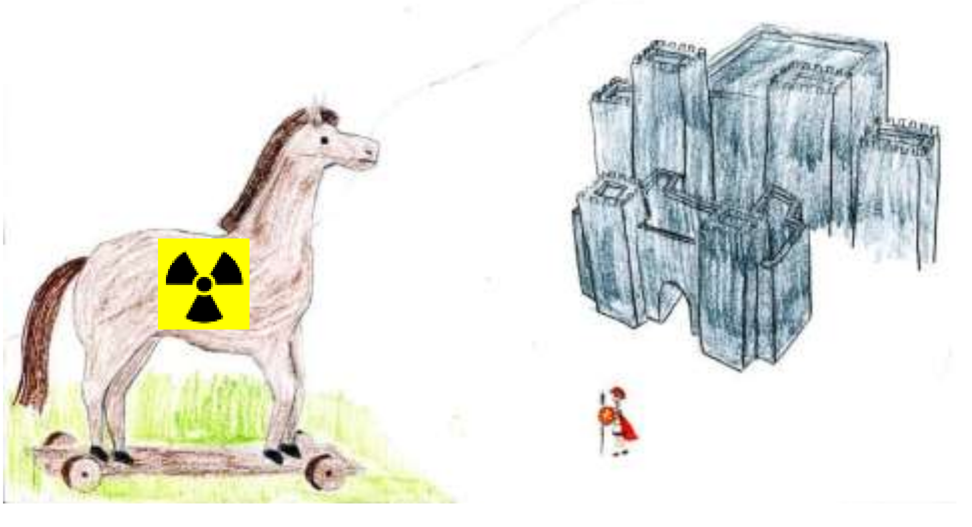


Q: How can one treat such patients?

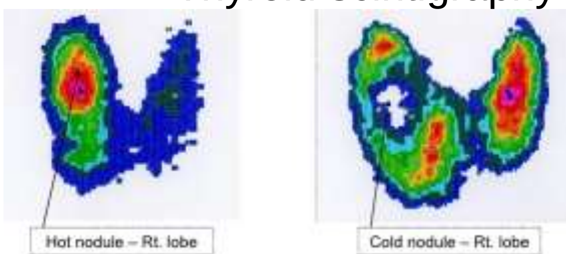


Learning from history

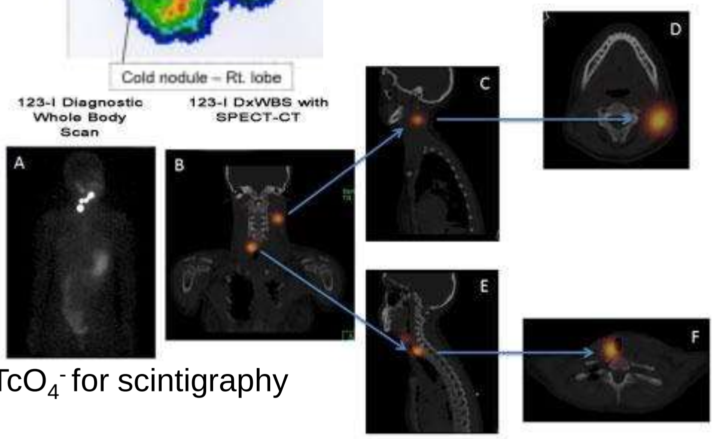
The principle of targeted therapies



Thyroid scintigraphy and therapy



I 123
13.2 h
ε
no β^+
γ 159

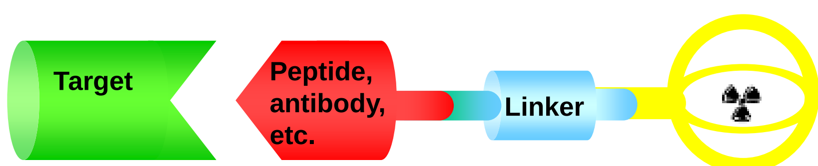


I 131
8.0 d
β^- 1.0, 1.8,…
γ 364, 637…

$^{123}I^-$, $^{131}I^-$ or $^{99m}TcO_4^-$ for scintigraphy
$^{131}I^-$ for therapy

(Papillary) thyroid cancer has the **highest survival** of all malignant cancers!

Multidisciplinary collaboration to fight cancer



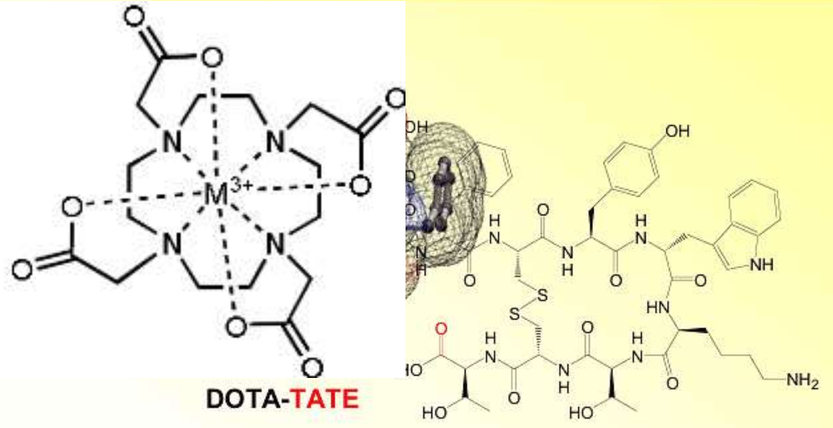
Immunology
Structural biology

Coordination chemistry

Nuclear physics and radiochemistry

Nuclear medicine and medical physics

Structural Formula of DOTA-TOC/TATE



DOTA-TATE

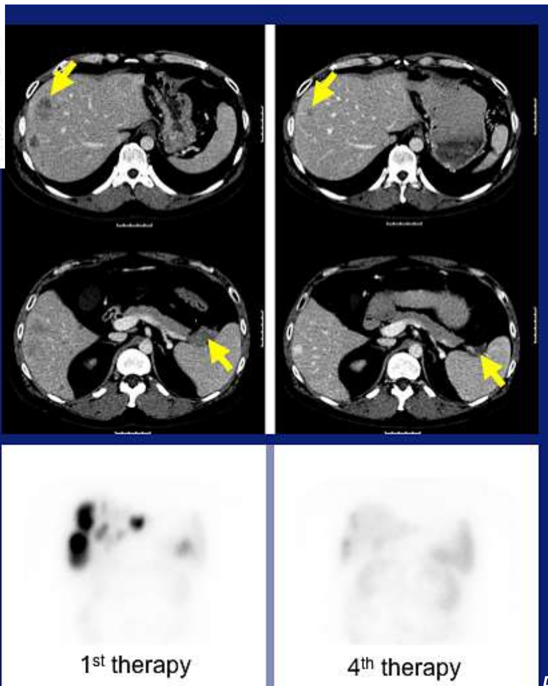
1,4,7,10-tetraazacyclododecantetraacetate

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

IC_{50} (Y^{III}) = 1.6 ± 0.4 nM

Helmut Maecke, EANM-2007.

Universitätsspital Basel



Male

36 years of age

Small cell pancreatic neuroendocrine tumour

Liver metastases

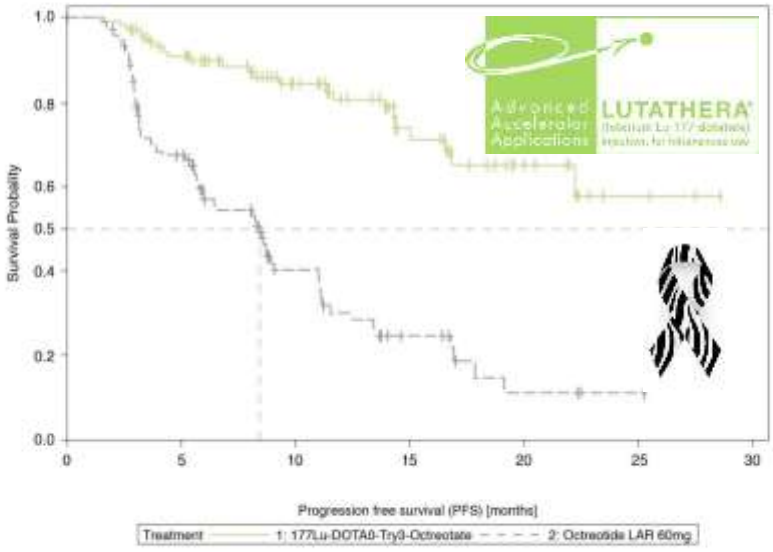
Ki-67 index 10-15% (liver biopsy)

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

Partial remission

Roelf Valkema, EANM-2008.

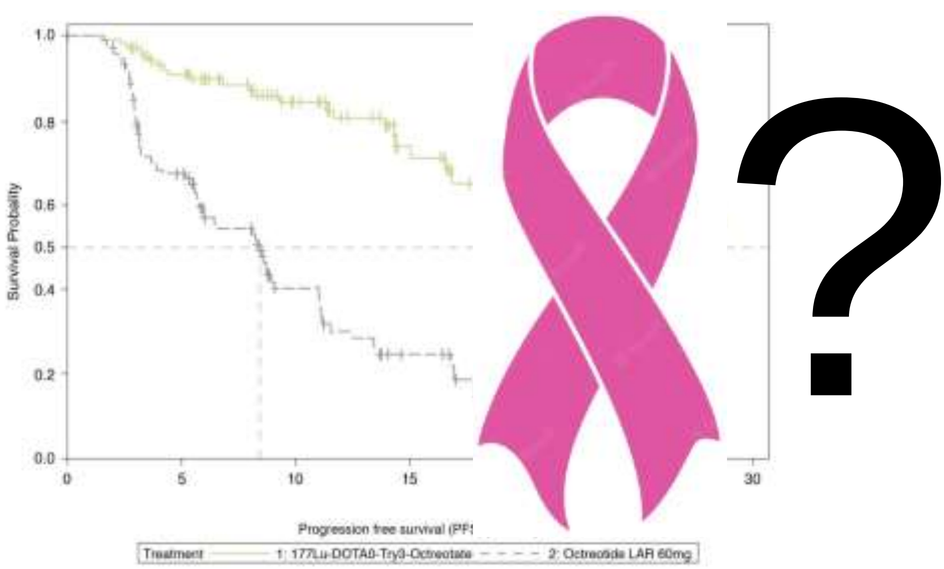
^{177}Lu-Peptide Receptor Radionuclide Therapy of midgut neuroendocrine tumors



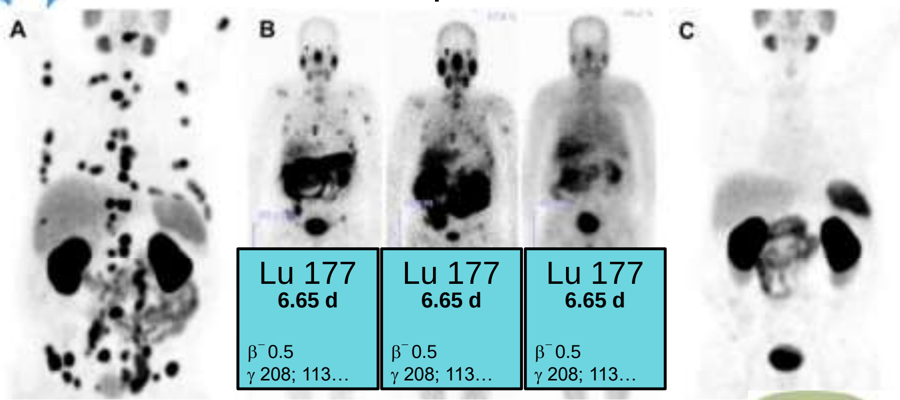
29.1.2018
FDA Approval
of Lutathera

J. Strosberg et al., N Engl J Med 2017;376:125.

Treatment of other cancers ?



