Radioisotopes for Nuclear Medicine

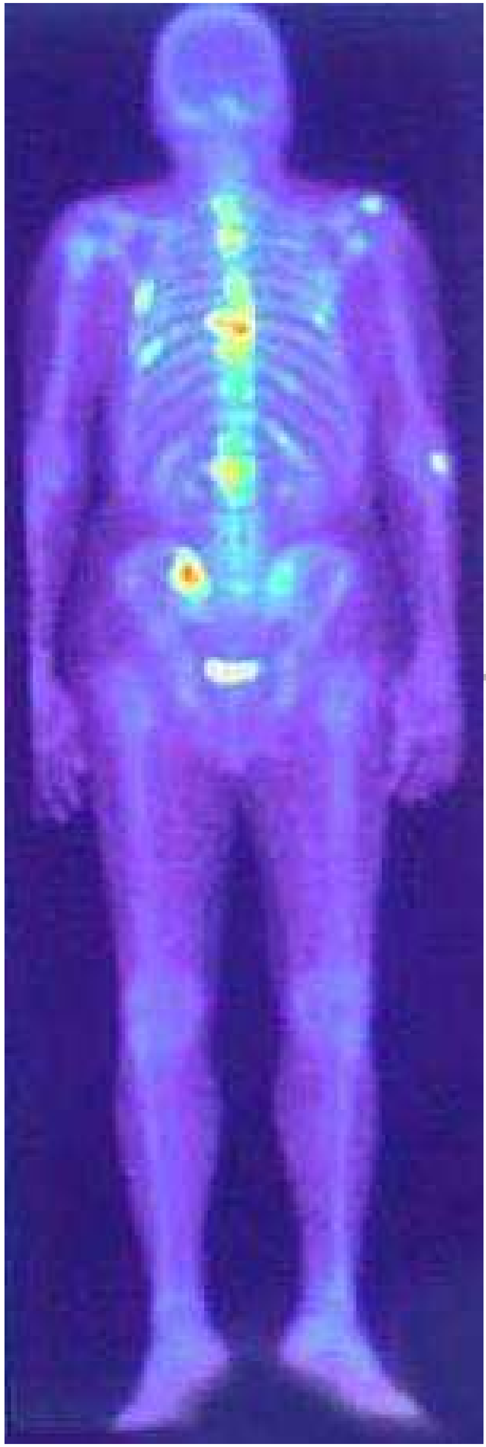
Ulli Köster

Institut Laue Langevin, Grenoble

ISOLDE
CERN

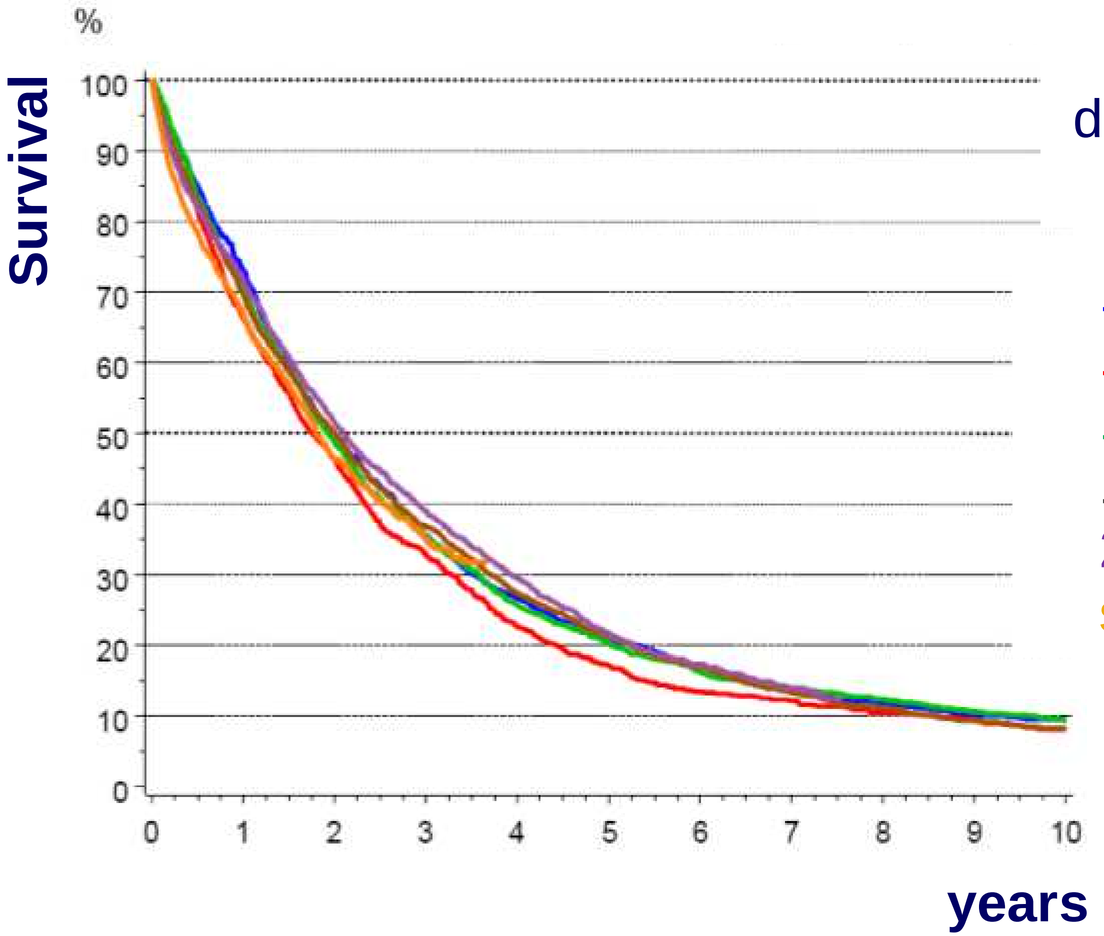
NEUTRONS FOR SCIENCE®

Radioisotopes for diagnosis



"I'd have been here sooner if it hadn't been for early detection."

