

Overview

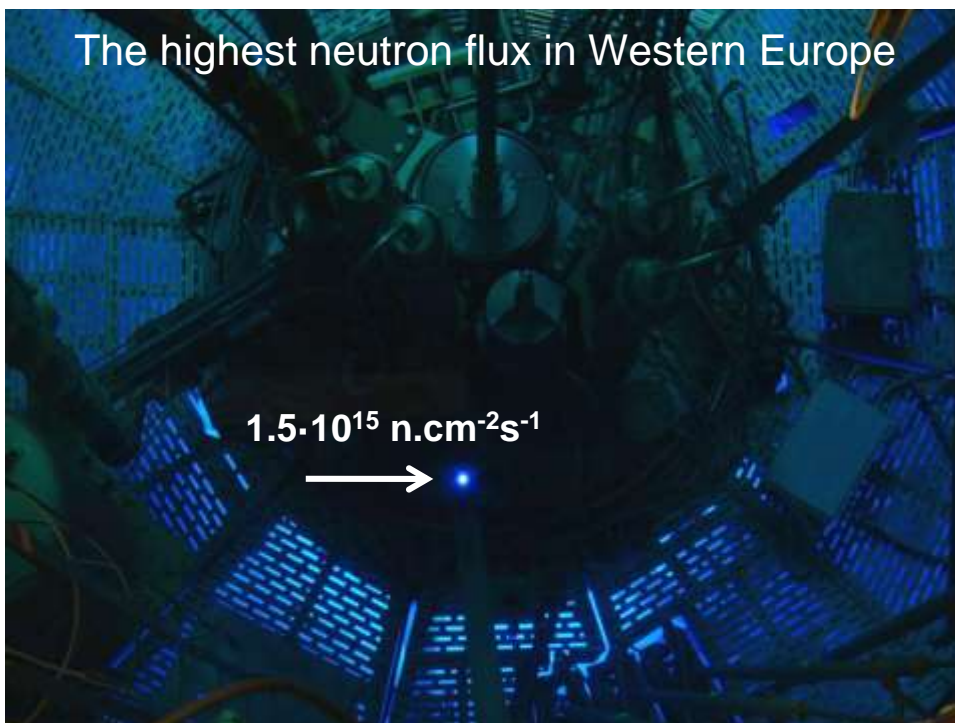
Ulli Köster

Institut Laue-Langevin, Grenoble



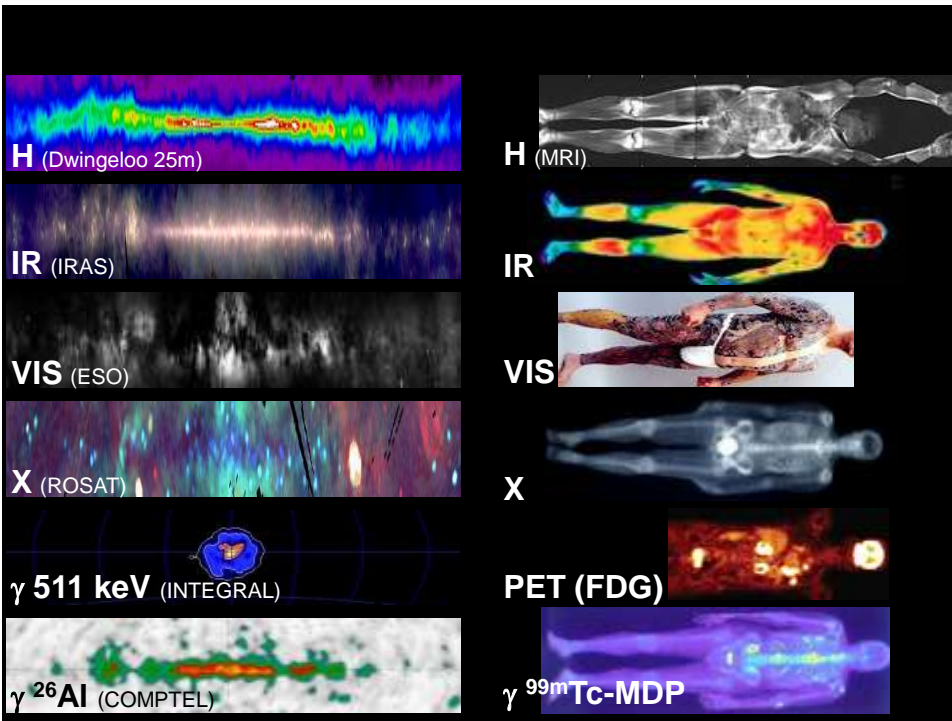
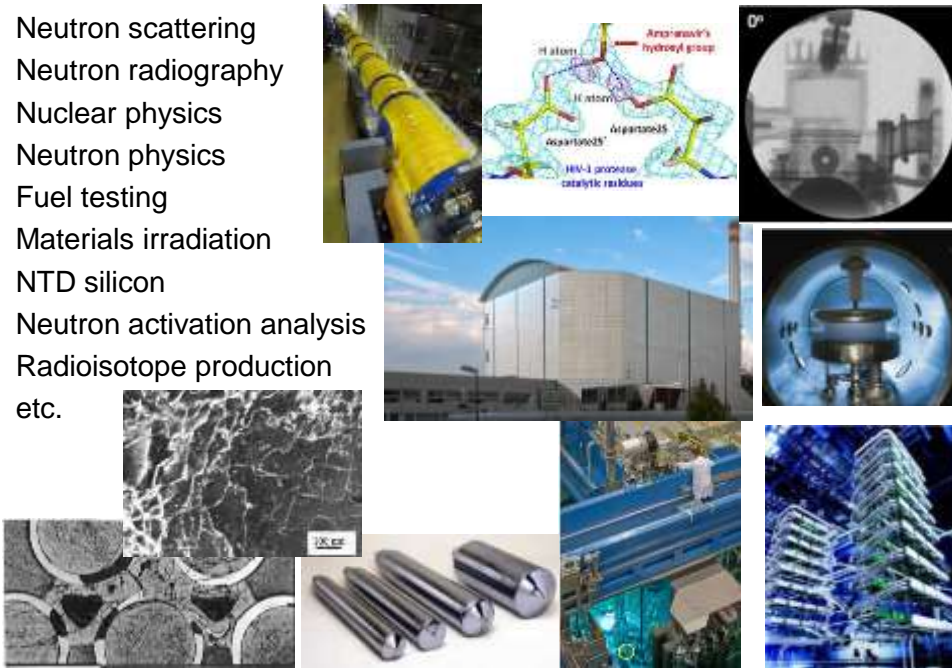
MEDICIS-PROMED

9 February 2016

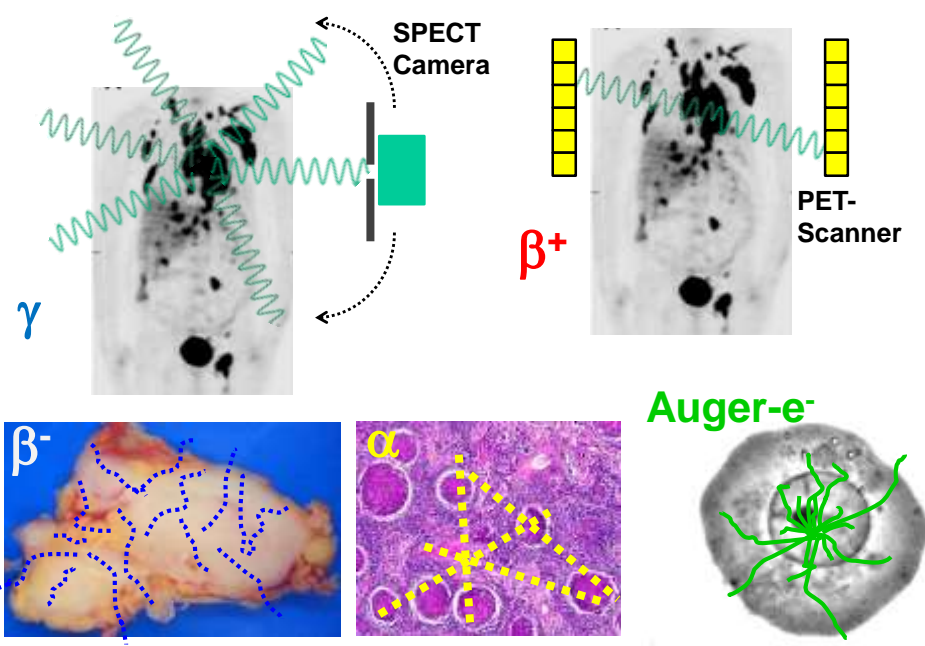


Research reactors are multi-use facilities

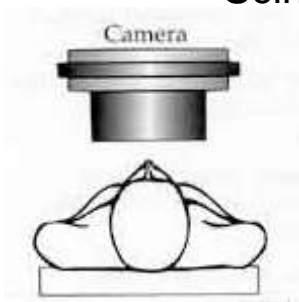
Neutron scattering
 Neutron radiography
 Nuclear physics
 Neutron physics
 Fuel testing
 Materials irradiation
 NTD silicon
 Neutron activation analysis
 Radioisotope production
 etc.



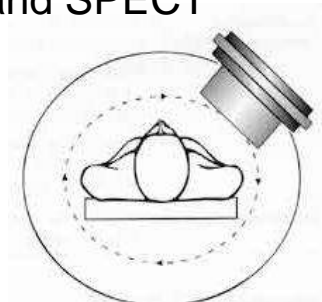
The Nuclear Medicine Alphabet



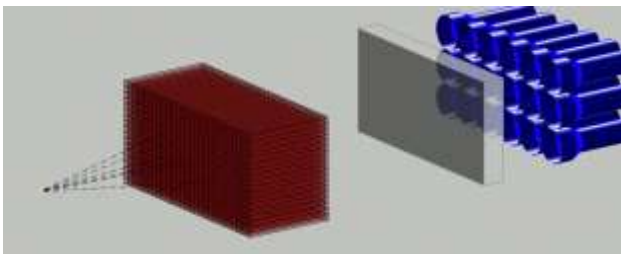
Scintigraphy and SPECT



2D: planar scan
(Gamma camera)

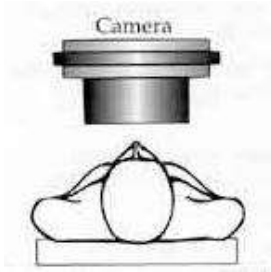


3D: SPECT: Single Photon Emission
Computer Tomography

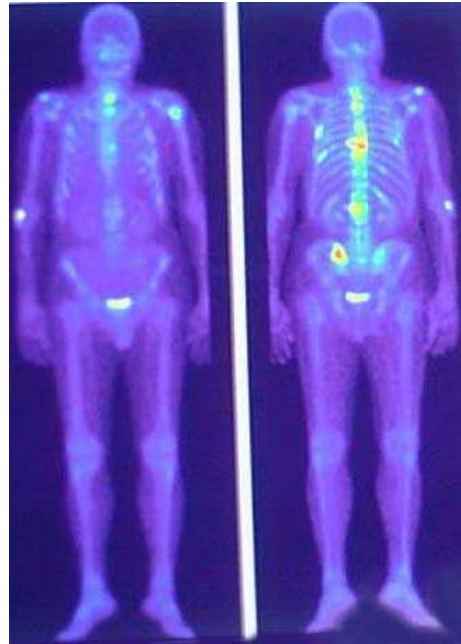


$E_{\gamma} > 60 \text{ keV}$
 $E_{\gamma} < 400 \text{ keV}$

Bone metastases

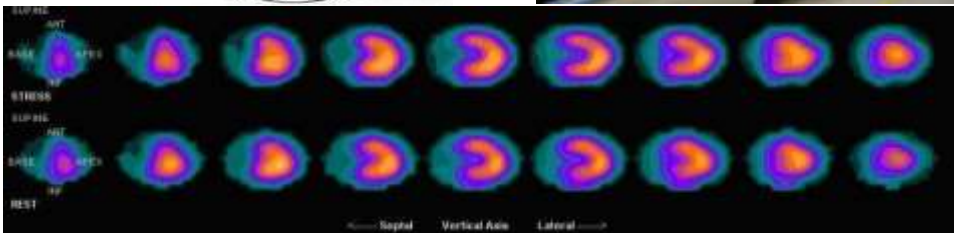
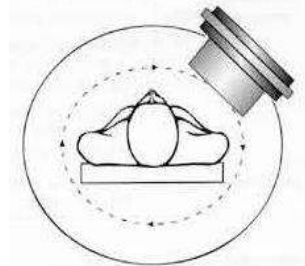