^{177}Lu-radioligand therapy of advanced prostate cancer

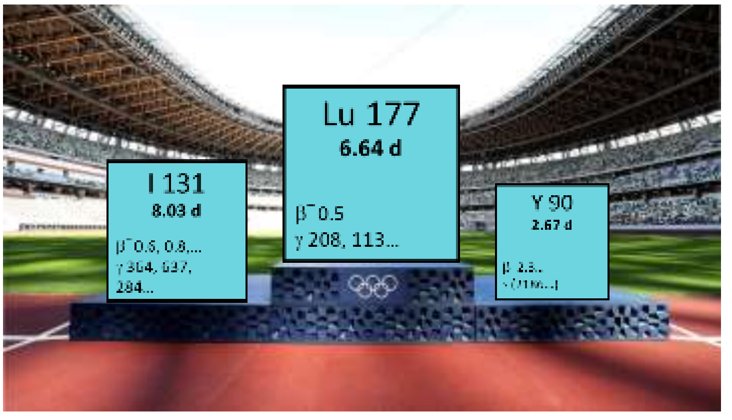


C. Kratochwil et al., Eur J Nucl Med Mol Imaging 2015;42:987.
M. Weineisen et al., J Nucl Med 2015;56:1169.
R.P. Baum et al., J Nucl Med 2016;57:1006.
C. Kratochwil et al., J Nucl Med 2016;57:1170.
K. Rahbar et al., J Nucl Med 2017;58:85.
M.S. Hofman et al., Lancet Oncol 2018;19:825.
O. Sartor et al., N Engl J Med 2021;385:1091.

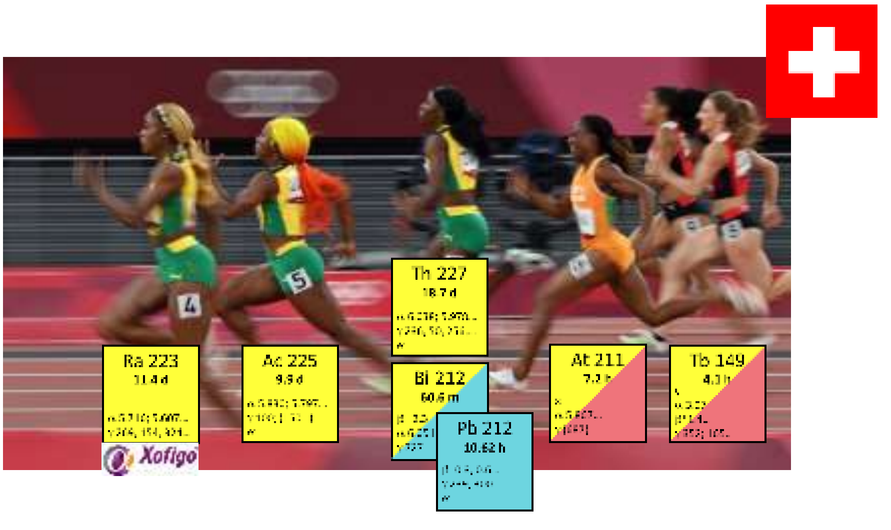
Approval
23.3.2022 FDA
9.12.2022 EMA

The “gold standard” for radionuclide therapy

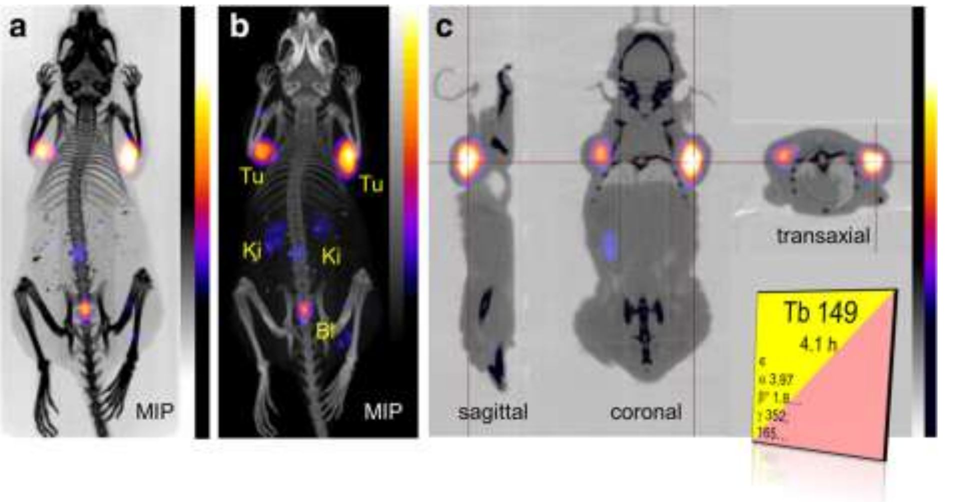
The beta emitter podium



The alpha emitter race

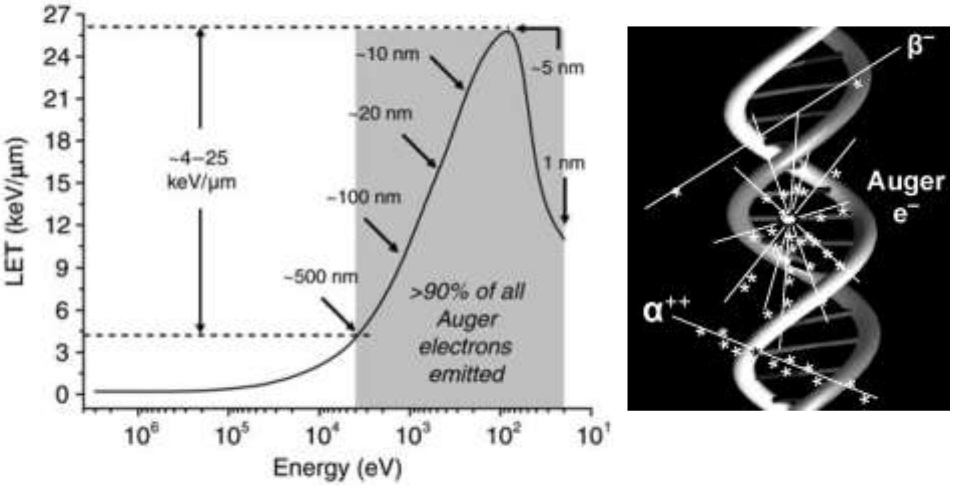


Alpha-PET with ^{149}Tb



C. Müller et al. EJNMMI Radiopharm Chem 2016;1:5.

Radiobiological effectiveness of Auger electrons



A.I. Kassis, Rad. Prot. Dosimetry 2011;143:241.

Which radionuclides will we need for medicine in 2030 ?

Today 30 million clinical applications per year !

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

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

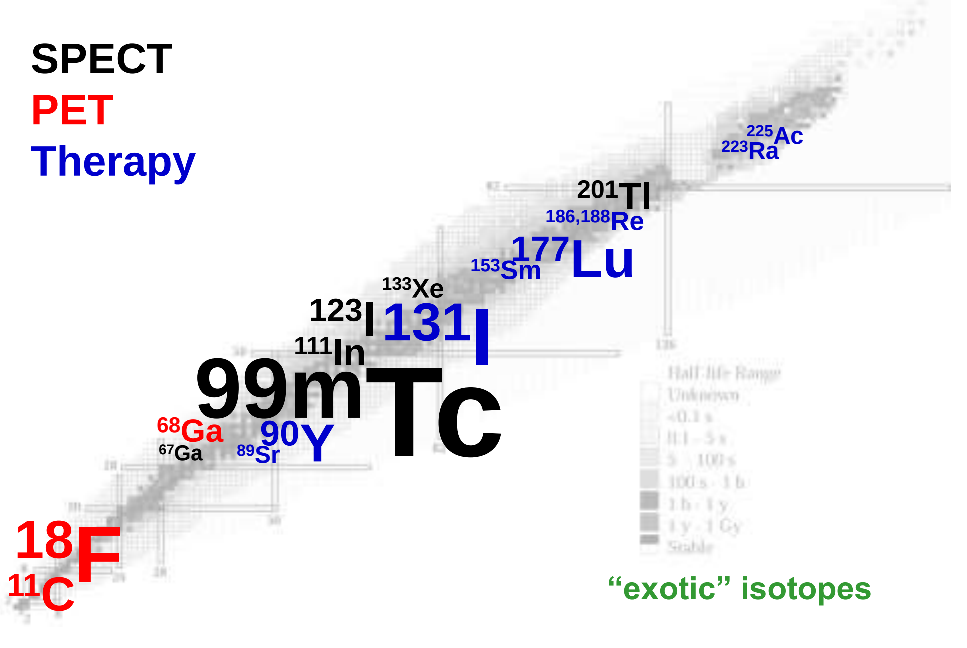
The New York Patent Group has carefully studied the information available relative to the above-identified item. The AEC does not at present desire to prepare a patent application on this item for the following reason:

"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."