Mammary Carcinoma
Survival time since diagnosis of metastases

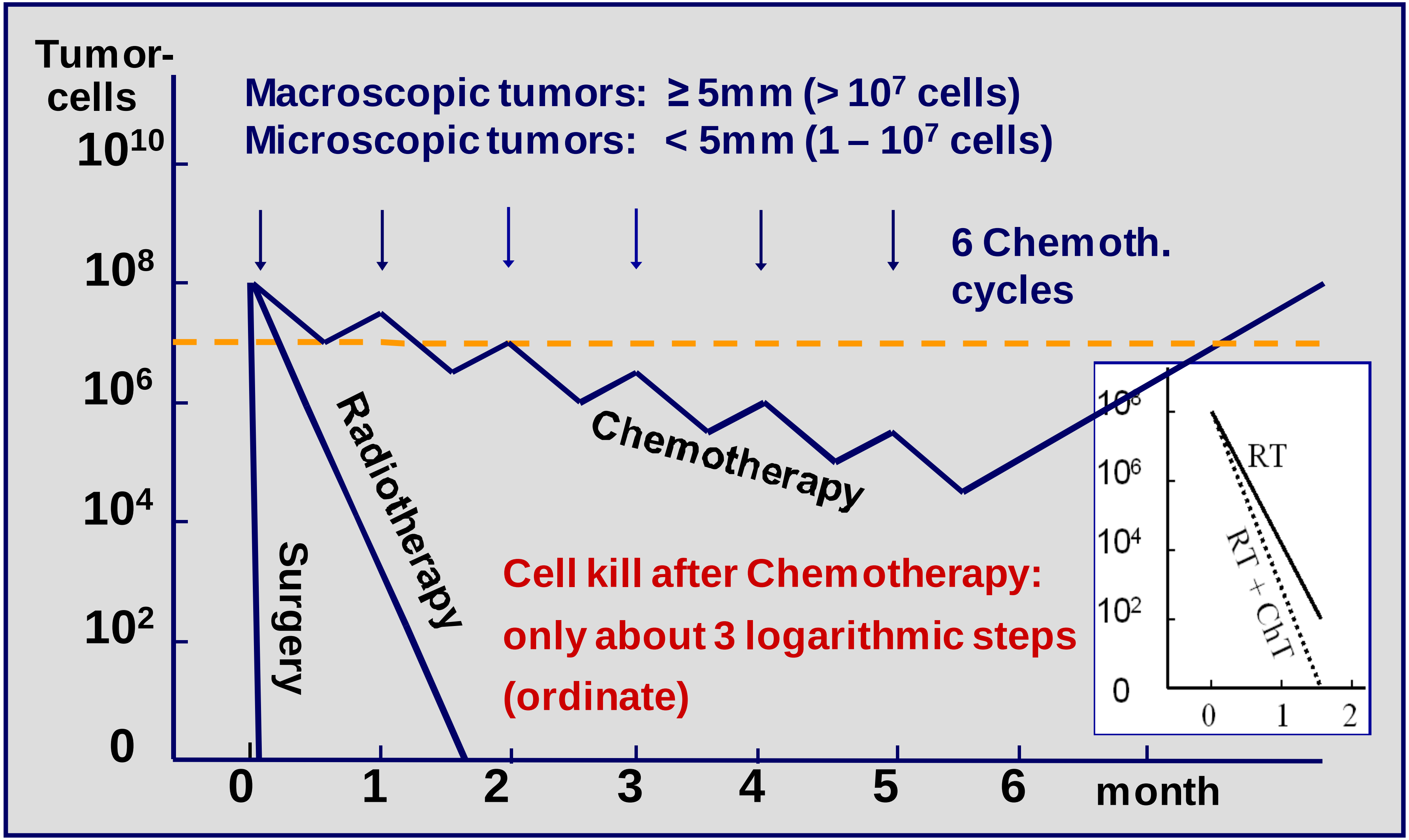


Results for 6 time periods
data from tumor centre Munich
n = 9228

1980-1984
1985-1989
1990-1994
1995-1999
2000-2003
since 2004