- planar or SPECT scan for bone metastases
- differentiate between local and generalized disease
- decide on treatment options: surgery or radiation therapy versus systemic therapy
- Bone: 35% of NM procedures in Europe



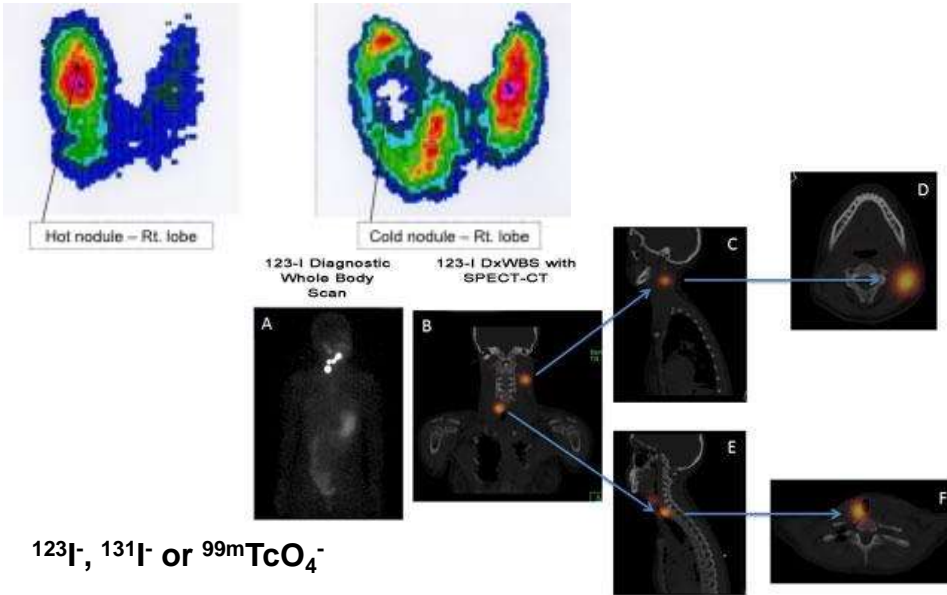
Ischemic heart disease

- diagnose by ECG, quantify by cardiac stress test with SPECT
- treatment by medication, angioplasty or bypass surgery
- 26% of NM procedures in Europe

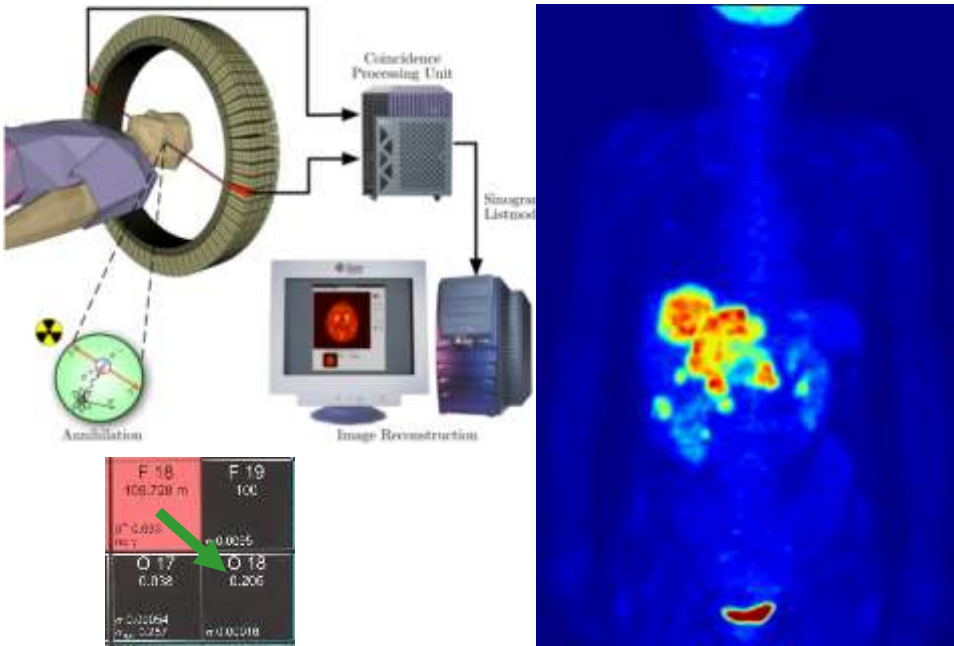


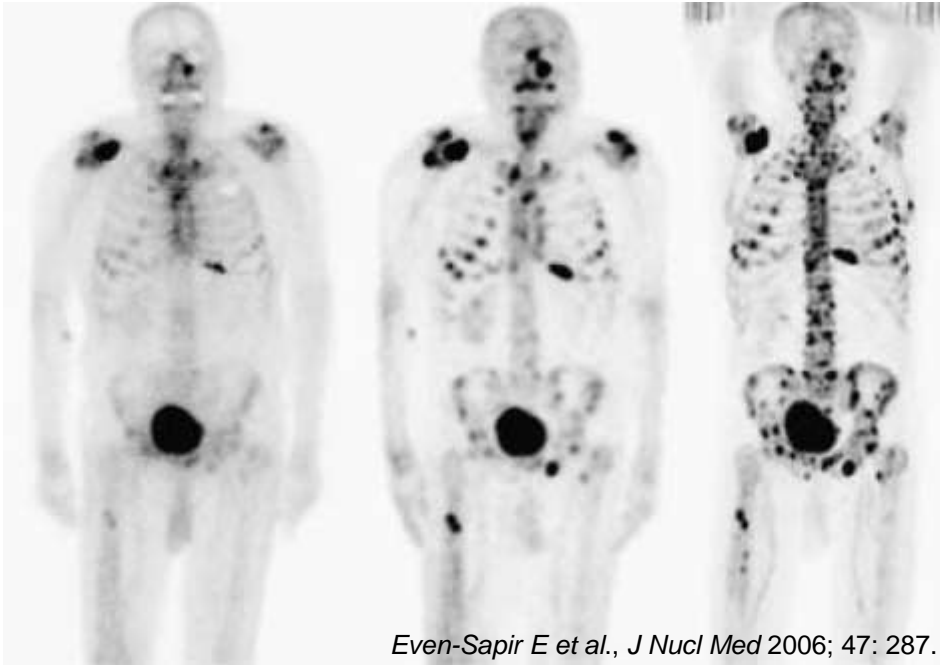
Thyroid scintigraphy

Thyroid: 12% of NM procedures in Europe



Positron Emission Tomography





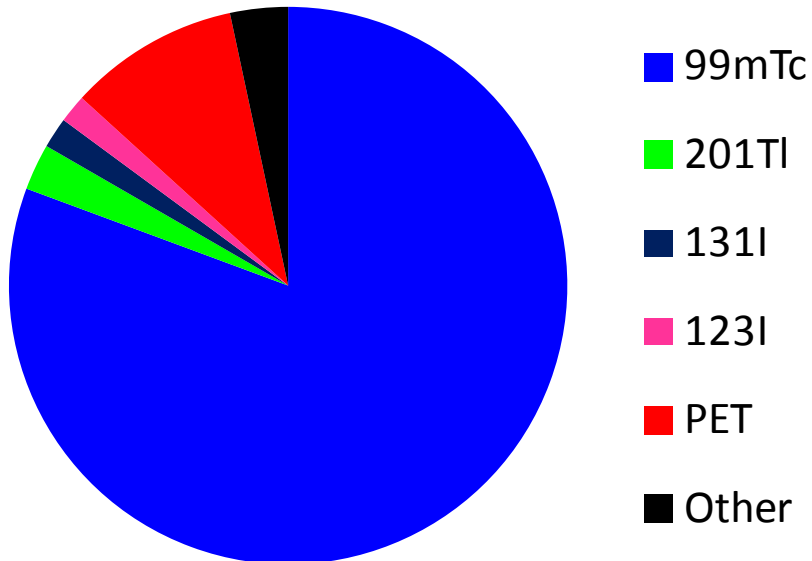
Even-Sapir E et al., J Nucl Med 2006; 47: 287.

^{99m}Tc -MDP planar

^{99m}Tc -MDP SPECT

^{18}F -PET

Cumulative use of diagnostic isotopes in Europe



<http://www.nupecc.org/npmed/npmed2014.pdf>

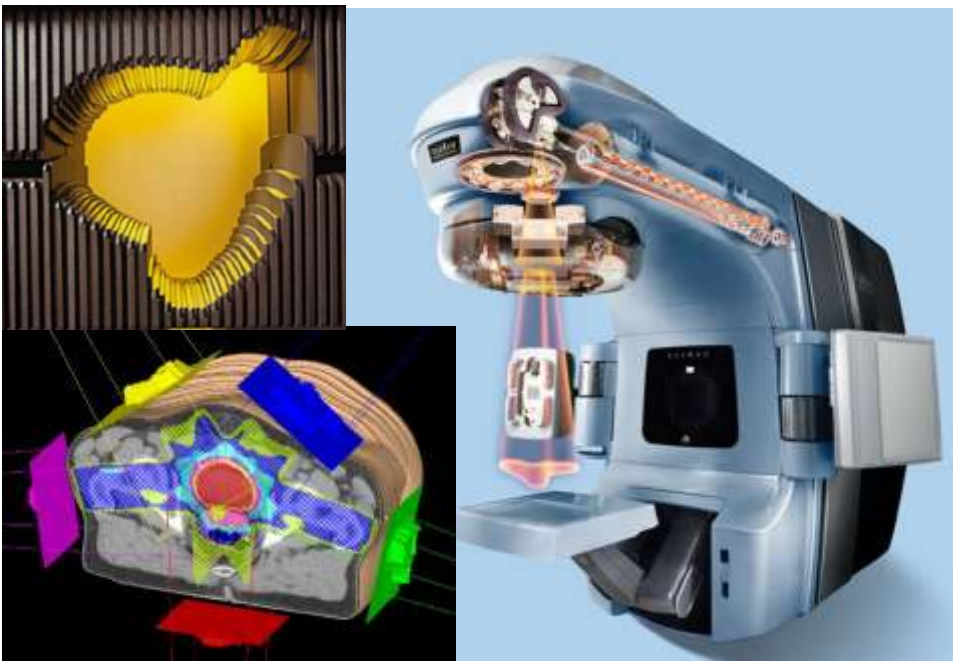
From diagnostics

The death and the radiologist.