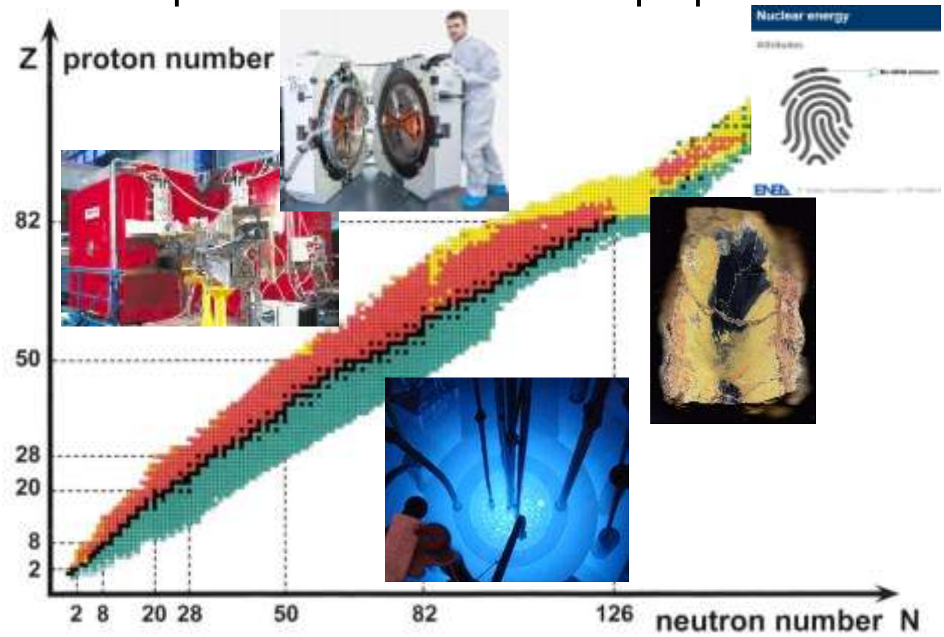
...

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."

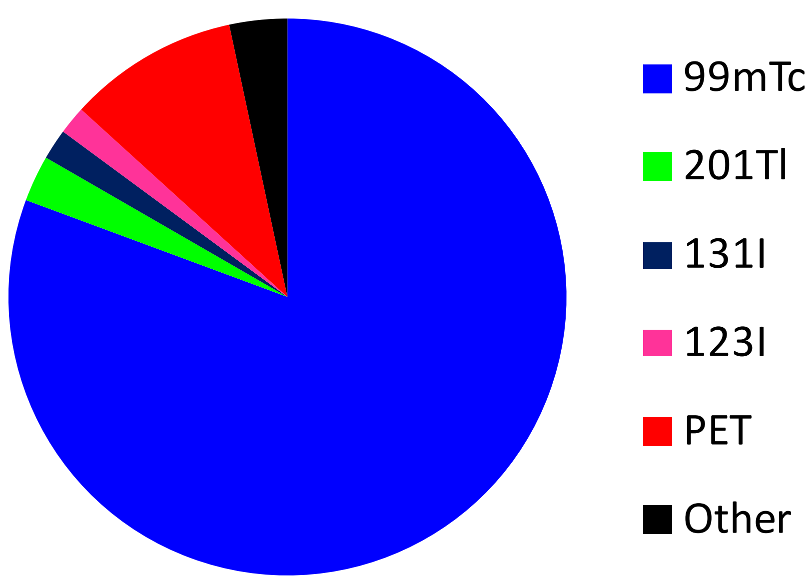
The chart of nuclides – nuclear medicine perspective



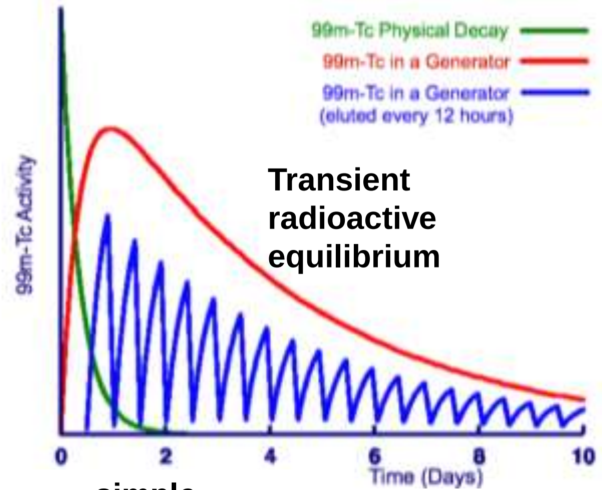
The “Alpine divide” of radioisotope production



Cumulative use of diagnostic isotopes in Europe



^{99}Mo/^{99m}Tc generator



- **simple**
- **reliable**
- **portable**
- **self-shielded**

^{99m}Tc supply: an industrial/commercial challenge

30 M patients/year

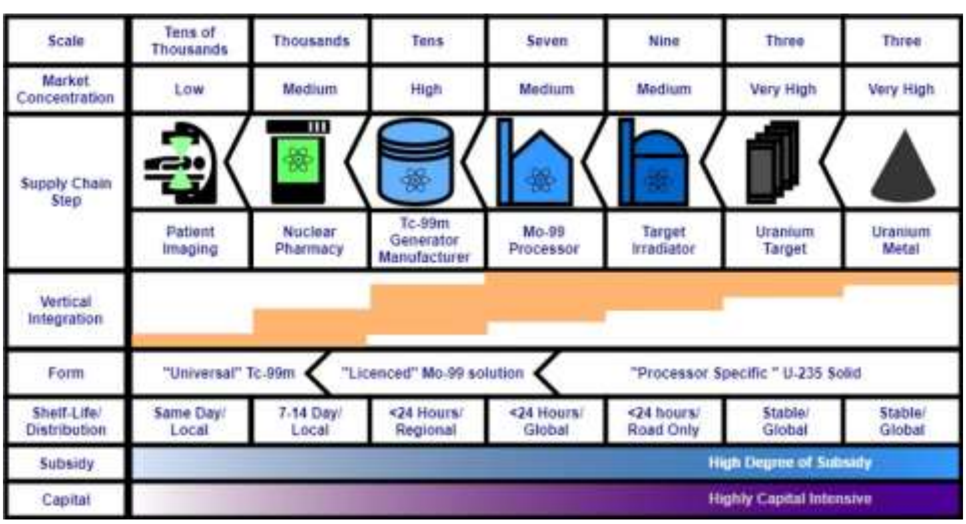
~ 20000 TBq injected ~ $6 \cdot 10^{20}$ atoms ≈ 0.1 g ^{99m}Tc

Out of scale of any “lab experiments”

Fission production

7 d irradiation, 2 d decay during transport and chemical processing:
$^{99}Mo/^{all}Mo \approx 10\%$, i.e. specific activity ≈1800 TBq/g

The $^{99}Mo/^{99m}Tc$ supply chain



The Supply of Medical Isotopes, OECD-NEA (2019)

Isotope shortage means a healthcare crisis

European hospitals cope with Mo-99 supply crisis

EUROPE MOLYBDENUM SUPPLY

L'inquiétante pénurie d'isotopes pour l'imagerie

Engpässe in der Tumormedizin

Medical isotope shortage reaches crisis level

Krebsärzten gehen die Diagnosemittel aus

Médecine nucléaire : il faut prolonger le réacteur Osiris

We Need to Expand Medical Isotope Production!

ANALYSIS | The made-in-Canada isotope shortage facing medical scans

Desperately Seeking Moly

Isotopes médicaux - Crise mondiale à l'horizon

Aucune solution n'existe pour résoudre le problème d'approvisionnement

Isotope shortage to get worse with closing of more reactors

L'OCDE s'inquiète des risques de pénurie d'isotopes médicaux

Mangel an medizinisch verwendbaren Isotopen

Szintigraphien fallen aus, für Februar droht der Notstand

Mo-99 crisis

Niowave broke ground last month on a $79 million isotope production facility that looks out on the runways of Capital Region International. The company expects to move in by the end of the year, to make its first medical isotopes early next year, to be producing them commercially by early 2016. It expects to add 90 jobs to its 70-member staff in the process.

UBC SCIENTISTS HELP AVERT A NUCLEAR MEDICINE MELTDOWN

January 8, 2015

Moly 99 reactor using Sandia design could lead to U.S. supply of isotope to track disease

Canada seeks to avoid medical isotope shortage, extends nuclear reactor

Isotope breakthrough may stave off shortage concerns

MARCH 12, 2015 BY PAUL MAYNE

Coquí Pharma completes design of medical isotope facility

09 April 2015

Lab confirms new commercial method for producing medical isotope

June 15, 2015 (Argonne)

NorthStar Medical Radioisotopes ready to begin Mo-99 production

Michael Walter Aug 31, 2015

It Takes Two: GE Healthcare and SHINE team up to solve longstanding radiopharmaceutical supply concerns in medical imaging

Successful generation of Tc-99m is a supply chain advancement that can help ensure patient access to critical medical imaging scans.

CHALFONT ST. GILES, UK – 9 November 2015 – Technetium-99m (Tc-99m) is used in more than 40

All ways lead to Rome; many ways lead to ^{99m}Tc

^{99}Mo production (for generator) **direct ^{99m}Tc production**

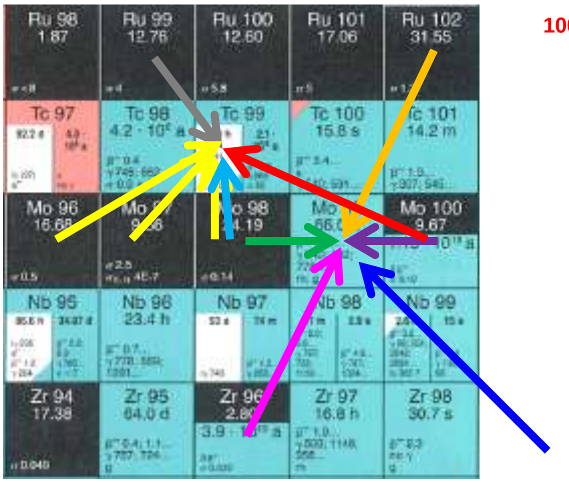
^{235}U(n_{th},f)
^{238}U(n_{fast},f)
^{238}U(γ,f)
^{238}U(p,f)

^{98}Mo(n,γ)
^{nat}Mo(n,γ)
^{100}Mo(d,p)

^{100}Mo(γ,n)
^{100}Mo(n,2n)
^{100}Mo(p,np)

^{96}Zr(α,n)

^{102}Ru(n,α)



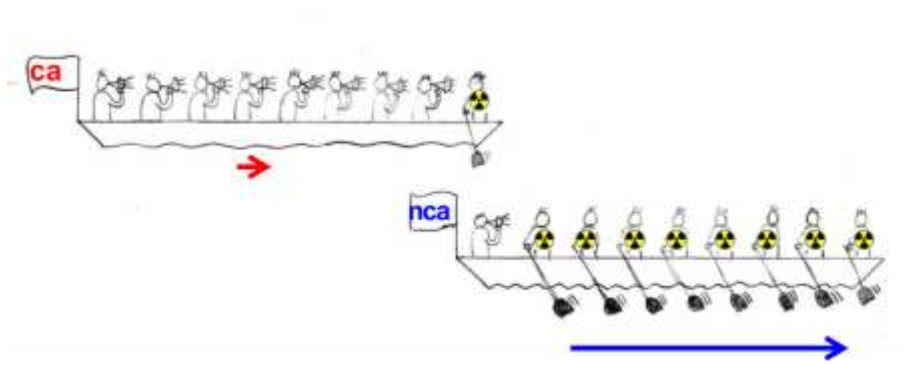
^{100}Mo(p,2n)
^{nat}Mo(α,x)
^{98}Mo(d,n)
^{99}Ru(n,p)

Reactions without practical interest:
^{99g}Tc(γ,γ')^{99m}Tc, ^{99}Ru(μ^-,ν_μ)^{99m}Tc, ^{197}Au(π^+,X)^{99m}Tc,...