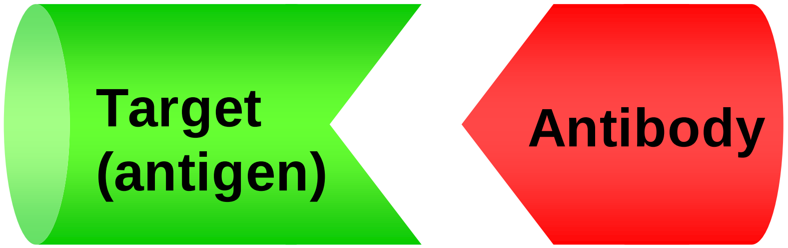
Little/no improvement with (modern) chemotherapies!

Comparison of Therapies

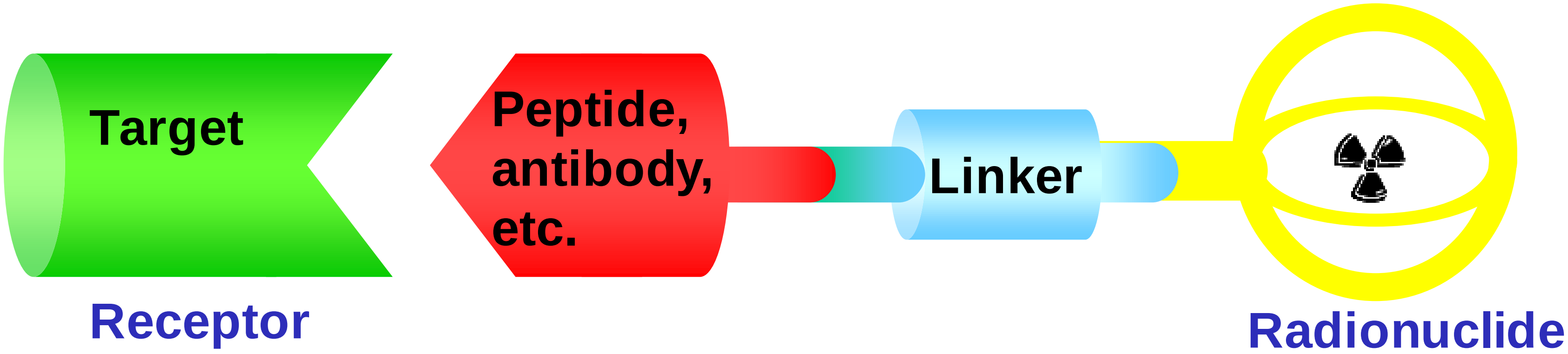


(Molls, TU München; according to Tannock: Lancet 1998, Nature 2006)