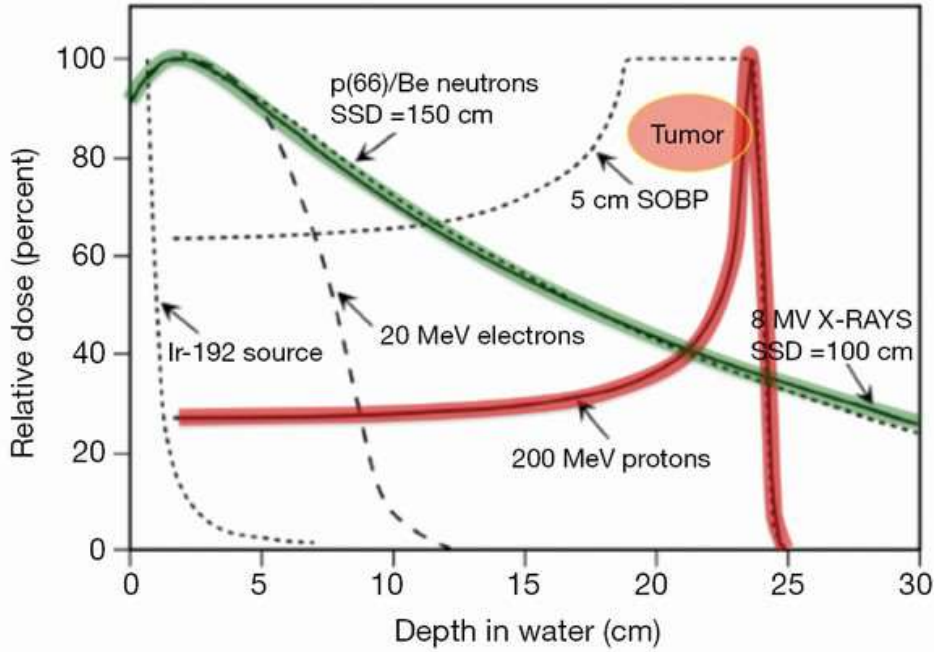


to therapy

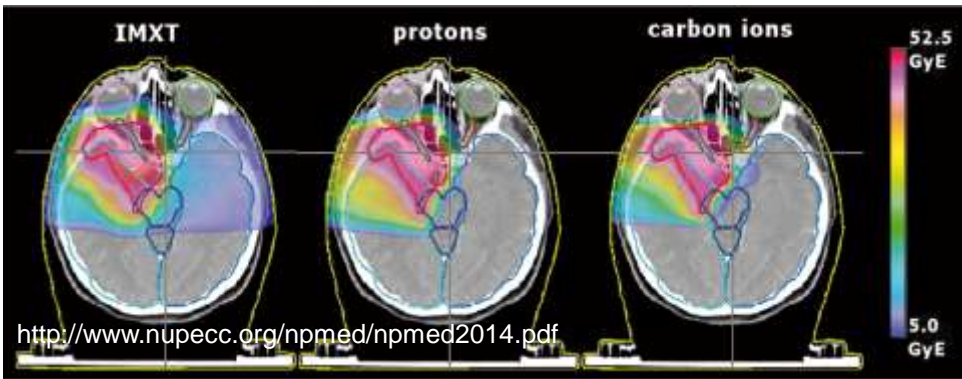
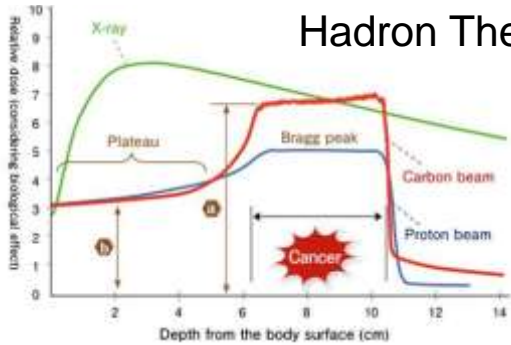
EBRT (External Beam Radiation Therapy)



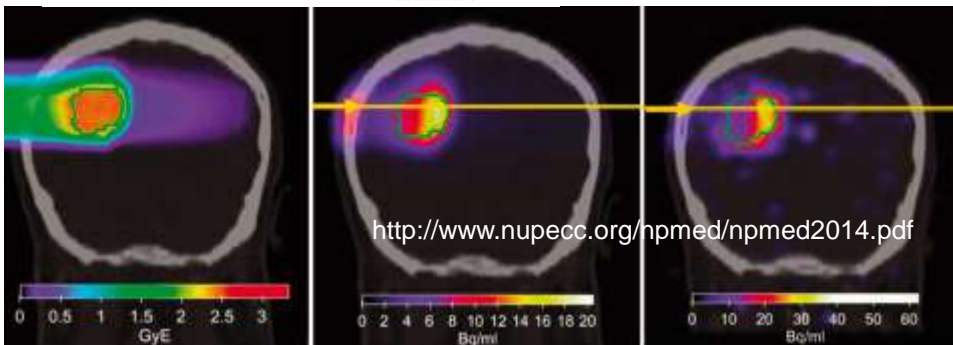
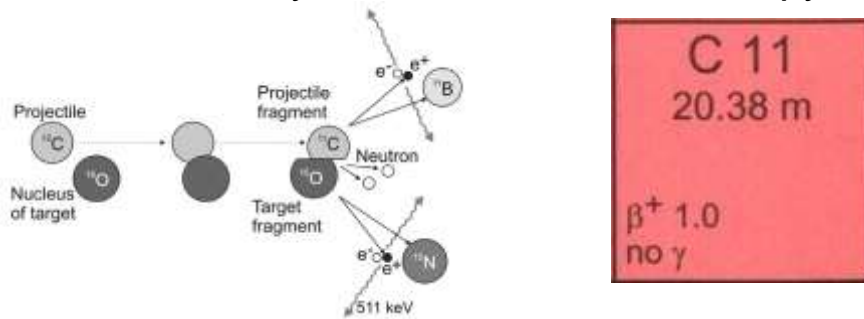
EBRT (External Beam Radiation Therapy)



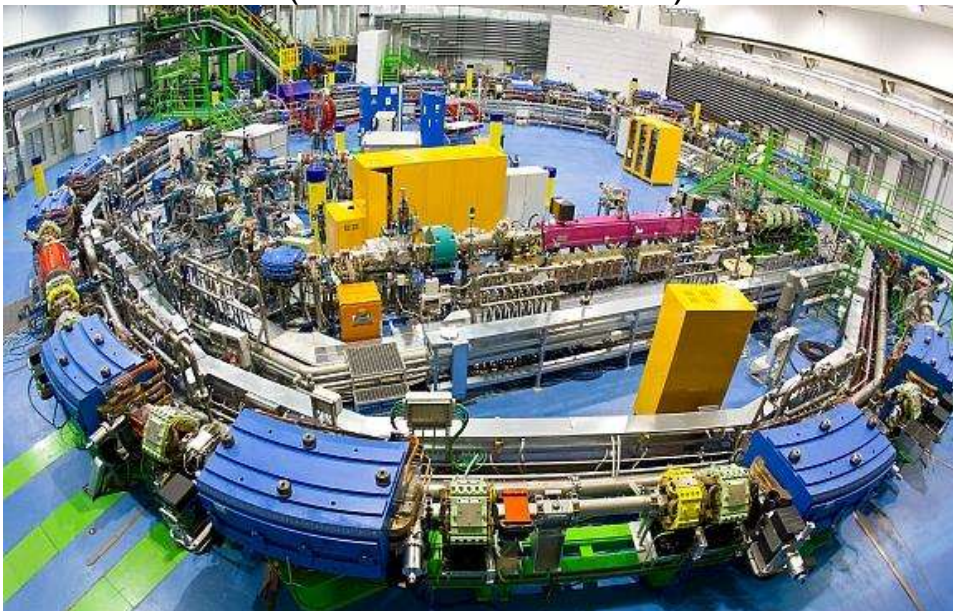
Hadron Therapy



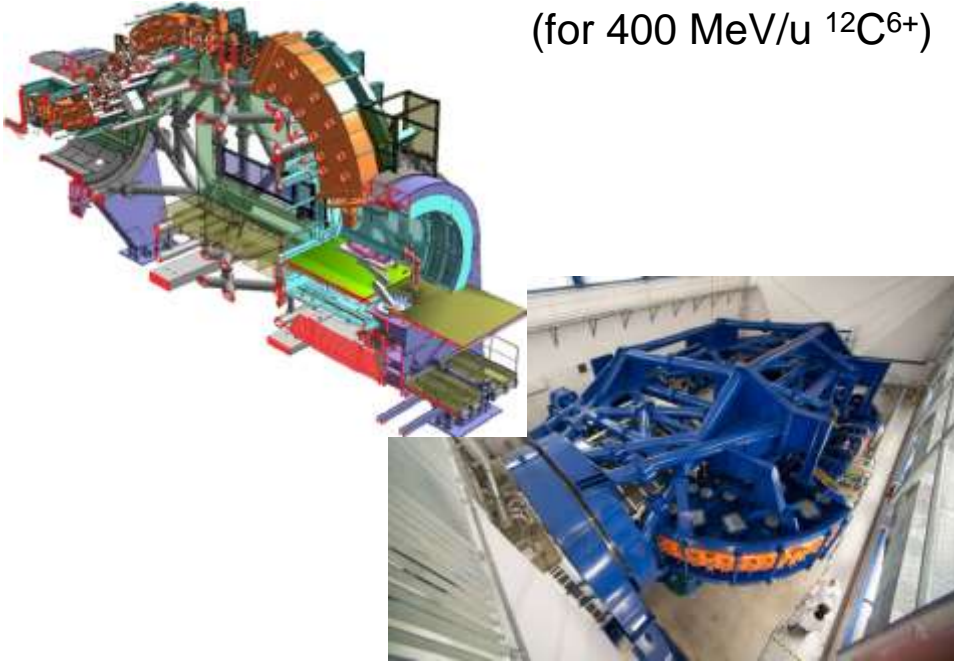
PET for Quality Control in Hadron Therapy



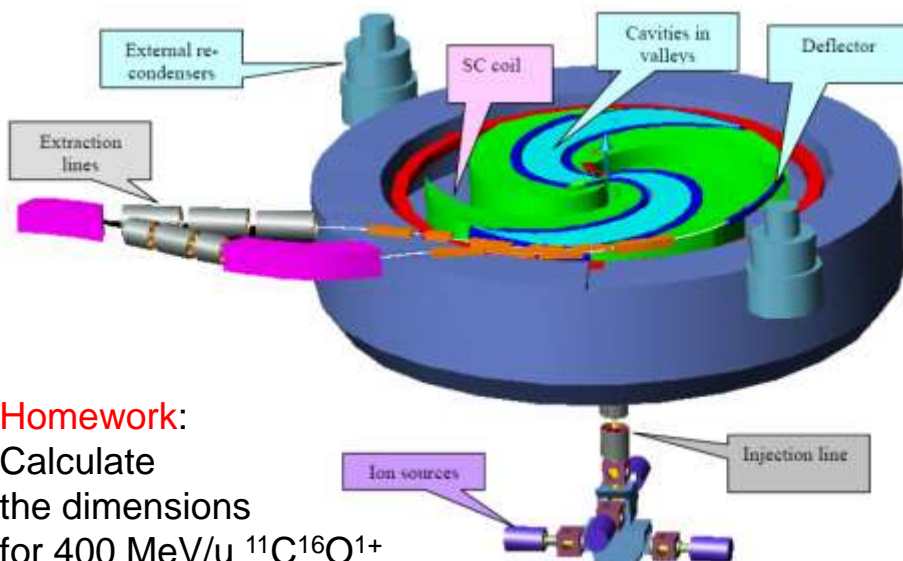
CNAO synchrotron: 78 m long, 25 m diameter
(for 400 MeV/u $^{12}\text{C}^{6+}$)



HIT gantry: 25 m long, 13 m diameter, 670 tons
(for 400 MeV/u $^{12}\text{C}^{6+}$)

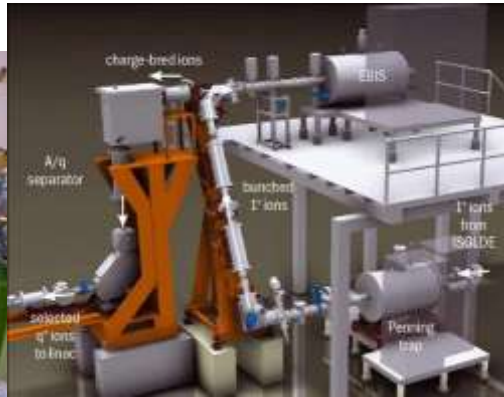
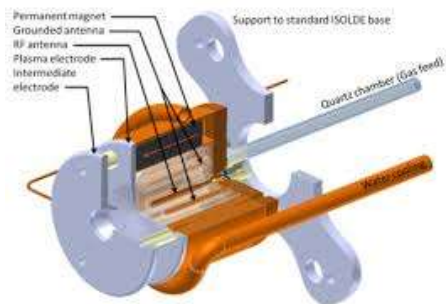


IBA C400 cyclotron: 6.6 m diameter, 700 tons
(for 400 MeV/u $^{12}\text{C}^{6+}$)



Homework:
Calculate
the dimensions
for 400 MeV/u $^{11}\text{C}^{16}\text{O}^{1+}$

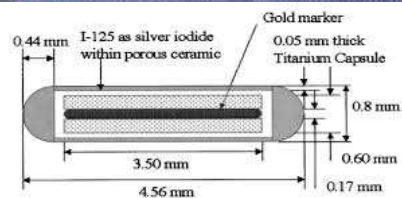
Molecular beams and charge breeding



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”)



Cancer and efficiency of treatments

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

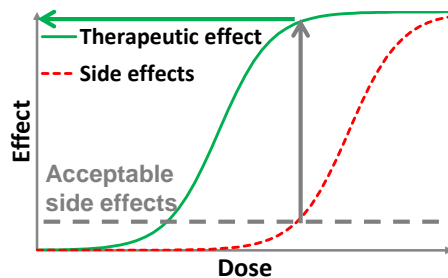
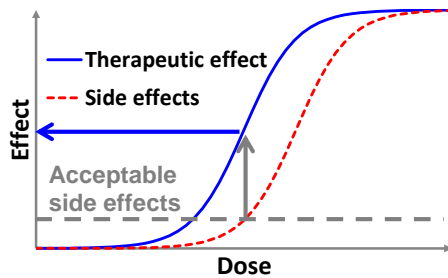
Over **one million deaths per year** from cancer in EU.