Production by ^{98}Mo(n,γ), ^{100}Mo(γ,n) or ^{100}Mo(n,2n)

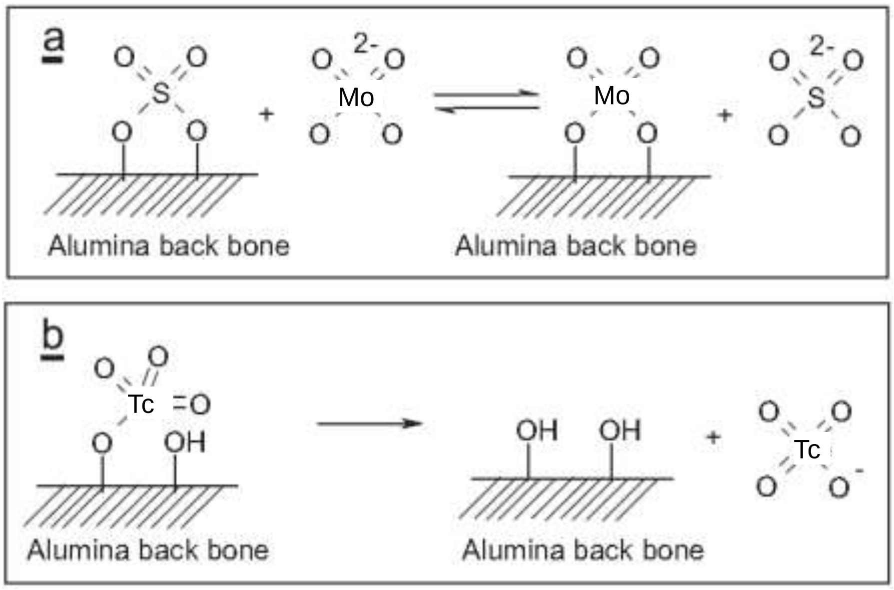
>1000 times lower specific activity than fission-moly

Carrier-added vs. no-carrier-added



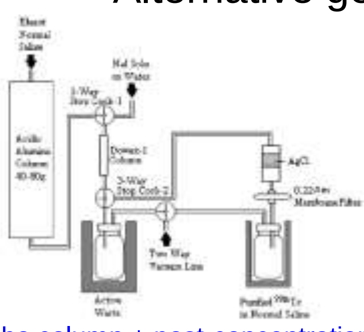
Molar activity of ^{99}Mo not produced by fission

Principle of alumina based generator

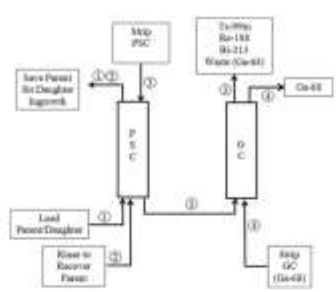


Sorption capacity ca. 2 mass% MoO_4^{2-} per Al_2O_3

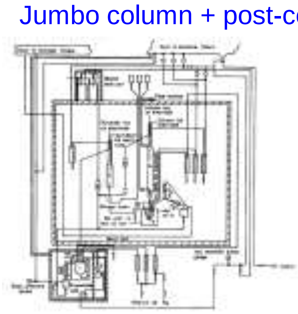
Alternative generator systems



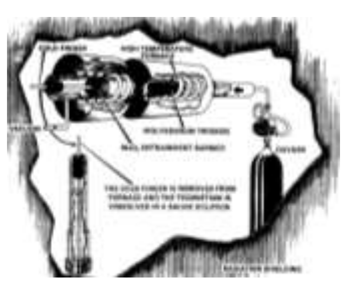
Jumbo column + post-concentration



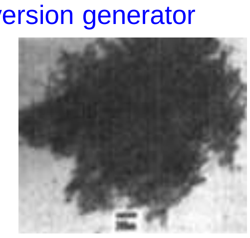
Multicolumn selectivity inversion generator



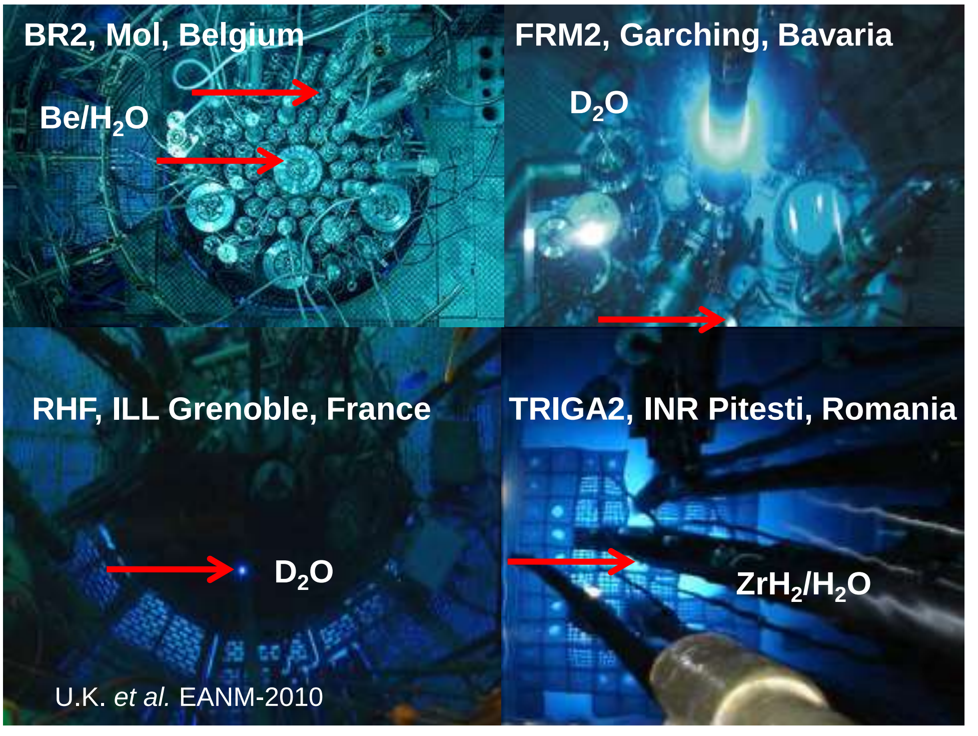
Solvent extraction

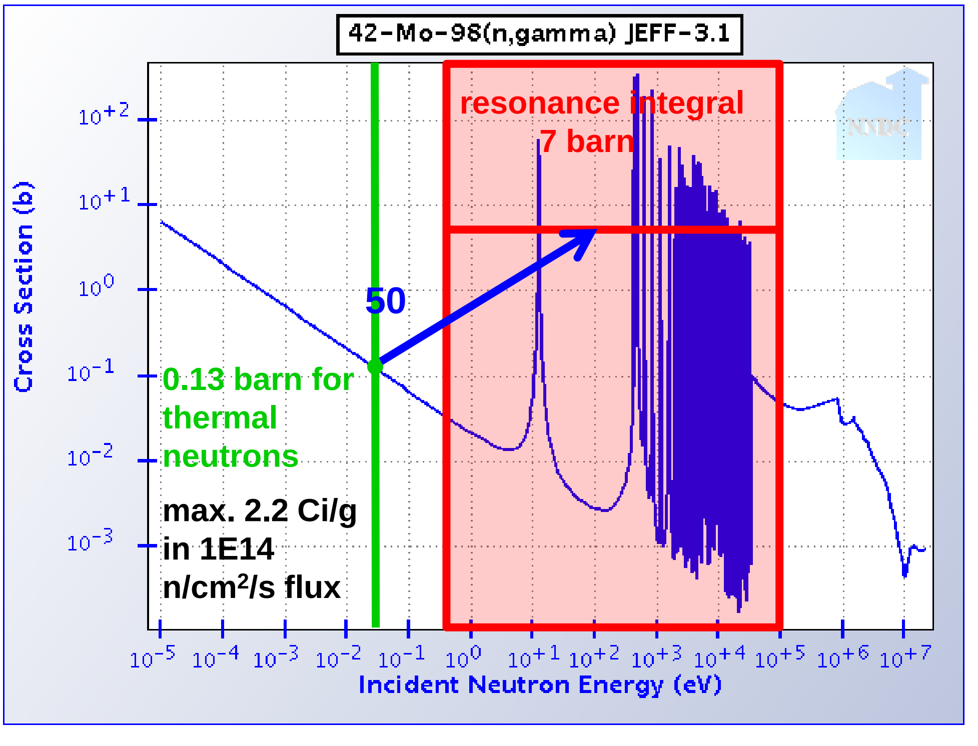


Sublimation generator

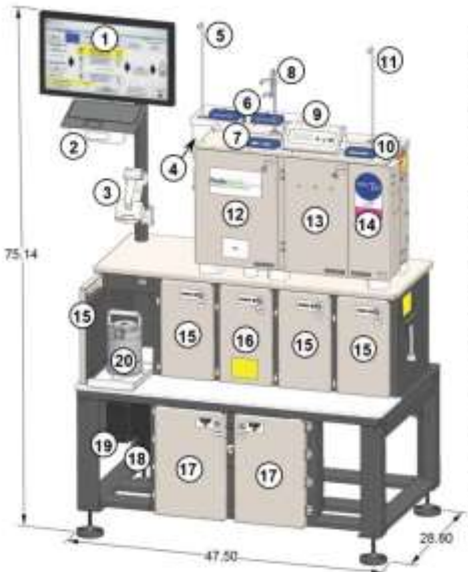


Gel generators
Polymer generators


BR2, Mol, Belgium
Be/H_2O
FRM2, Garching, Bavaria
D_2O
RHF, ILL Grenoble, France
D_2O
TRIGA2, INR Pitesti, Romania
ZrH_2/H_2O
U.K. *et al.* EANM-2010


42-Mo-98(n,gamma) JEFF-3.1
resonance integral
7 barn
50
0.13 barn for
thermal
neutrons
max. 2.2 Ci/g
in 1E14
n/cm²/s flux
Cross Section (b)
Incident Neutron Energy (eV)

Specific activity matters !