Immunology approach



Multidisciplinary collaboration to fight cancer

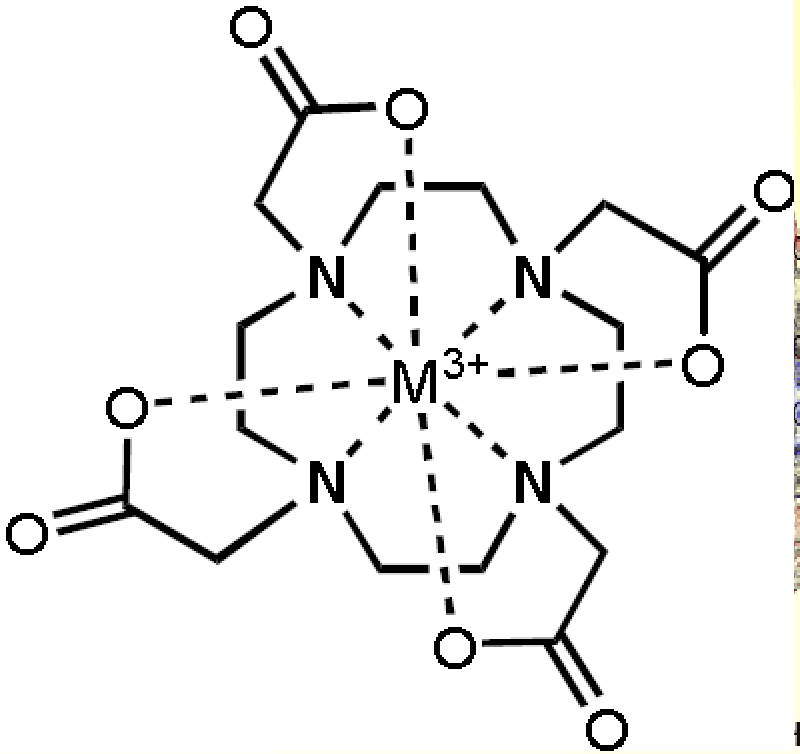


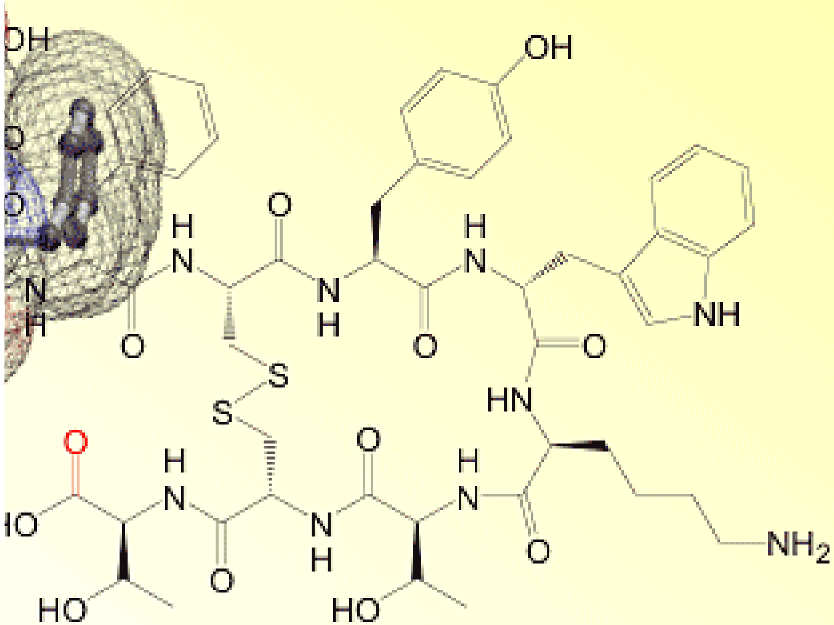
Immunology
Structural biology

Coordination chemistry

Nuclear physics and radiochemistry

Structural Formula of DOTA-TOC/TATE