- ⇒ improve early diagnosis
- ⇒ improve systemic treatments

Targeted therapies

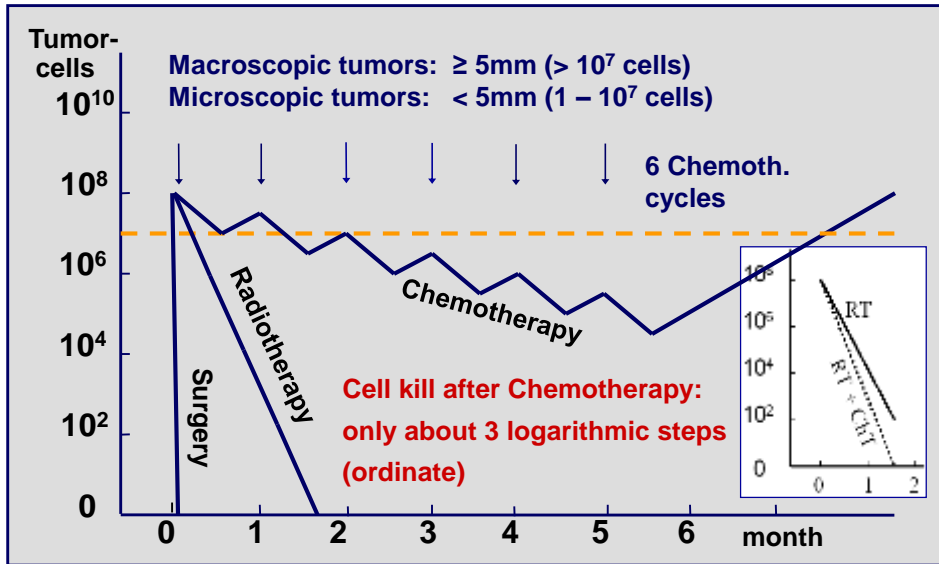


Paracelsus (1493-1541)
“All things are poison, and nothing is without poison; only the dose permits something not to be poisonous.”



Selective targeting is essential to widen the therapeutic window!

Comparison of Therapies



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



Klinik und Poliklinik für Strahlentherapie und Radiologische Onkologie

Prof. Molls



Learning from history

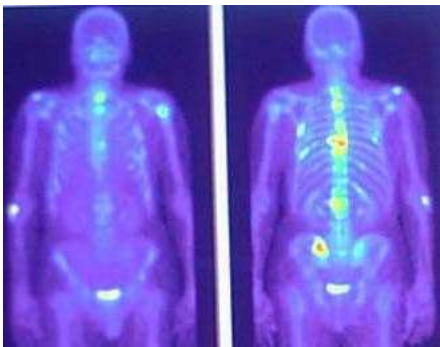


The principle of targeted therapies

- “attractive” vector > high uptake by the target
- transportable
- good in-vivo stability
- warriors “not visible”
- delayed uptake > suitable half-life
- limited space > high specific activity
- optimum arms
- specific



Metabolic targeting



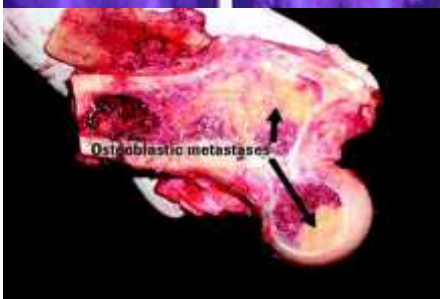
Thyroid cancer

$^{123}\text{I}^-$ for imaging
 $^{131}\text{I}^-$ for therapy

Bone metastases

1.5 million patients world-wide

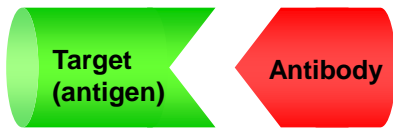
$^{99\text{m}}\text{Tc}$ -MDP for SPECT imaging
 ^{18}F for PET imaging



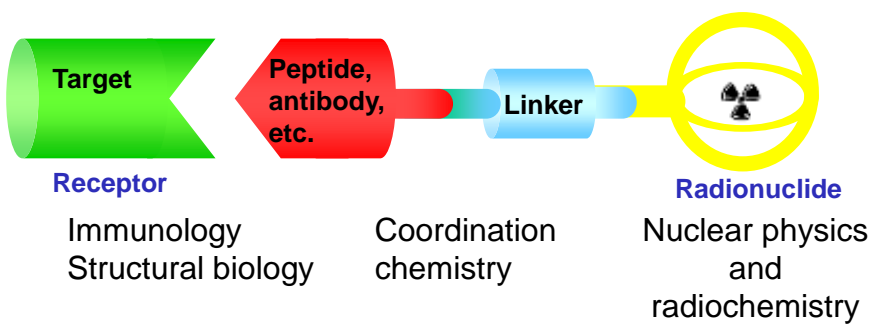
Therapy

^{153}Sm -EDTMP (Quadramet)
 $^{89}\text{Sr}^{2+}$ (Metastron)
 $^{223}\text{Ra}^{2+}$ (Xofigo/Alpharadin)

Immunology approach

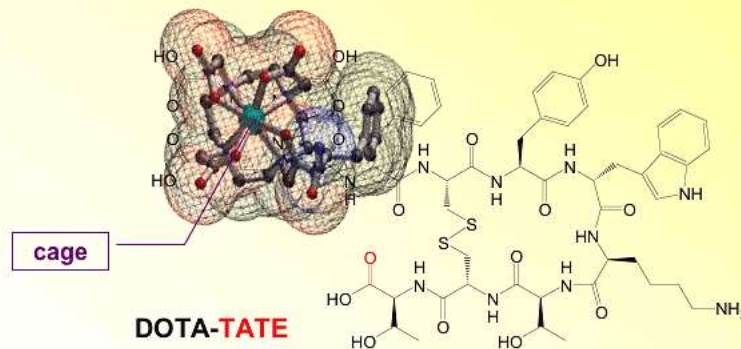


Multidisciplinary collaboration to fight cancer



Nuclear medicine and medical physics

Structural Formula of DOTA-TOC/TATE



1,4,7,10-tetraazacyclododecantetraacetate

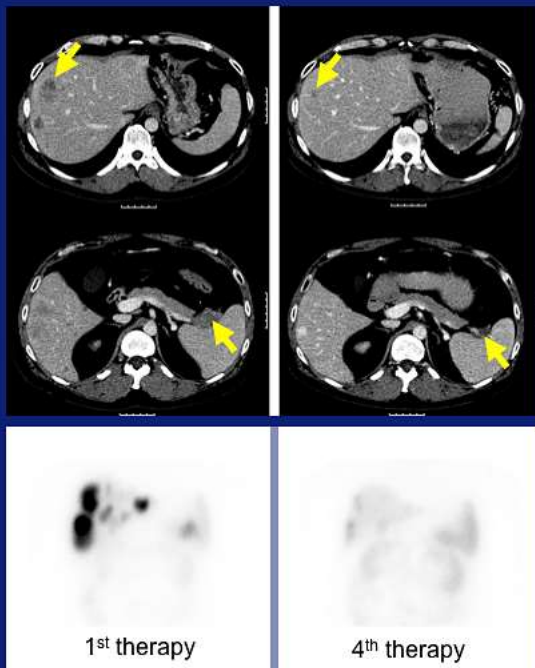
^{111}In ^{90}Y

^{67}Ga ^{177}Lu

^{68}Ga ^{213}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}Lu -
octreotate and
capecitabine

Partial remission

Roelf Valkema, EANM-2008.

What success does PRRT offer?

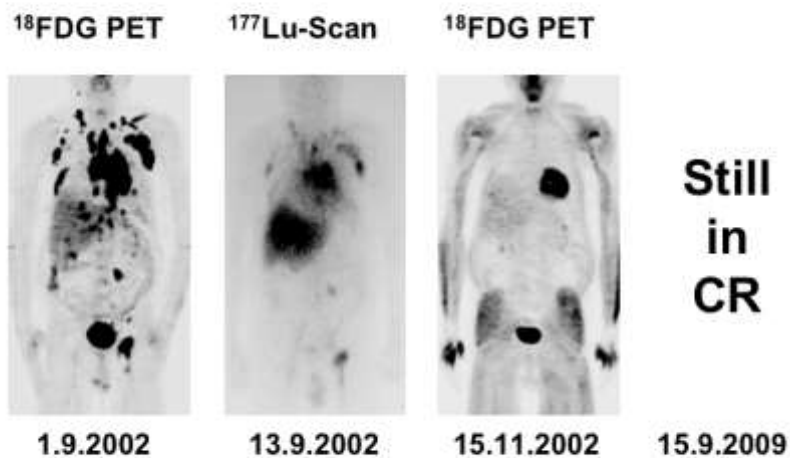
- ✓ CR+ PR + MR in about 50% of patients: **YES**
- ✓ Reduce symptoms and improve quality of life: **YES**
- ✓ Increase survival time: **YES**
- ✓ Safety and tolerability: **YES**

Roelf Valkema, EANM-2008.



Lymphoma therapy: RITUXIMAB+¹⁷⁷Lu

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



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



University Hospital Basel, CH



Radionuclides for targeted radionuclide therapy

Radio-nuclide	Half-life (d)	E mean (keV)	E _γ (B.R.) (keV)	Range	
Y-90	2.7	934 β	-	12 mm	Established isotopes
I-131	8.0	182 β	364 (82%)	3 mm	
Lu-177	6.7	134 β	208 (10%) 113 (6%)	2 mm	Emerging isotope

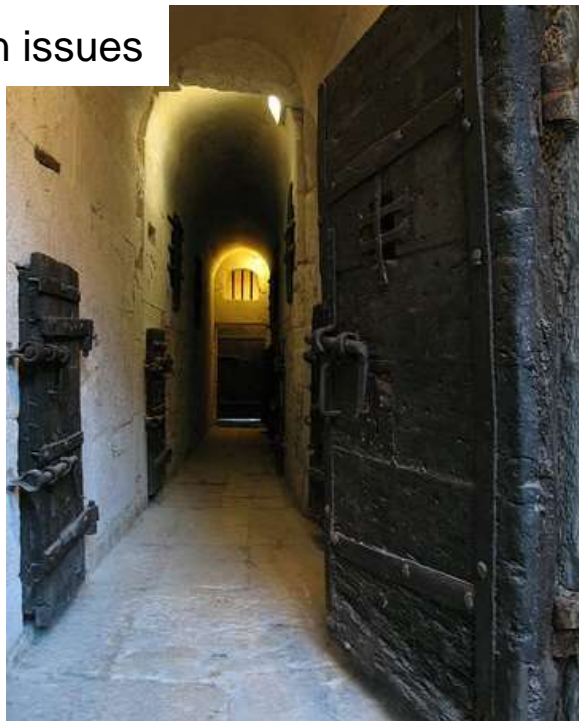
¹³¹I: radioprotection issues

364 keV gamma ray emitted with 82% B.R.