RadioGenix System 1.2 Components

1. Touch Screen Monitor
2. Workstation Keyboard
3. Barcode Scanner
4. Ozone Generator and Purge Water Reservoir
5. Sterile Water Hanger
6. Sterile Tubing Docking Station
7. NaOH Port
8. NaOH Bottle Hanger
9. Instrument Display
10. Saline Port
11. Saline Container Hanger
12. Service Door
13. PSC Door
14. Product Door
15. Source Vessel Bays (4)
16. Transfer Bay
17. Discarded Material Bays (2)
18. RadioGenix Computer
19. UPS Battery Backup
20. Source Vessel

Figure 1. The NorthStar RadioGenix® Mo-99/Tc-99m Generator System Model 1.2[1] with the

NorthStar to end production of Mo-99

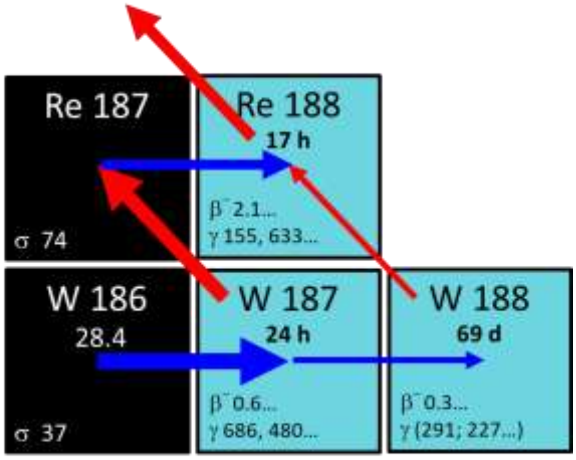
Will Morton
Oct 9, 2023

NorthStar Medical Radioisotopes will shut down its molybdenum-99 (Mo-99) production facilities in Beloit, WI, by the end of 2023, citing increasing costs and competition, the company reported.

According to a statement, NorthStar is currently reaching out to all active customers and suppliers to mitigate any disruptions in the supply chain.

"With a global market environment dominated by foreign-government subsidized competitors and new entrants in the wings, and given steadily increasing costs for raw materials, reactor irradiation, and processing, we have concluded that the Mo-99 program is no longer sustainable," NorthStar President and CEO Frank Sholz, PhD, said in response to a query from *AuntMinnie.com*.

^{188}W/^{188}Re generator

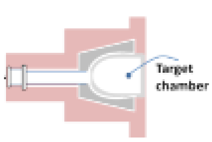


SECURE

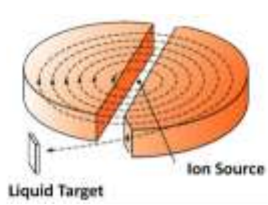
Funded by the European Union

This project has received funding from the European Union's Horizon Europe research and innovation programme.

^{18}F production via ^{18}O(p,n)

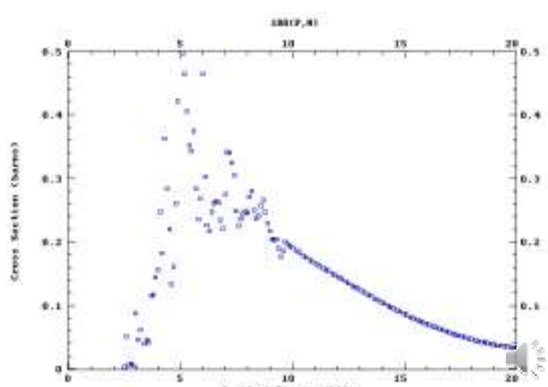


$H_2{}^{18}O$ (water)



Cyclotron irradiation

Transformation into FDG

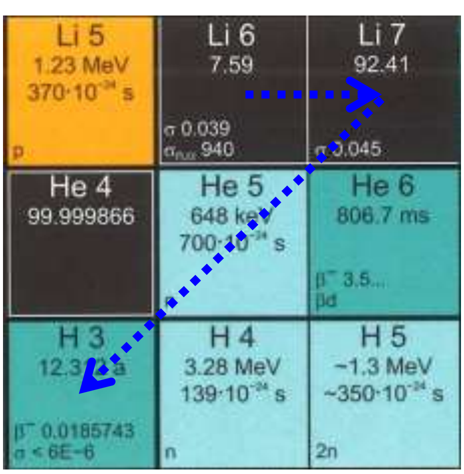


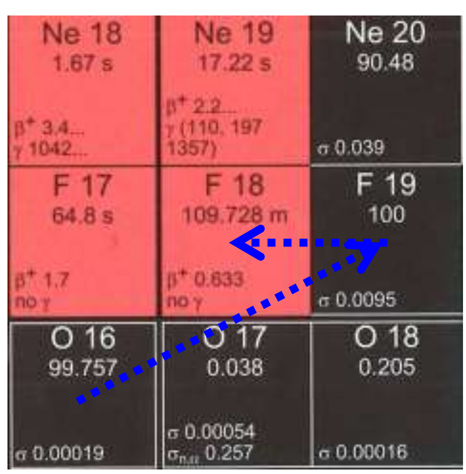
Question

Can one produce ^{18}F in a nuclear reactor?

Answer: YES

1. irradiation of Li_2O or Li_2CO_3 with thermal neutrons
2. ^{6}Li(n,α)^{3}H produces 2.7 MeV tritons
3. tritons induce ^{16}O(t,n)^{18}F reaction Q=+1.27 MeV





Crossing the Alpine Divide !

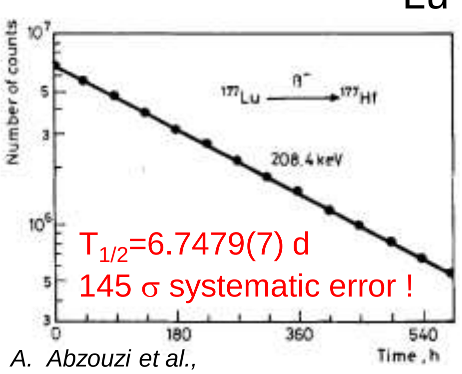
Report of an International Atomic Energy Agency's Consultants' Meeting on Fluorine 18: Reactor Production and Utilization

HERNAN VERA RUIZ

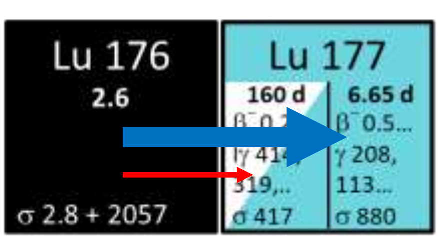
Department of Research and Isotopes, IAEA, P.O. Box 100, A-1400 Vienna, Austria

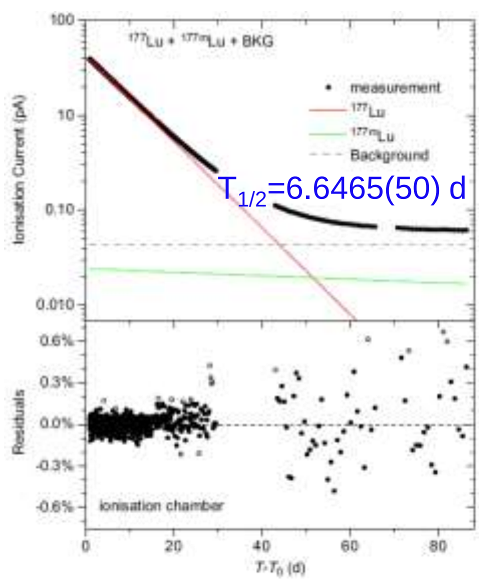
H. Vera Ruiz, Appl Radiat Isot 1988;39:31.

^{177}Lu half-life



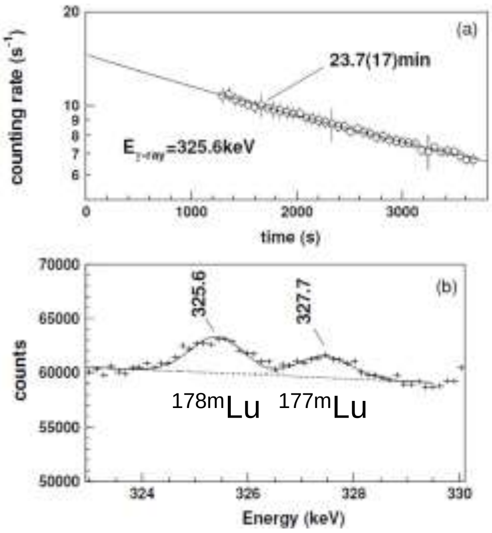
A. Abzouzi et al.,
J Radioanal Nucl Chem Lett 1990;144:359.

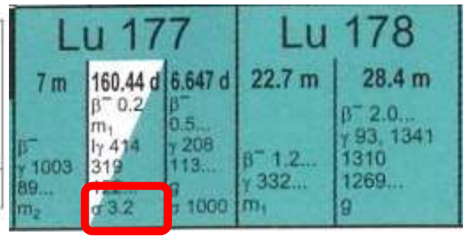


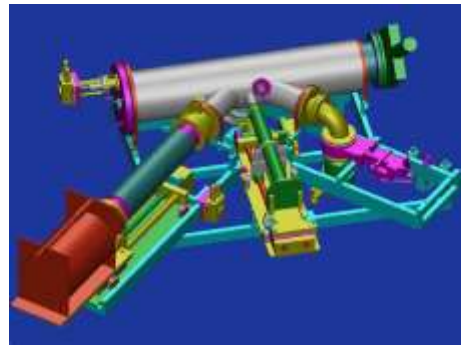


S. Pommé et al.,
Appl Radiat Isot 2011;69:1267.

$^{177m}Lu(n,\gamma)^{178m}Lu$



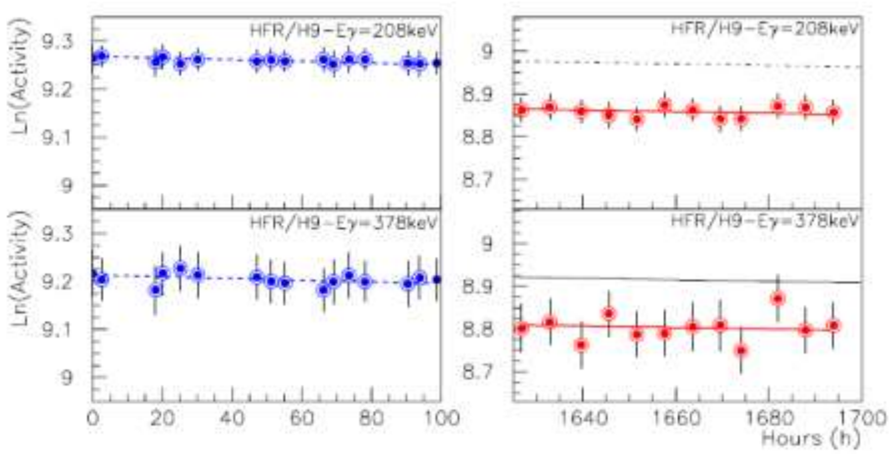




$\sigma[^{177m}Lu(n,\gamma)] = 368(26)$ b

G. Bélier et al.
Phys Rev C71, 014603 (2006)

Measurement of burnup cross-section



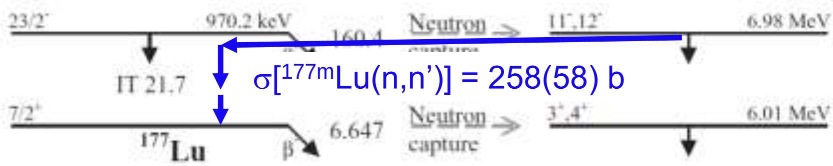
$\sigma[^{177m}Lu(n,X)] = 626(45)$ b

Why is $\sigma[^{177m}Lu(n,X)] >> \sigma[^{177m}Lu(n,\gamma)]$??