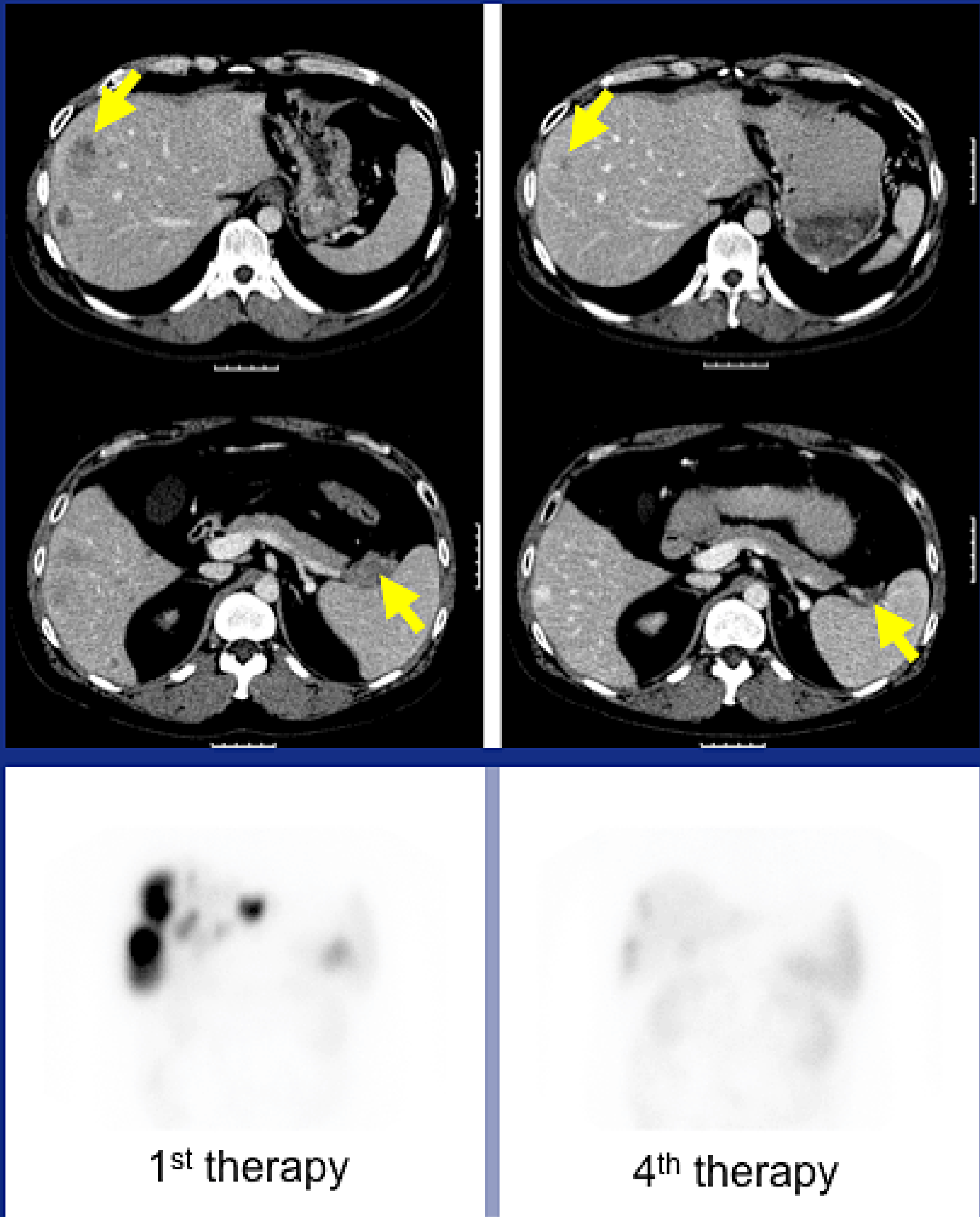
DOTA-TATE

1,4,7,10-tetraazacyclododecantetraacetate

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

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

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.