**3.7 GBq patient dose
⇒ 0.2 mSv/h at 1 m**

**“hot zone”
(IAEA/NRCP)**

**requires dedicated
shielded treatment
rooms**



^{90}Y : collateral damage from long range betas ?

$Q_{\beta^-} = 2.28 \text{ MeV}$
up to 12 mm range



The rising star
for therapy



Production of ^{177}Lu

Ta 175 10.5 h	Ta 176 8.1 h	Ta 177 56.6 h	Ta 178 9.23 m 2.45 h	Ta 179 665 d	Ta 180 0.012	Ta 181 99.988
Hf 174 0.16 $2.0 \cdot 10^{15}$ a	Hf 175 70.0 d	Hf 176 5.26	Hf 177 51 m 1.1 s 18.60	Hf 178 31 a 4.0 s 27.28	Hf 179 25 d 18.7 s 13.62	Hf 180 5.3 h 35.06
Lu 173 1.37 a	Lu 174 142 d 3.31 a	Lu 175 97.41	Lu 176 2.59 3.68 h $3.8 \cdot 10^{10}$ a	Lu 177 160.1 d 0.71 d	Lu 178 22.7 m 28.4 m	Lu 179 4.6 h
Yb 172 21.83	Yb 173 16.13	Yb 174 31.83	Yb 175 4.2 d	Yb 176 12 s 12.76	Yb 177 6.5 s 1.9 h	Yb 178 74 m
Tm 171 1.92 a	Tm 172 63.6 h	Tm 173 8.2 h	Tm 174 1.57 a	Tm 175 15.2 m	Tm 176 1.9 m	Tm 177 85 s

Waste problem for hospitals!

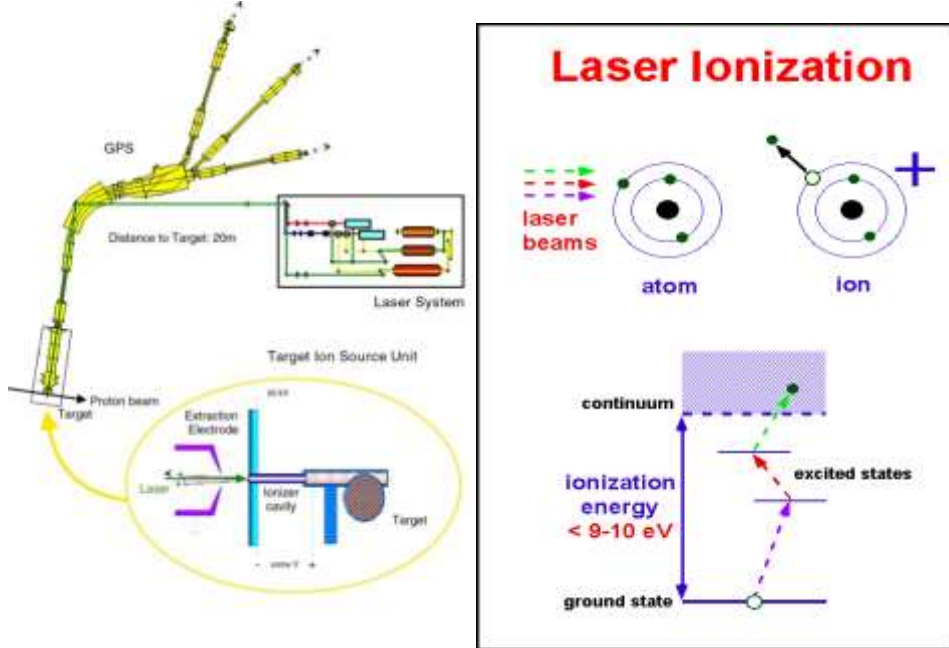
R. Henkelmann et al., *Eur. J. Nucl. Med. Mol. Imag.* 36 (2009) S260.

Question

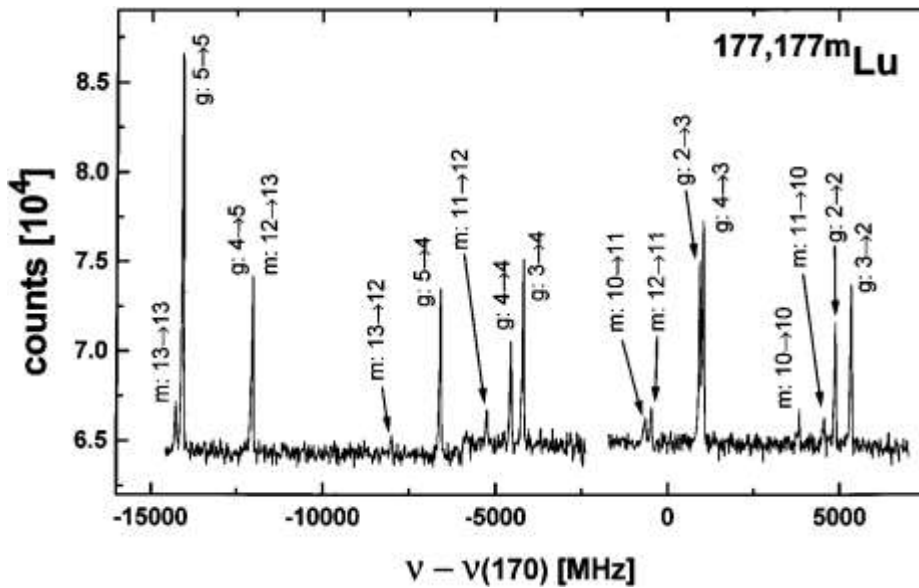
How to get ^{177g}Lu without ^{177m}Lu contamination ?

Hf 176 5.26	Hf 177 51 m 1.1 s 18.60	Hf 178 31 a 4.0 s 27.28	Hf 179 25 d 18.7 s 13.62
Lu 175 97.41	Lu 176 2.59 3.68 h $3.8 \cdot 10^{10}$ a	Lu 177 160.1 d 0.71 d	Lu 178 22.7 m 28.4 m
Yb 174 31.83	Yb 175 4.2 d	Yb 176 12 s 12.76	Yb 177 6.5 s 1.9 h

Resonance Ionization Laser Ion Source



Hyperfine Structure of $^{177g/m}\text{Lu}$



U. Georg et al. Eur. Phys. J. A 3 (1998) 225.

“Clean” production route to ^{177}Lu

Ta 175 10.5 h	Ta 176 8.1 h	Ta 177 56.6 h	Ta 178 0.23 m 2.45 h	Ta 179 665 d	Ta 180 0.012 A15 h	Ta 181 99.988
Hf 174 0.16 2.0 · 10 ¹⁵ a	Hf 175 70.0 d	Hf 176 5.26	Hf 177 51 m 1.1 s 18.60	Hf 178 31 a 4.0 s 27.28	Hf 179 25 d 18.7 s 13.62	Hf 180 5.3 h 35.06
Lu 173 1.37 a	Lu 174 142 d 3.31 a	Lu 175 97.41	Lu 176 2.59 3.58 h 1.8 · 10 ¹⁰ a	Lu 177 160.1 d 0.71 d	Lu 178 32.7 m 28.4 m	Lu 179 4.6 h
Yb 172 21.83	Yb 173 16.13	Yb 174 31.83	Yb 175 4.2 d	Yb 176 12 s 12.78	Yb 177 6.5 s 1.9 h	Yb 178 74 m

- Free of long-lived isomer
- Non-carrier-added quality
- Requires high-flux reactor and advanced radiochemistry

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}Lu from irradiated Yb
by ITG Garching



“Clean” production route to ¹⁷⁷Lu

Ta 175 10.5 h	Ta 176 8.1 h	Ta 177 56.6 h	Ta 178 0.23 m 2.45 h	Ta 179 665 d	Ta 180 0.012 1.15 h	Ta 181 99.988
Hf 174 0.16 2.0 · 10 ¹⁵ a	Hf 175 70.0 d	Hf 176 5.26	Hf 177 51 m 1.1 s 18.60	Hf 178 31 a 4.0 s 27.28	Hf 179 25 d 58.7 s 13.62	Hf 180 5.3 h 35.06
Lu 173 1.37 a	Lu 174 142 d 3.31 a	Lu 175 97.41	Lu 176 2.59	Lu 177 160.1 d 0.71 d	Lu 178 32.7 m 28.4 m	Lu 179 4.6 h
Yb 172 21.83	Yb 173 16.13	Yb 174 31.83	Yb 175 4.2 d	Yb 176 12 s 12.78	Yb 177 6.3 s 1.9 h	Yb 178 74 m

- Free of long-lived isomer
- Non-carrier-added quality
- Requires high-flux reactor and advanced radiochemistry

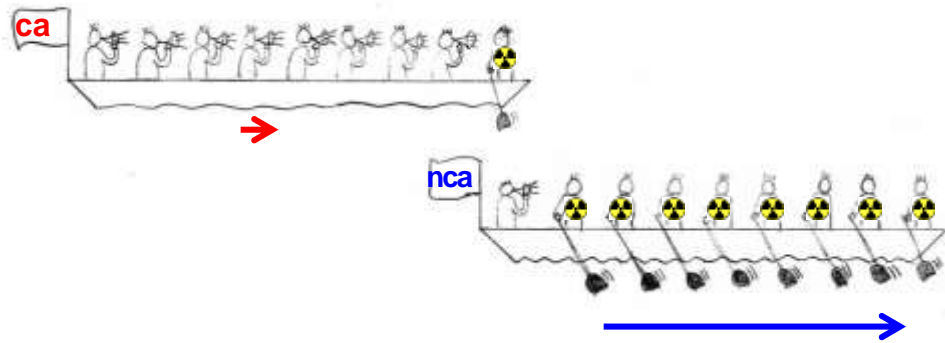


Specific activity

Physical quantity describing the activity per mass (GBq/mg, Ci/mg),

basically the ratio of radioactive atoms to all atoms (including stable ones).