O. Roig et al. Phys Rev C71, 014603 (2006)

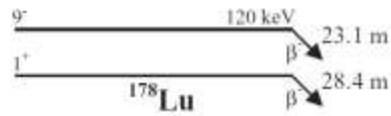
Inelastic neutron acceleration (INNA)

σ[177mLu(n,X)] = 626(45) b



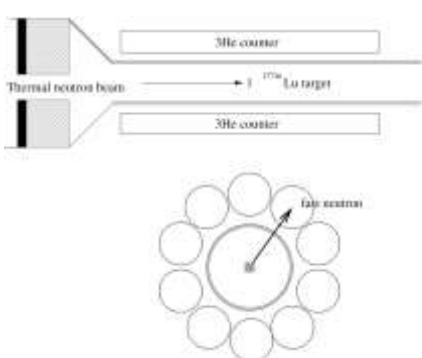
σ[177mLu(n,n')] = 258(58) b

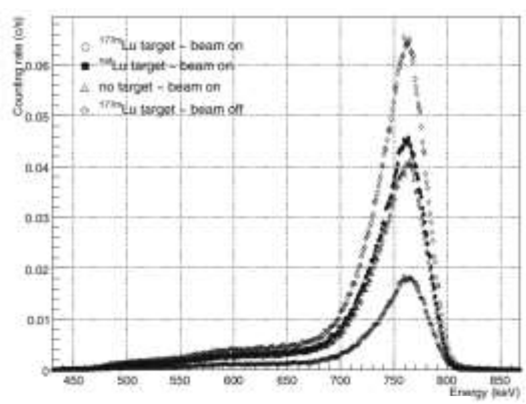
σ[177mLu(n,γ)] = 368(26) b



O. Roig et al. Phys Rev C71, 014603 (2006)

Direct observation of INNA





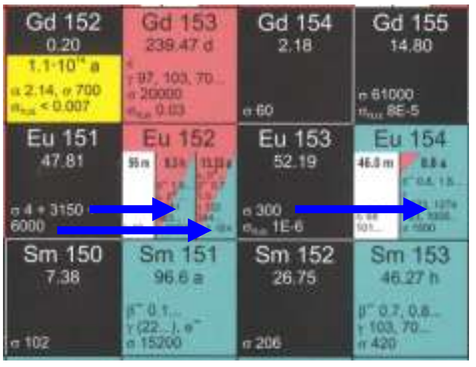
σ_{INNA} (cold) = 363(48) b

<< 642(151) b

(1/v scaling from thermal)

E. Bauge et al. Eur. Phys. J A48, 113 (2012)

What is produced when Eu is irradiated with n ?



Consider “product burn-up” in high neutron flux:
$\lambda[^{152m}\mathrm{Eu}(n,\gamma)] = \sigma \cdot \Phi = 68000 \cdot 10^{-24}\ \mathrm{cm}^2 \cdot 10^{15}\ \mathrm{cm}^{-2}\mathrm{s}^{-1}$
$\Rightarrow T_{1/2}(n,\gamma) = \ln(2) / \lambda(n,\gamma) = 2.8$ h, i.e. most ^{152m}Eu nuclei will capture a second neutron instead of decaying

Transmutation - Radioactivity Calculation

- ***Transmutation calculations:***

$$\frac{dN_i(t)}{dt} = -(\lambda_i + r_i) \cdot N_i(t) + \sum_{i \neq j} (\lambda_{j \to i} + r_{j \to i}) \cdot N_j(t) + PF_i$$

$$PF_i = \sum_h N_h \cdot \int_0^\infty dE \cdot \phi(E) \cdot \gamma_{h \to i}(E) \cdot \sigma_{f,h}(E)$$

Bateman transmutation equation

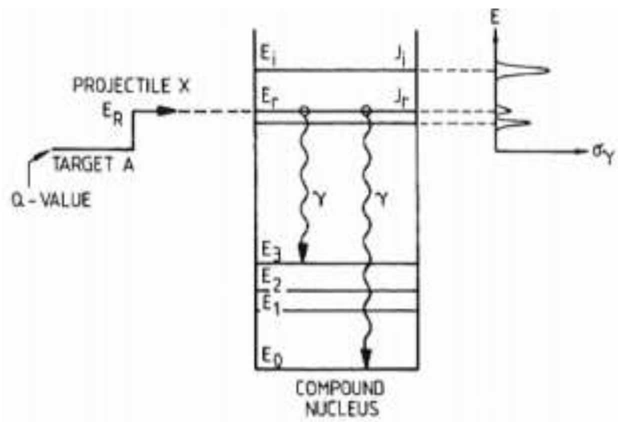
Responses: *Inventory (atoms), Activity (Bq), Dose (Sv), Decay Heat (W), Material damage (gas generation and dpa), neutron/gamma emission,...*

- ***Burnup calculation****: Neutron transport + Transmutation/Depletion*
- ***Reactor Safety Analysis****: “Multiphysics” problem*
  Neutron transport + Transmutation + Thermo-hydraulic + Fuel performance

24

Oscar Cabellos, 23 Jan 2024

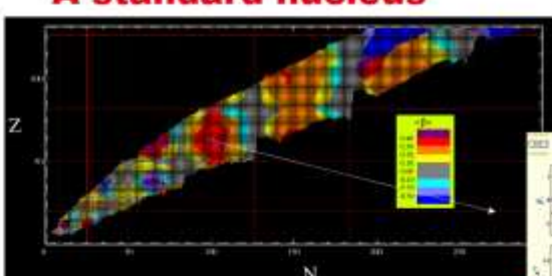
Resonance reactions



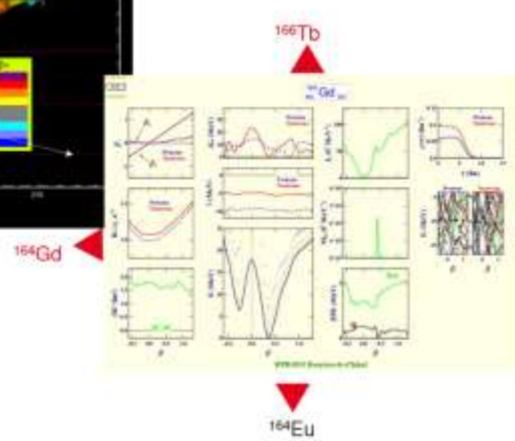
Enhanced cross-section (resonance) when energy matches excited state in compound nucleus.

High level density increases chance of hitting a resonance.

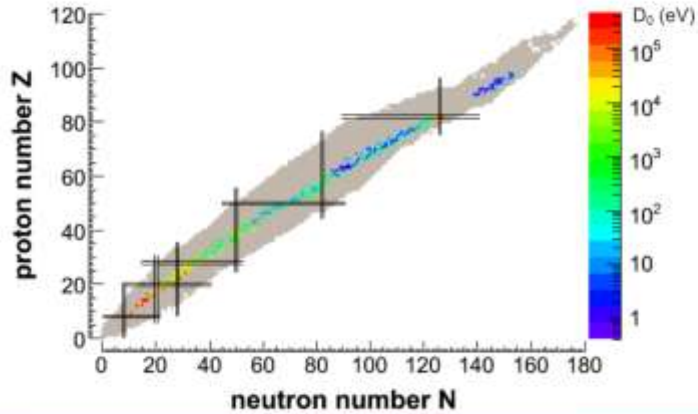
A standard nucleus



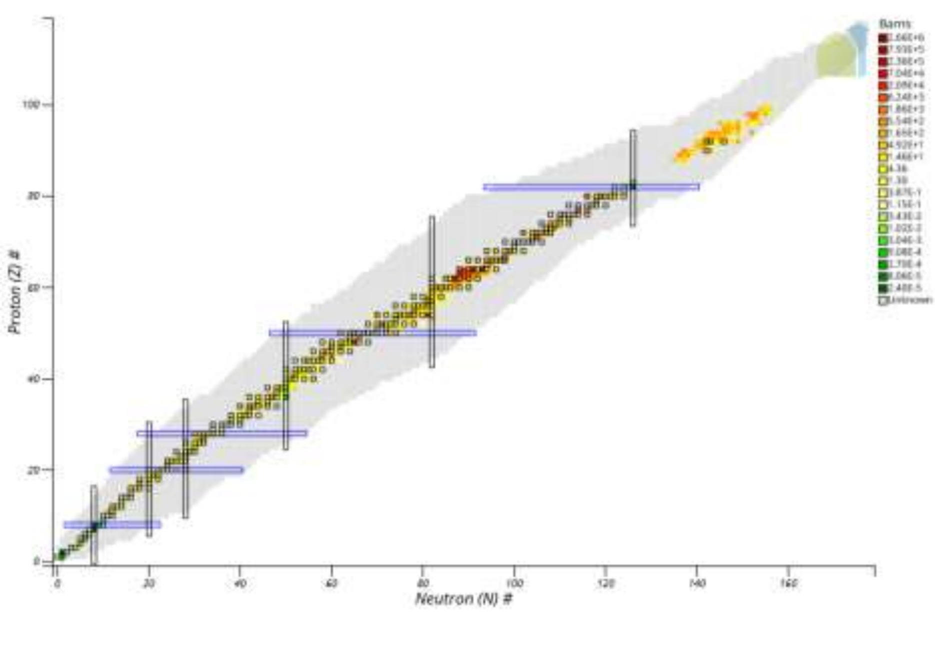
http://www-phynu.cea.fr/HFB-Gogny_eng.htm;
S. Hilaire & M. Girod, EPJ **A33** (2007) 237



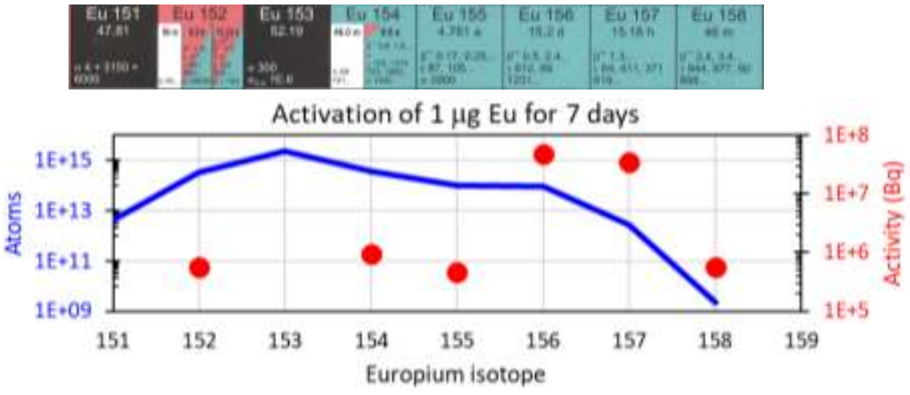
Nuclear level densities: level spacing D_0



Thermal neutron capture cross-sections



Multi neutron capture



$\Phi = 1.1\cdot10^{15}$ cm^{-2}s^{-1} , v = 2200 m/s
$\Rightarrow N_{n\text{-}th} = 5\cdot10^{9}$ cm^{-3}

$\sigma_{th} \approx$ 1000x higher compared to keV cross-sections
$\Rightarrow$ equivalent $N_{n\text{-}keV} \approx 5\cdot10^{12}$ cm^{-3}

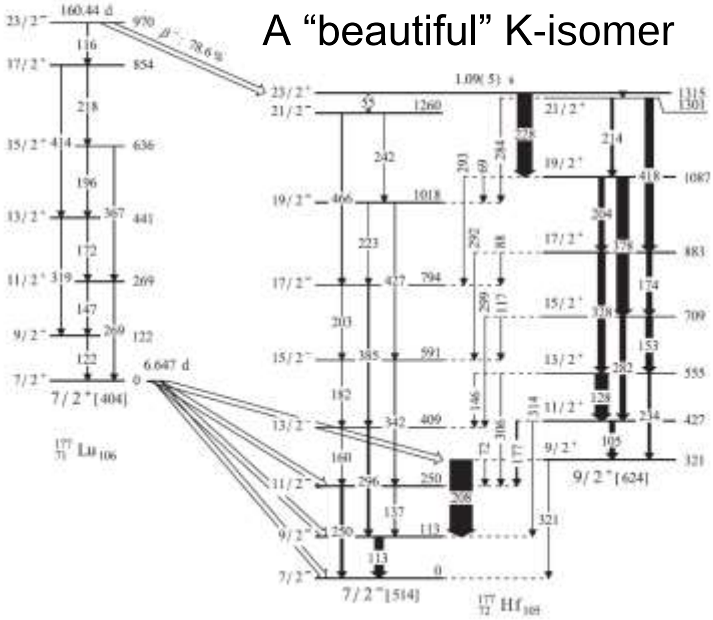
Q: stellar neutron capture process at such N_n?

List of neutron capture processes

- The **r process** (neutrino-wind, NS mergers, jet-SNe, etc) - $N_n > 10^{20}$ n cm^{-3};
- The **n process** (explosive He-burning in CCSN) - 10^{18} n cm$^{-3} < N_n <$ few 10^{20} n cm^{-3};
- The **i process** (H ingestion in convective He burning conditions) - 10^{13} n cm$^{-3} < N_n < 10^{16}$ n cm^{-3};
- Neutron capture triggered by the Ne22(α,n)Mg25 in massive AGB stars and super-AGB stars - $N_n < 10^{14}$ n cm^{-3};
- The **s process** (s process in AGB stars, s process in massive stars and fast rotators) – $N_n <$ few 10^{12} n cm^{-3}.

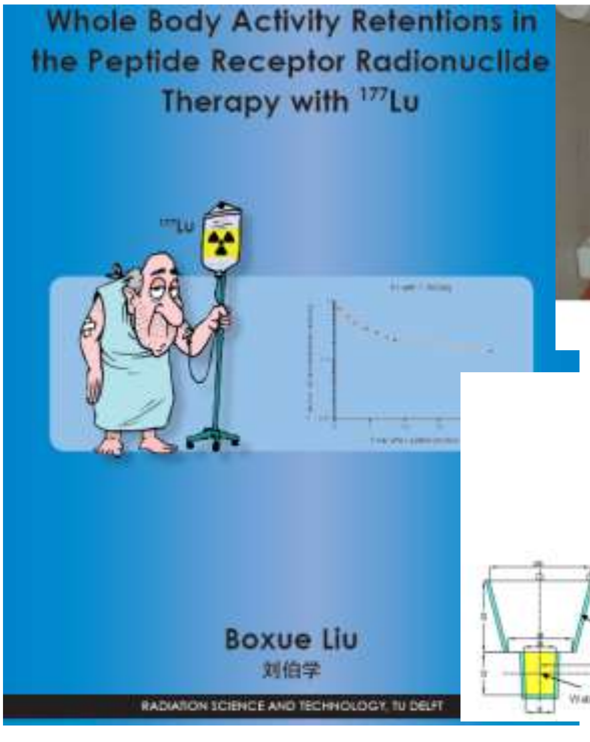
Marco Pignatari, 24 Jan 2024

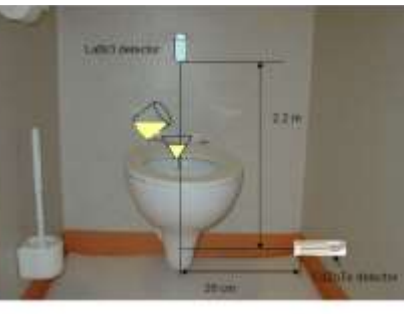
A “beautiful” K-isomer



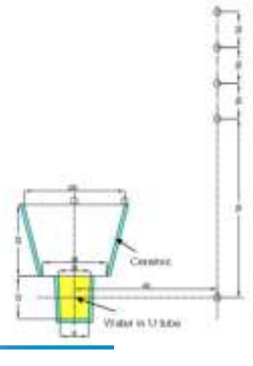
Lu 177	
160 d	6.65 d
β^- 0.2 Iγ 414, 319,..	β^- 0.5… γ 208, 113…

F. Kondev et al., Phys Rev C 2012;85:027304.
F. Kondev et al., Appl Rad Isot 2012;70:1867.
L. Knafla et al., Phys Rev C 2020;102:054322.



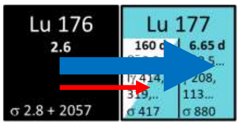


a. Toilet pot and experimental setup



b. Top view of the toilet pot

The curse of the K-isomer



Direct production:
≈0.01% ^{177m}Lu/^{177g}Lu (Bq/Bq) in c.a. ^{177}Lu

Waste problem for hospitals

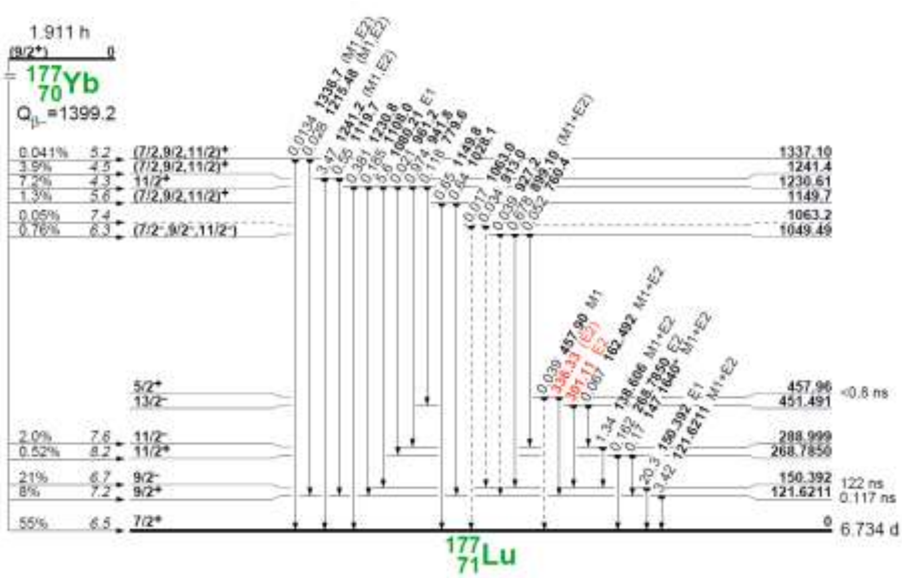
A. Brown, EANM'9, OP-549.
Eur J Nucl Med Mol Imag 2019;46 Suppl 1:S212.

~ 100 k patients/year

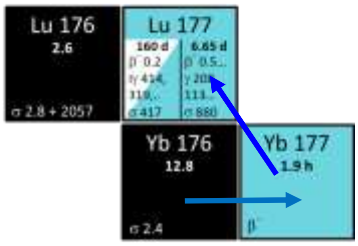
~ 4000 TBq injected ~ 3·10^{21} atoms ≈ 1 g ^{177}Lu

Isomer separation out of scale of any "lab experiments"

^{177}Yb decay to 7/2$^+$ ground state



Indirect production of no-carrier-added ^{177}Lu

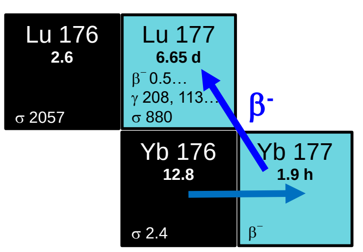


Indirect production:
no ^{177m}Lu in n.c.a. ^{177}Lu

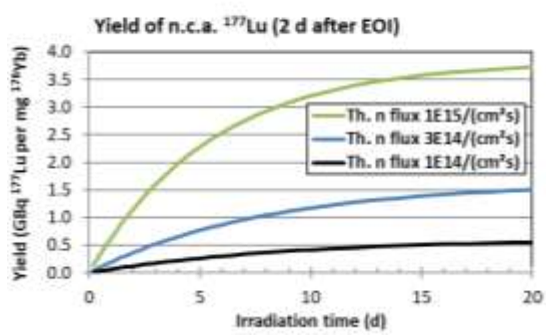
Accelerator production of ^{177}Lu is NOT competitive in terms of yield and would produce even more ^{177m}Lu!