Carrier added vs. non-carrier added



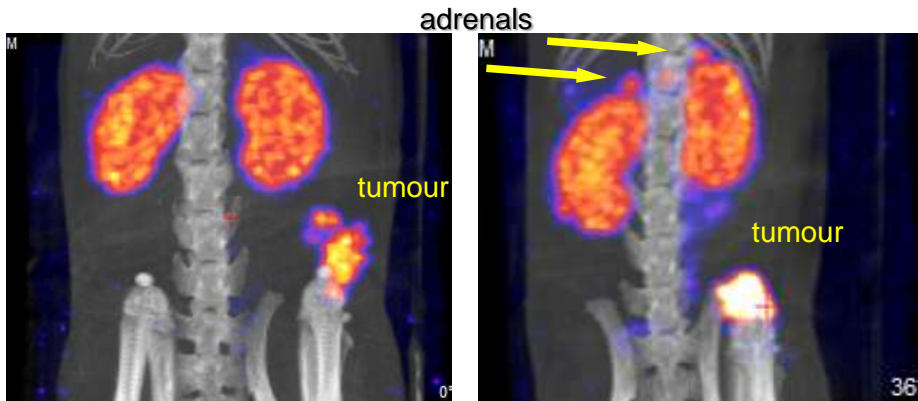
Saturation of selective receptors per cell



SPECT/CT day 1 p.t. Lu-octreotate

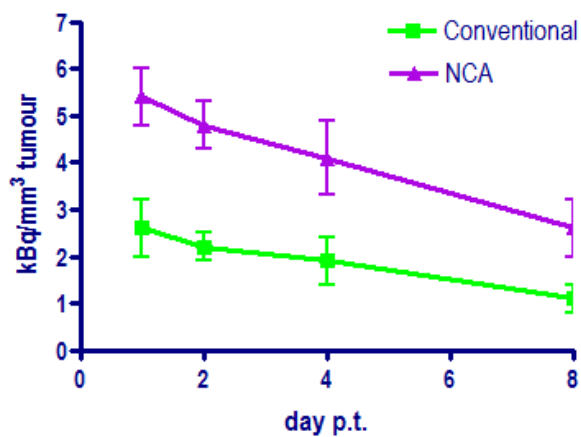
Conv. ^{177}Lu -octreotate, 11 μg

NCA ^{177}Lu -octreotate, 2 μg



M. de Jong, ICTR-PHE 2012

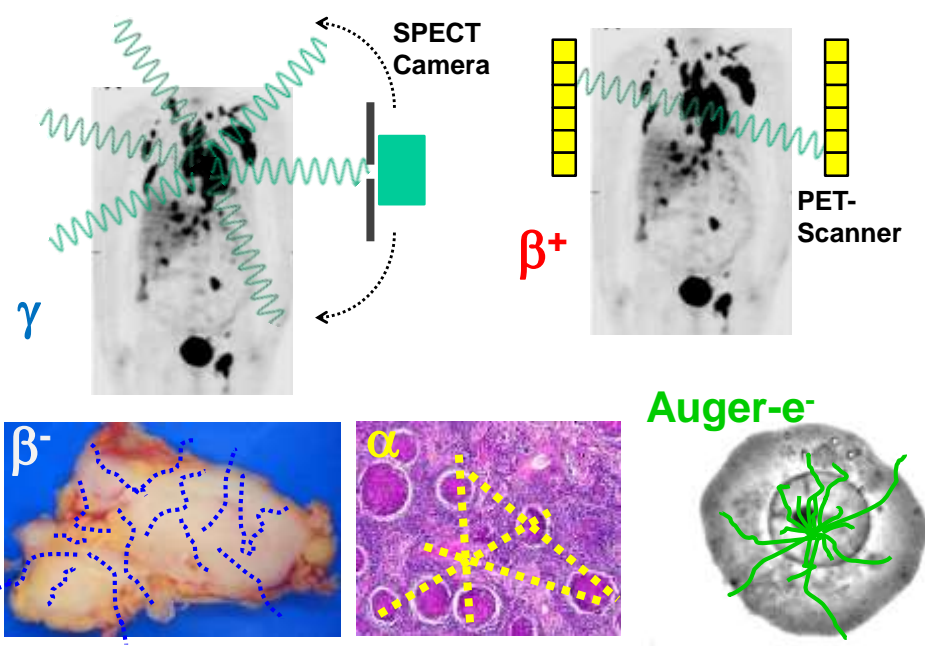
Tumour uptake, based on SPECT quantification



NCA ^{177}Lu -octreotate: ~2x higher tumour uptake
→ 70 vs. 35 Gy tumour dose

M. de Jong, ICTR-PHE 2012

The Nuclear Medicine Alphabet

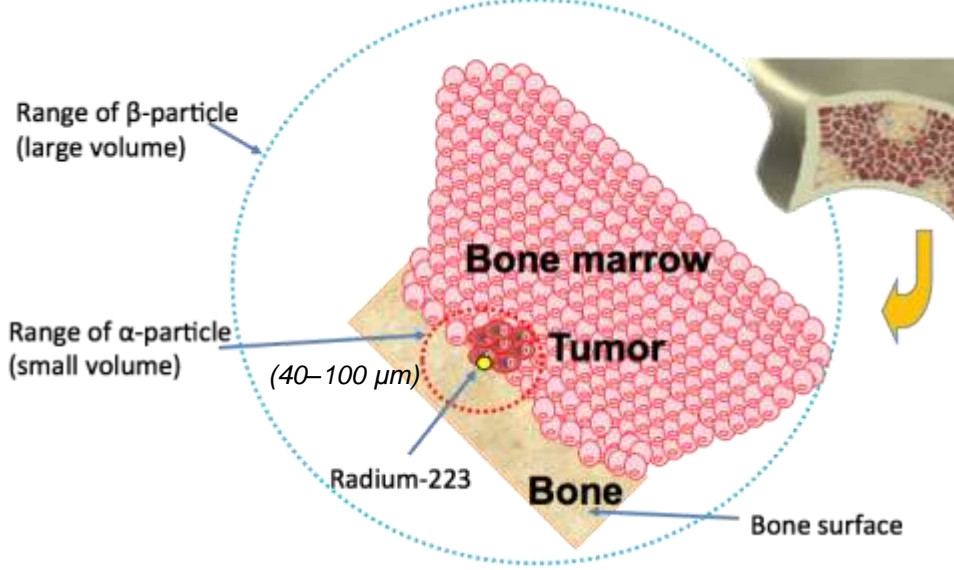


Radio-nuclide	Half-life	Daughters	Half-life	Cumulative α /decay	E_{α} mean (MeV)	Range (μ m)
Tb-149	4.1 h			0.17	3.97	25
<i>Pb-212</i>	10.6 h	Bi-212 Po-212	1.01 h 0.3 μ s	1	7.74	65
Bi-212	1.01 h	Po-212	0.3 μ s	1	7.74	65
<i>Bi-213</i>	0.76 h	Po-213	4 μ s	1	8.34	75
At-211	7.2 h	Po-211	0.5 s	1	6.78	55
Ra-223	11.4 d	Rn-219 Po-215 <i>Pb-211</i> Bi-211	4 s 1.8 ms 0.6 h 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 10.6 h 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 0.76 h 4 μ s	4	6.88	>50

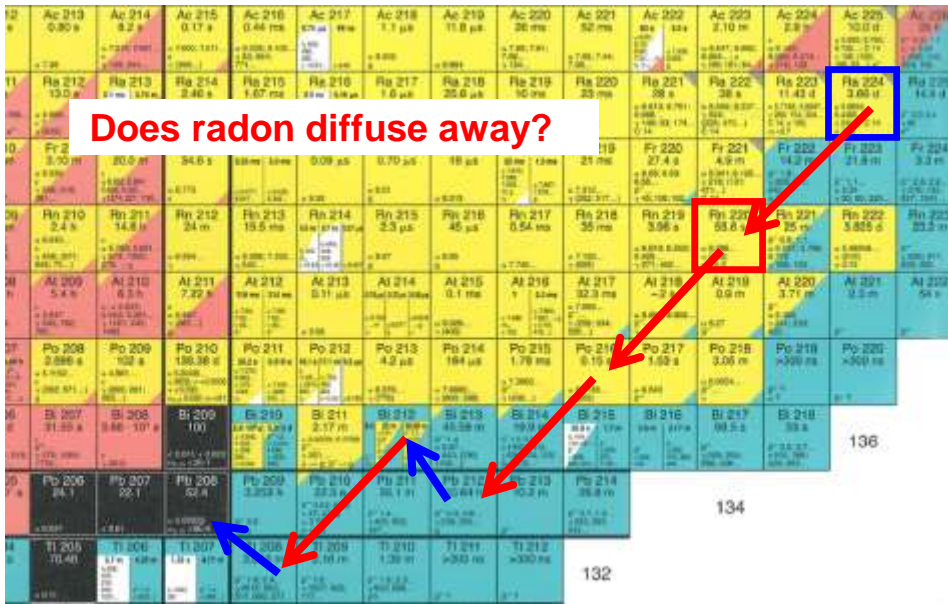
Isotopes for targeted alpha therapy

212 Ac 213 0.30 s	Ac 214 9.2 s	Ac 215 0.17 s	Ac 216 0.44 ms	Ac 217 49 ns	Ac 218 7.7 μs	Ac 219 11.8 μs	Ac 220 26 ms	Ac 221 50 ms	Ac 222 84 s	Ac 223 44 s	Ac 224 2.10 m	Ac 225 10.0 d	Ac 226 15.0 d	Ac 227 21.8 y
211 Ra 212 13.0 s	Ra 213 4.7 ms	Ra 214 3.40 s	Ra 215 1.07 ms	Ra 216 4.9 μs	Ra 217 1.0 μs	Ra 218 20.0 μs	Ra 219 10 ms	Ra 220 23 ms	Ra 221 28 s	Ra 222 38 s	Ra 223 11.43 d	Ra 224 3.66 d	Ra 225 14.8 d	Ra 226 1600 y
210 Fr 211 3.70 m	Fr 212 20.5 m	Fr 213 34.5 s	Fr 214 18 ms	Fr 215 0.09 μs	Fr 216 0.70 μs	Fr 217 18 μs	Fr 218 80 ns	Fr 219 21 ns	Fr 220 27.4 s	Fr 221 4.9 m	Fr 222 14.2 m	Fr 223 21.9 m	Fr 224 3.2 m	Fr 225 149 d
209 Rn 210 2.4 s	Rn 211 14.5 ms	Rn 212 24 ms	Rn 213 19.5 ms	Rn 214 18 ms	Rn 215 2.3 μs	Rn 216 45 μs	Rn 217 0.54 ms	Rn 218 35 ms	Rn 219 3.06 s	Rn 220 55.5 s	Rn 221 25 ms	Rn 222 3.823 s	Rn 223 23.3 m	Rn 224 3.48 m
208 At 209 5.4 s	At 210 6.3 s	At 211 7.27 s	At 212 100 ns	At 213 32 ns	At 214 0.1 ns	At 215 1 ns	At 216 32.3 ms	At 217 -2 s	At 218 0.9 m	At 219 3.77 m	At 220 1.2 m	At 221 2.2 m	At 222 54 s	At 223 45 s
207 Po 208 2.886 s	Po 209 102 s	Po 210 138.38 s	Po 211 3.2 s	Po 212 0.14 s	Po 213 4.2 μs	Po 214 164 μs	Po 215 1.78 ms	Po 216 0.15 s	Po 217 1.02 s	Po 218 3.05 m	Po 219 >300 m	Po 220 >300 m	Po 221 >300 m	Po 222 >300 m
206 Bi 207 31.55 y	Bi 208 3.84 × 10 ⁸ y	Bi 209 100 y	Bi 210 5.012 × 10 ⁶ y	Bi 211 2.17 m	Bi 212 10.2 m	Bi 213 45.58 m	Bi 214 19.9 m	Bi 215 8.07 × 10 ⁶ y	Bi 216 117 y	Bi 217 47.83 d	Bi 218 35 s	Bi 219 33.7 d	Bi 220 3.03 d	Bi 221 1.21 d
205 Pb 205 15.3 y	Pb 206 12.42 × 10 ¹⁰ y	Pb 207 22.3 y	Pb 208 62.4 y	Pb 209 3.383 s	Pb 210 22.3 s	Pb 211 36.1 m	Pb 212 10.64 h	Pb 213 10.3 m	Pb 214 26.8 m	Pb 215 151 m	Pb 216 35.8 d	Pb 217 1.6 × 10 ⁶ y	Pb 218 3.1 × 10 ⁶ y	Pb 219 3.8 × 10 ⁶ y
134 Tl 205 70.40 d	Tl 206 4.2 × 10 ⁵ y	Tl 207 4.77 × 10 ⁵ y	Tl 208 3.055 y	Tl 209 2.10 y	Tl 210 1.30 m	Tl 211 >300 m	Tl 212 >300 m	Tl 213 4.77 × 10 ⁶ y	Tl 214 3.1 × 10 ⁶ y	Tl 215 3.1 × 10 ⁶ y	Tl 216 3.1 × 10 ⁶ y	Tl 217 3.1 × 10 ⁶ y	Tl 218 3.1 × 10 ⁶ y	Tl 219 3.1 × 10 ⁶ y

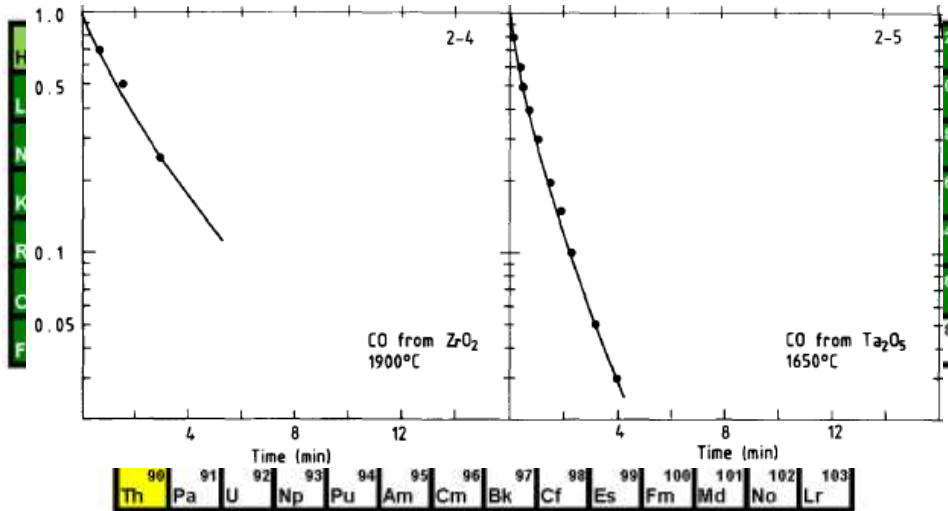
Alpha versus beta for therapy



Isotopes for targeted alpha therapy



Radioisotopes available at ISOLDE-CERN

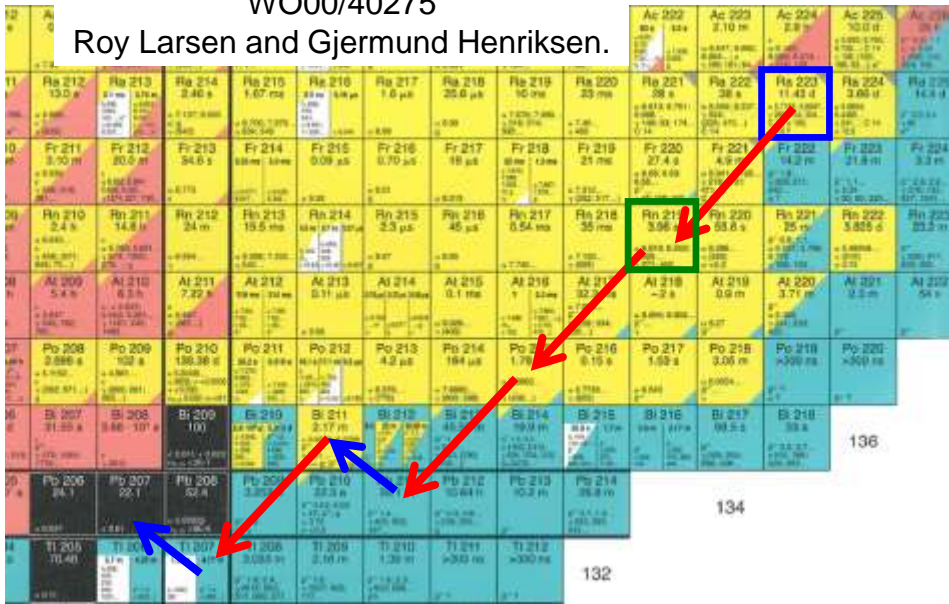


Diffusion and release measurements to develop new beams
 e.g. P. Hoff et al., NIM 221 (1984) 313.

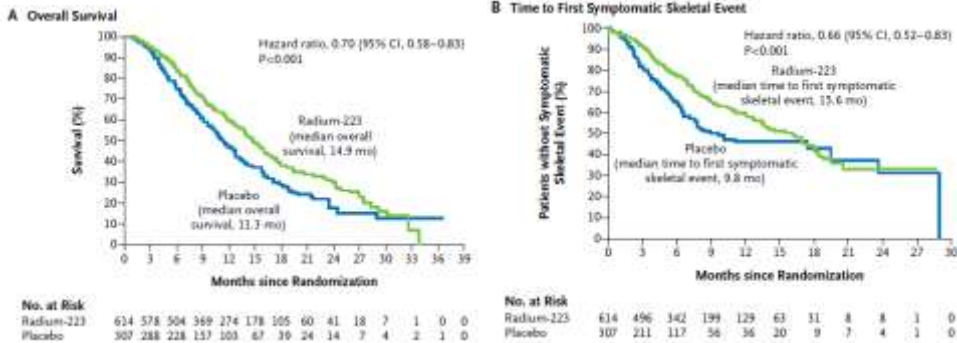
Isotopes for targeted alpha therapy

WO00/40275

Roy Larsen and Gjermund Henriksen.



²²³Ra: Xofigo



C. Parker, S. Nilsson, D. Heinrich, S.I. Helle, J.M. O'Sullivan, S.D. Fossà, 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[®]

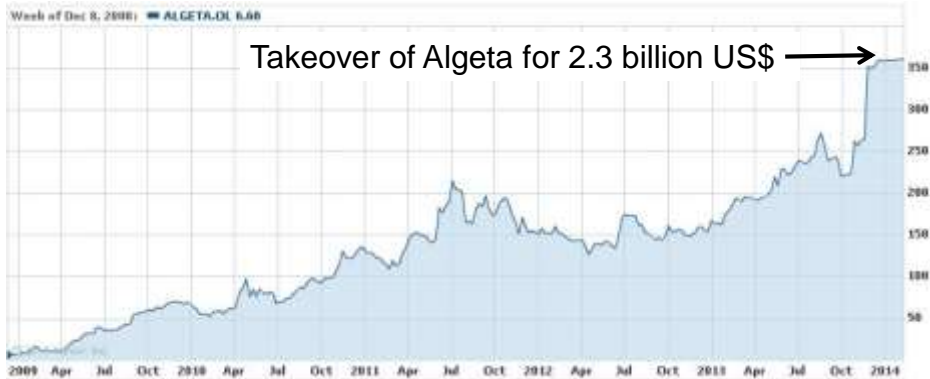


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Prospects of targeted alpha therapies ?



Radionuclides for RIT and PRRT

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

cross-fire

↑ Established isotopes

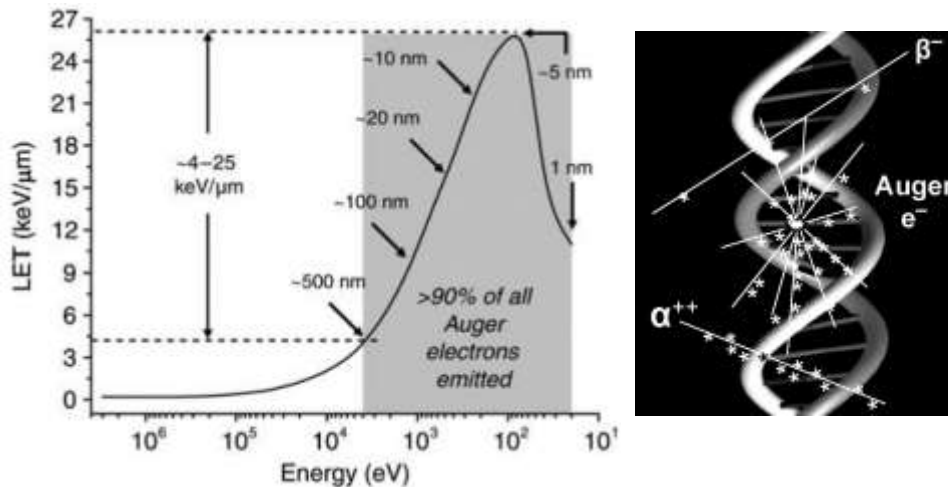
Emerging isotopes

R&D isotopes: supply-limited!

↓ localized

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

Radiobiological effectiveness of Auger electrons



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

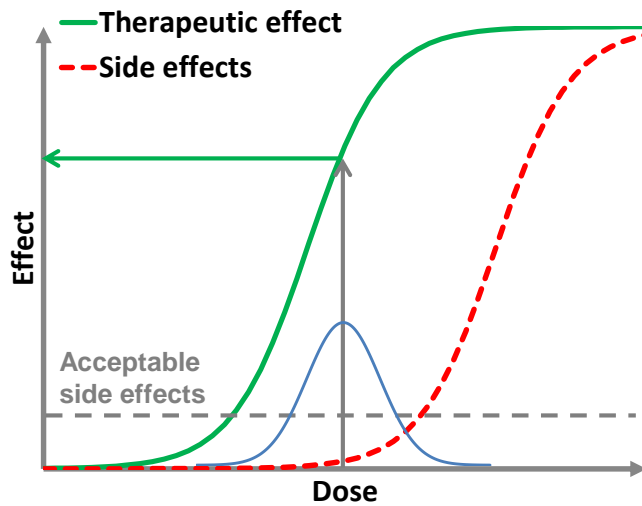
Auger therapy: a long-term project

The **ideal agent for cancer therapy** would consist of **heavy elements capable of emitting radiations of molecular dimensions**, which could be administered to the organism and selectively fixed in the protoplasm of cells one seeks to destroy. While this is perhaps not impossible to achieve, the attempts so far have been unsuccessful.

C. Regaud, A. Lacassagne, *Radiophysiologie et Radiotherapie* **1927**;1:95.

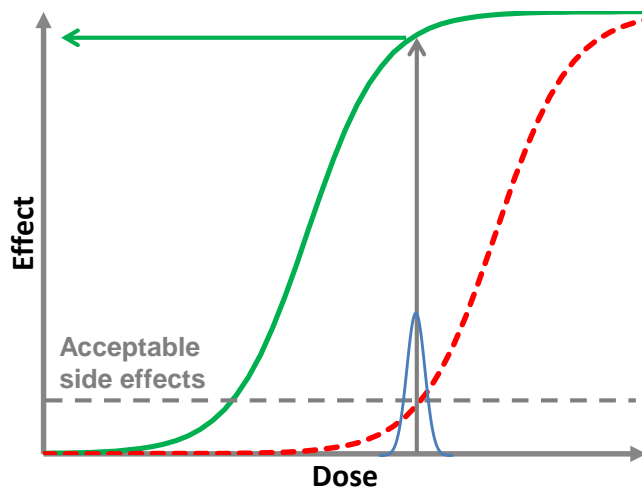


Theranostics



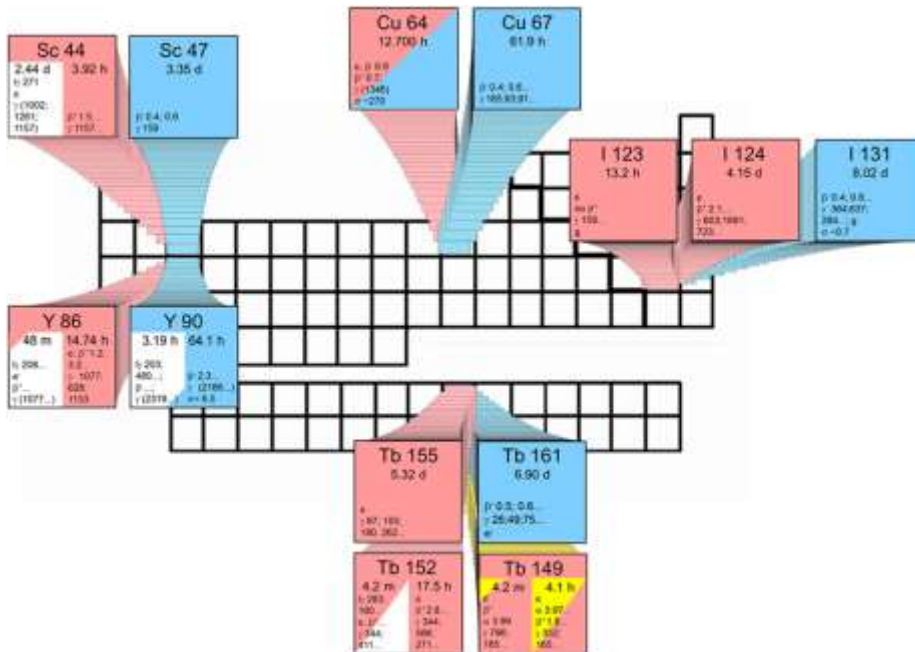
Accurate dosimetry is essential for optimum use of the therapeutic window.