Production of no-carrier-added ^{177}Lu

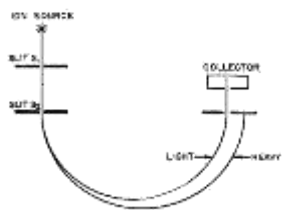
Indirect production



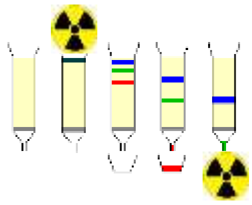
Specific activity ≈ theoretical
Yield depends on σ and Φ



Estimate for 100% enriched ^{176}Yb;
depends in reality also on neutron spectrum, self shielding, etc.



Calutron enrichment of ^{176}Yb



Radiochemical ^{177}Lu/^{176}Yb separation

Competitive advantage of higher neutron flux

Enriched ^{176}Yb

Reactor irradiation

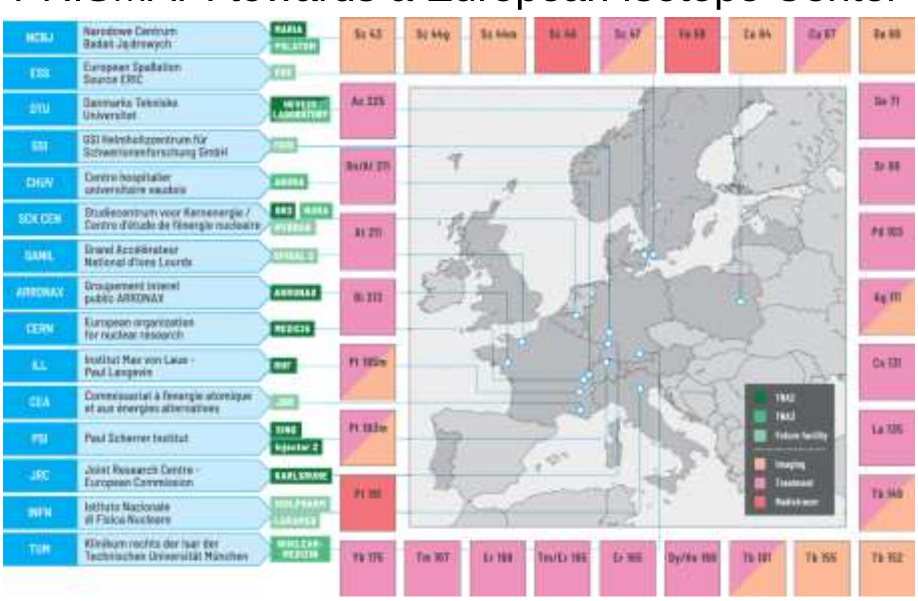
Radio-chemical separation

Radioisotope production in high flux reactors

High flux reactor	Operator	Location	Thermal flux (10^{14} cm^{-2}s^{-1})
HFIR	ORNL	Oak Ridge, US	–25
SM3	SSC RIAR	Dimitrovgrad, RU	–19 (tank)
RHF	**ILL**	**Grenoble, FR**	**–15**
BR2	SCK-CEN	Mol, BE	10 (tank), 2–4 (pool)
FRM2	TUM	Garching, DE	1.3 / 3-4 (new)
HFR	NRG	Petten, NL	2–4
MURR	Univ. Missouri	Columbia, US	2–4
SAFARI	NECSA	Pelindaba, ZA	2–3
OPAL	ANSTO	Lucas Heights, AU	2–3
MARIA	NCBJ	Swierk, PL	2–3
BRUCE Unit 7	Bruce Power	Tiverton, CA	2

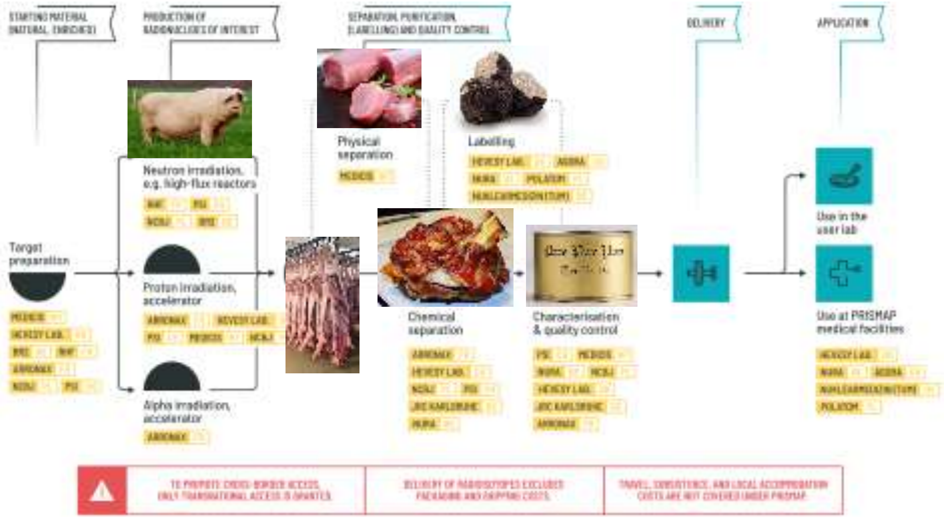
Red are irradiation positions in the tank where samples stay in for the entire reactor cycle (too long for ^{177}Lu production).

PRISMAP: towards a European Isotope Center



This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP).

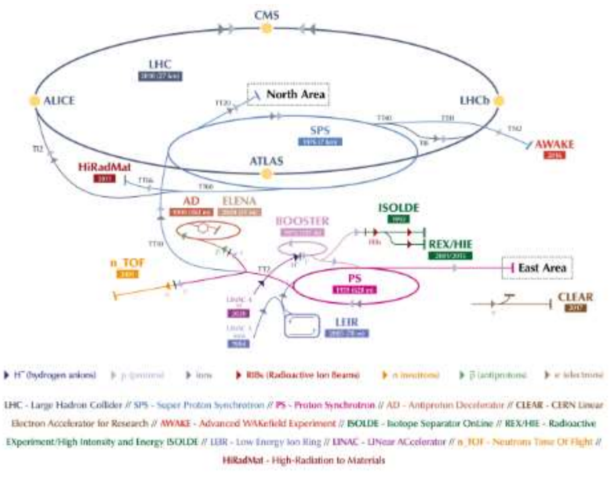
The flowchart of PRISMAP facilities



WP2-TNA2 Production and dispatch of non-conventional radioisotopes

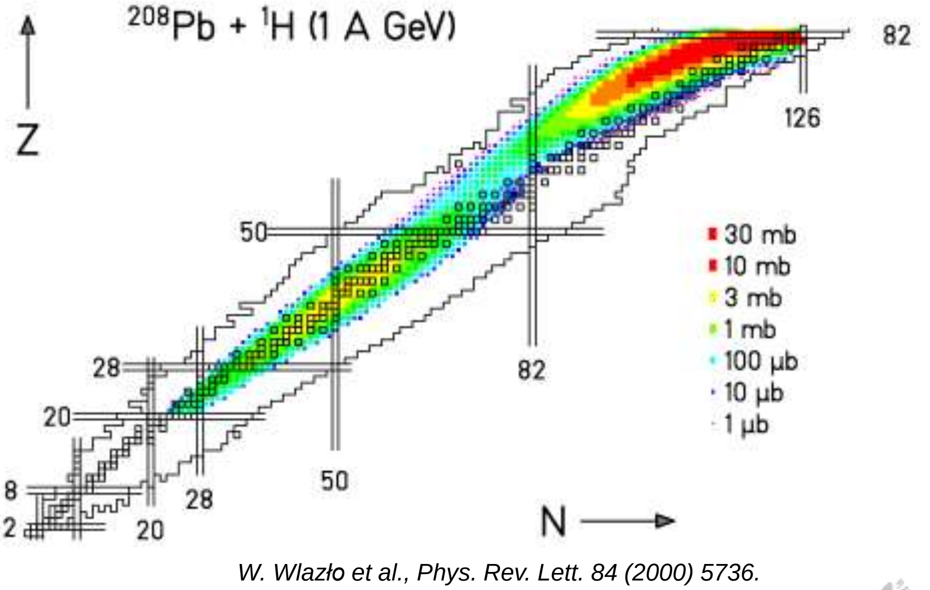
Terbium: a unique element for nuclear medicine

The accelerator complex of CERN



Ion source	90 keV
LINAC4	160 MeV
PSB	1.4 GeV
PS	25 GeV
SPS	450 GeV
LHC	7000 GeV

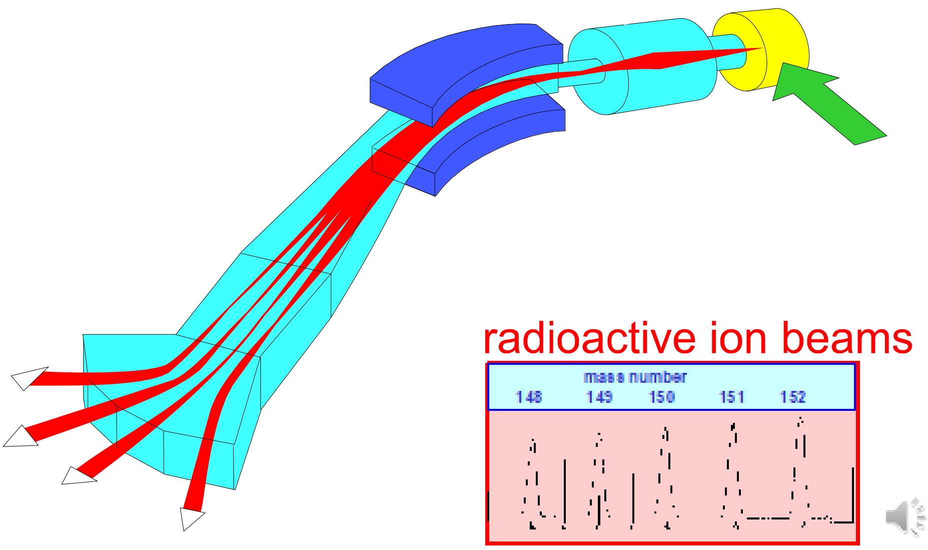
Spallation + Fragmentation + Fission



W. Wlazło et al., Phys. Rev. Lett. 84 (2000) 5736.

T. Enqvist et al., Nucl. Phys. A 686 (2001) 481.

Production of ^{149}Tb, ^{152}Tb and ^{155}Tb at ISOLDE



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- Cyclotron Produced Radionuclides: Physical Characteristics and Production Methods, IAEA Vienna 2009, Tech. Rep 468.
- Lectures on Theranostics by Richard Baum:

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- (Free) medical review papers from http://pubmed.gov
- Information on on-going clinical trials: http://clinicaltrials.gov
- Infos on: https://www.prismap.eu/