Theranostics



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

Matched pairs for theranostics



Terbium: a unique element for nuclear medicine

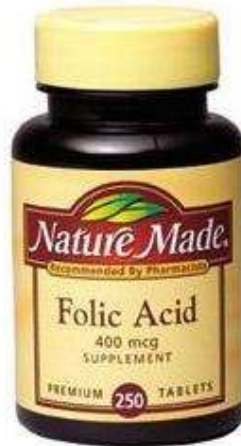


Dy 150 7.2 h	Dy 151 17 m	Dy 152 2.4 h	Dy 153 0.09 h	Dy 154 3.0 · 10 ⁴ a	Dy 156 0.050	Dy 156 0.090	Dy 157 8.1 h	Dy 158 0.095	Dy 158 144.4 d	Dy 160 2.329	Dy 161 18.889	Dy 162 21.475
Tb 149 4.1 h	Tb 150 10.3 h	Tb 151 1.6 h	Tb 152 1.0 h	Tb 153 2.34 d	Tb 154 1.0 h	Tb 155 5.32 d	Tb 156 1.0 h	Tb 157 1.0 h	Tb 158 1.0 h	Tb 159 1.0 h	Tb 160 72.3 d	Tb 161 6.90 d
Gd 143 74.6 a	Gd 145 9.06 d	Gd 150 1.8 · 10 ⁴ a	Gd 151 1.0 d	Gd 152 0.20	Gd 153 230.47 d	Gd 154 2.18	Gd 155 14.20	Gd 156 20.47	Gd 157 15.50	Gd 158 24.84	Gd 159 10.49 h	Gd 160 21.86

Folate-receptor positive cancers

Frequent overexpression of folate receptor in cancer of:

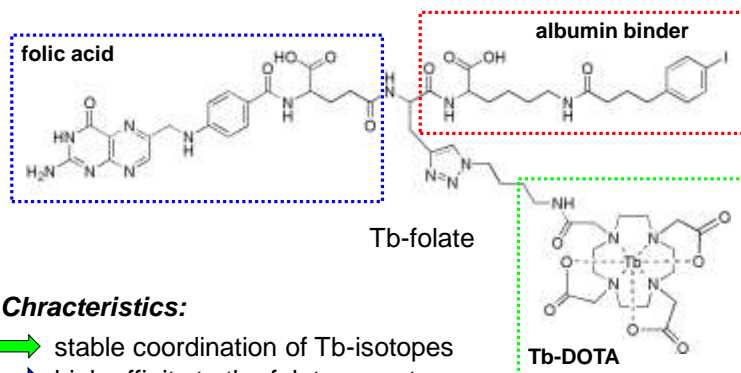
- ovaries
- cervix uteri
- lung
- kidney
- brain
- colon
- breast
- leukemia



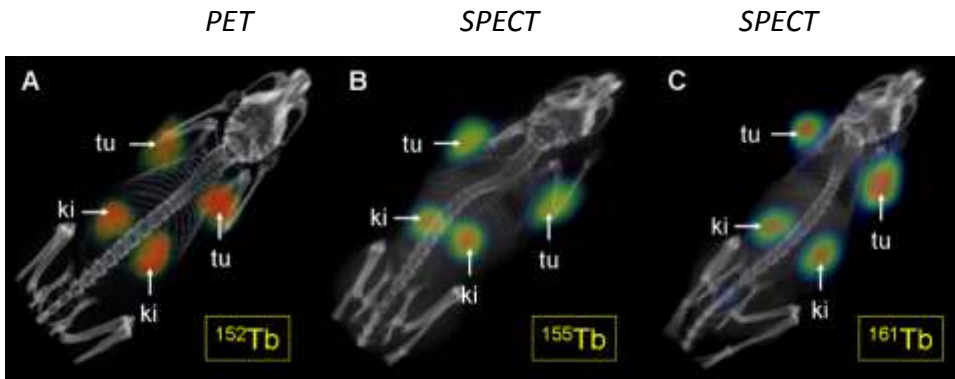
foliac acid = vitamine B9

C. Müller, Curr. Pharmaceut. Design 2012;18:1058.

Tumor Targeting Agent for Tb-Coordination Chemical Structure with 3 Functionalities



Theranostics with terbium isotopes



ISOLDE



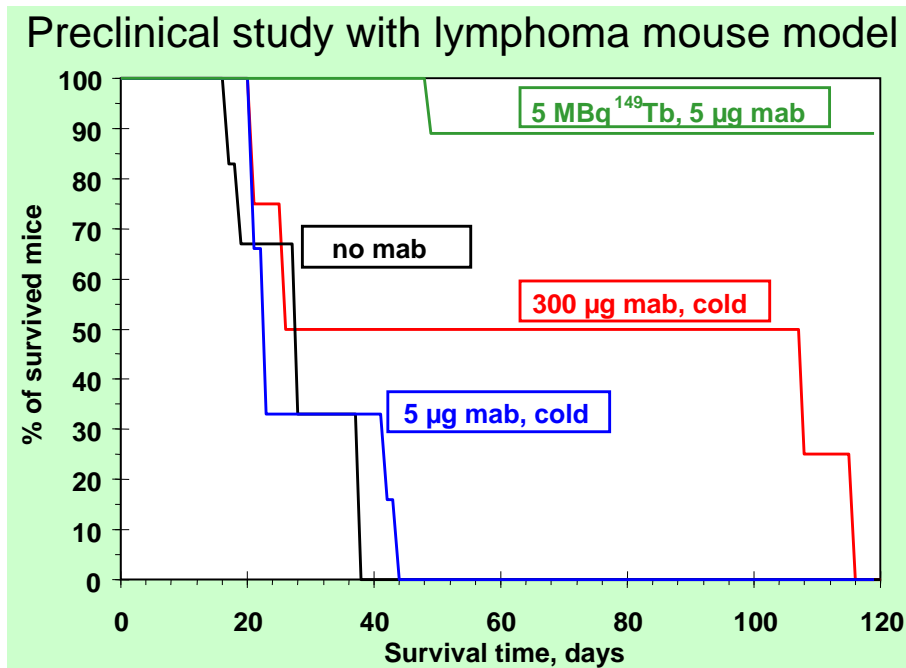
ISOLDE

PAUL SCHERRER INSTITUT



NEUTRONS FOR SCIENCE

IS528 Collaboration: C. Müller et al., *J. Nucl. Med.* 2012;53:1951.



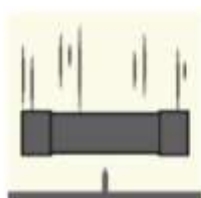
G.J. Beyer et al., *Eur J Nucl Med Molec Imaging* 2004;31:547.

Radioactive transport

Isotope	A2 (GBq)
^{18}F	600
$^{99\text{m}}\text{Tc}$	4000
^{131}I	700
^{177}Lu	700
^{211}At	500
^{161}Tb ($\beta\gamma$)	20
^{149}Tb (α)	0.09



FREE DROP
A 1-metre (30-foot) free-fall onto an unyielding surface



PUNCTURE
A 1-metre (48-inch) free-fall onto a steel rod

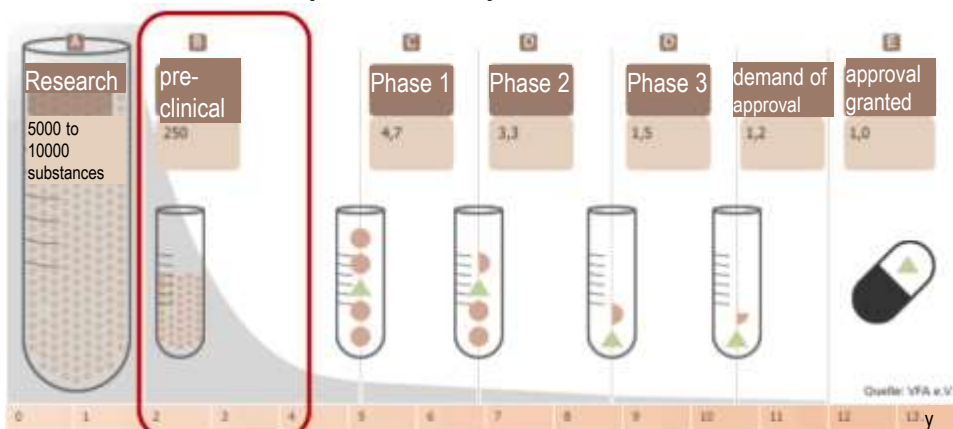


THERMAL
A 30-minute, fully-engulfing fire at 800° (1475°)



IMMERSION
An 8-hour immersion under water

Development of pharmaceuticals



Screening *in vitro* tests
animal exp.

tests with humans

toxicity
side effects

wanted effect

comparison
with standard

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

Cost effectiveness ?

2010 TARMED prices:

650 mg rituximab 3939 CHF **16x rituximab 63024 CHF**
1x Zevalin 24330 CHF **1x Zevalin is >2.6x cheaper!**
(⁹⁰Y-anti-CD20-ibritimumab)

6.2x more expensive?

“A single infusion of ZEVALIN matched roughly 16 infusions of rituximab in terms of achieving the same increase in progression free survival. I leave it up to the audience to draw conclusions about cost effectiveness. Thus, in conclusion, RIT represents the most effective single drug in the treatment of follicular NHL.”

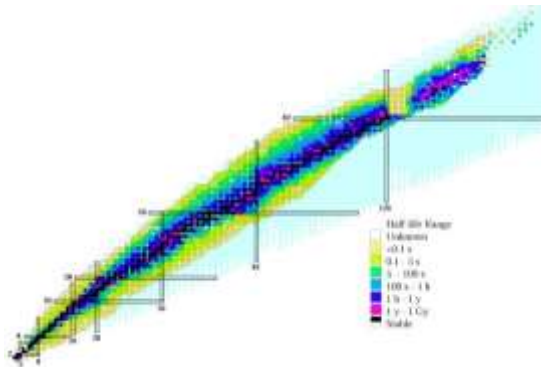
Dr. Anton Hagenbeek, the Academic Medical Center, Amsterdam, NL, on "Controversies in Follicular Lymphomas"



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.”

ESR	
1	Molecule (CO, CO ₂ , CH _x) breakup in RFQ
2	Facility development and safety (149/152Tb)
3	Charge breeding REX
4	Graphene coating of UCx target
5	RILIS installation at HUG (Lu, Tb, Er)
6	Mass separation of cyclotron produced radioisotopes (47Sc..)
7	U nanofiber target
8	Radiopharmaceuticals for Auger therapy (161Tb)
9	Tracers to follow tumour response in hadron therapy
10	Container for radioisotope shipping
11	Molecular beams (CO ⁺ , etc.)
CH1	Ovarian cancer bimodal imaging
CH2	RIT and imaging of ovarian cancer (translation preclinical>clinical)
CH3	Robotic placement of brachytherapy (brain, ovarian, pancreatic)
CH4	Radiopharmaceutical synthesis for ovarian cancer (fluorescent & PET)

“Main lines” of MEDICIS-PROMED

1. Mass separated isotopes, e.g. Tb
(ESR2, 4, 5, 7, 10)
2. ¹¹C (“tracer ammunition” for hadron therapy)
(ESR3, 9, 11, ESRCH1, 4)
3. Targeted therapies for ovarian cancer
(ESR1, 6, 8, ESRCH2, 3)