Erasmus MC

Lymphoma therapy: RITUXIMAB+^{177}Lu

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

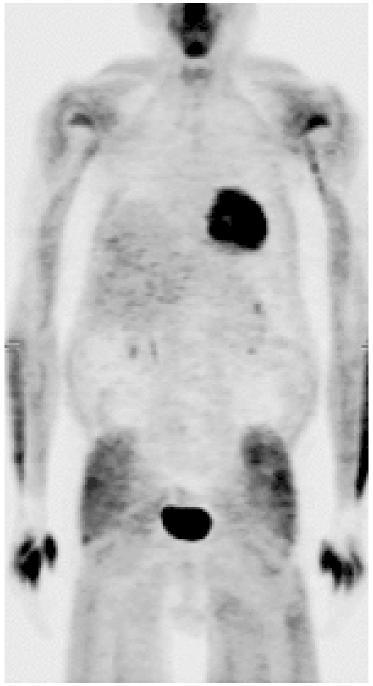
^{18}FDG PET

1.9.2002

^{177}Lu-Scan

13.9.2002

^{18}FDG PET

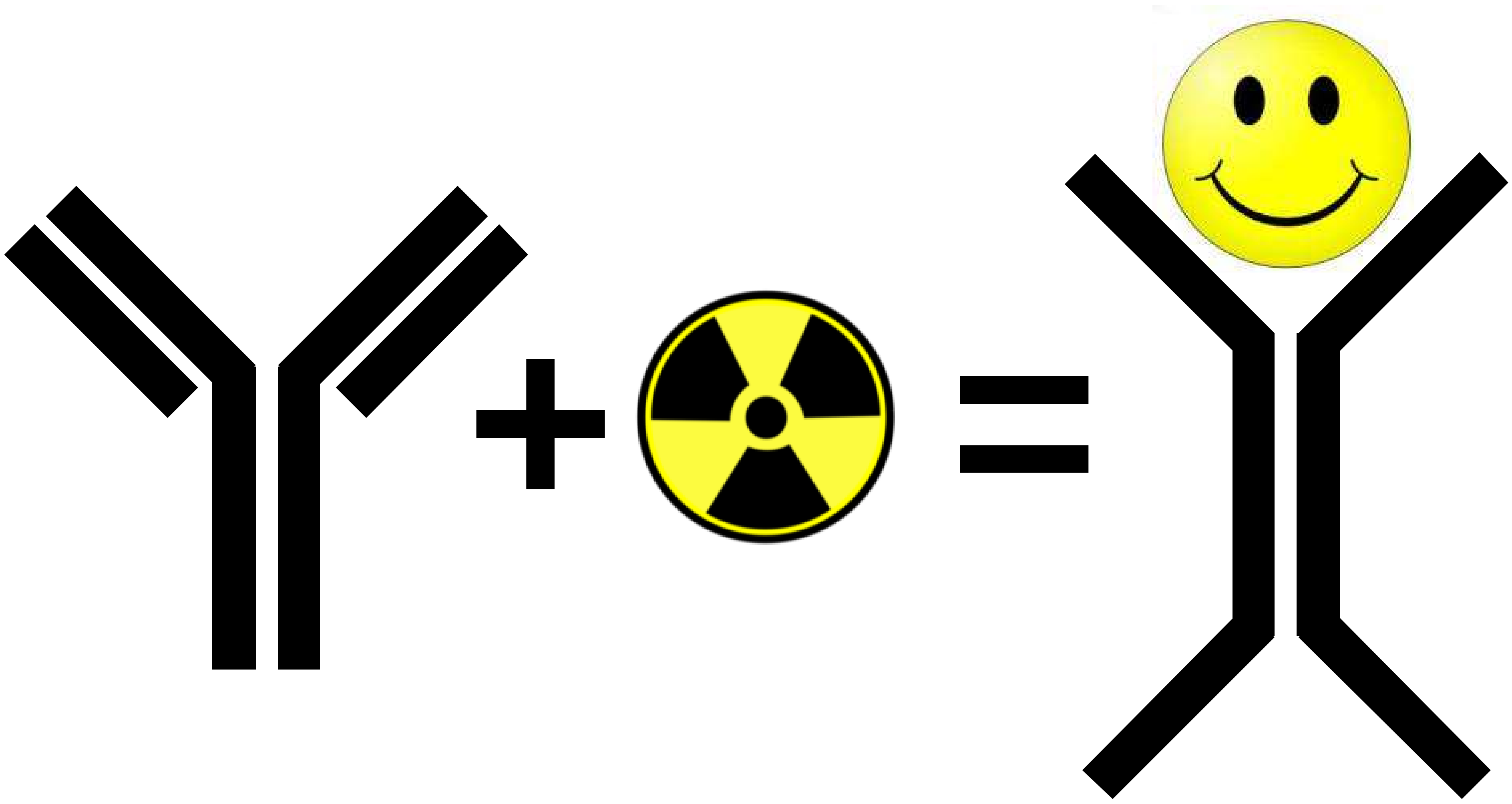


15.11.2002

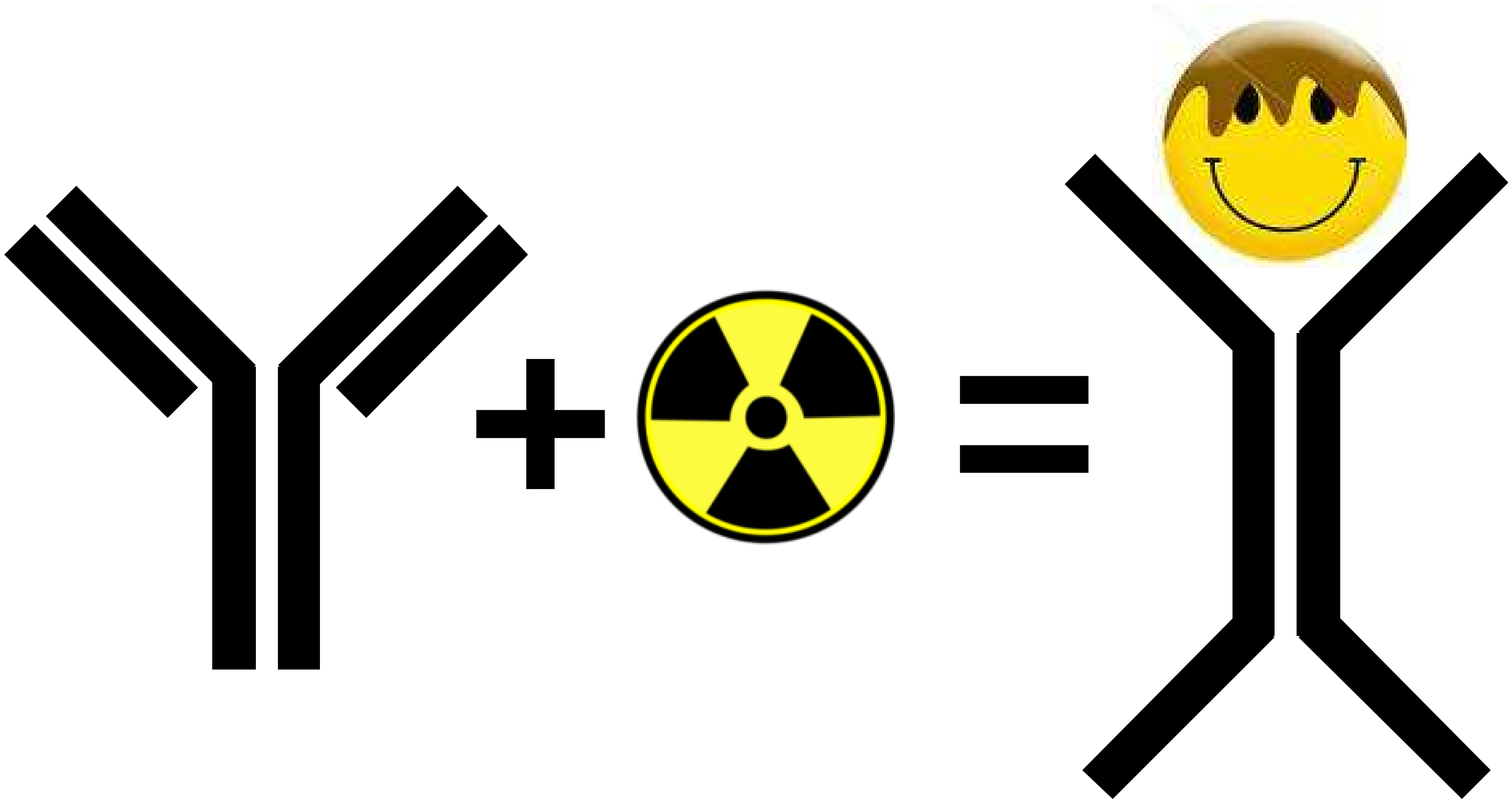
Still in CR

15.9.2009

Radioimmunotherapy

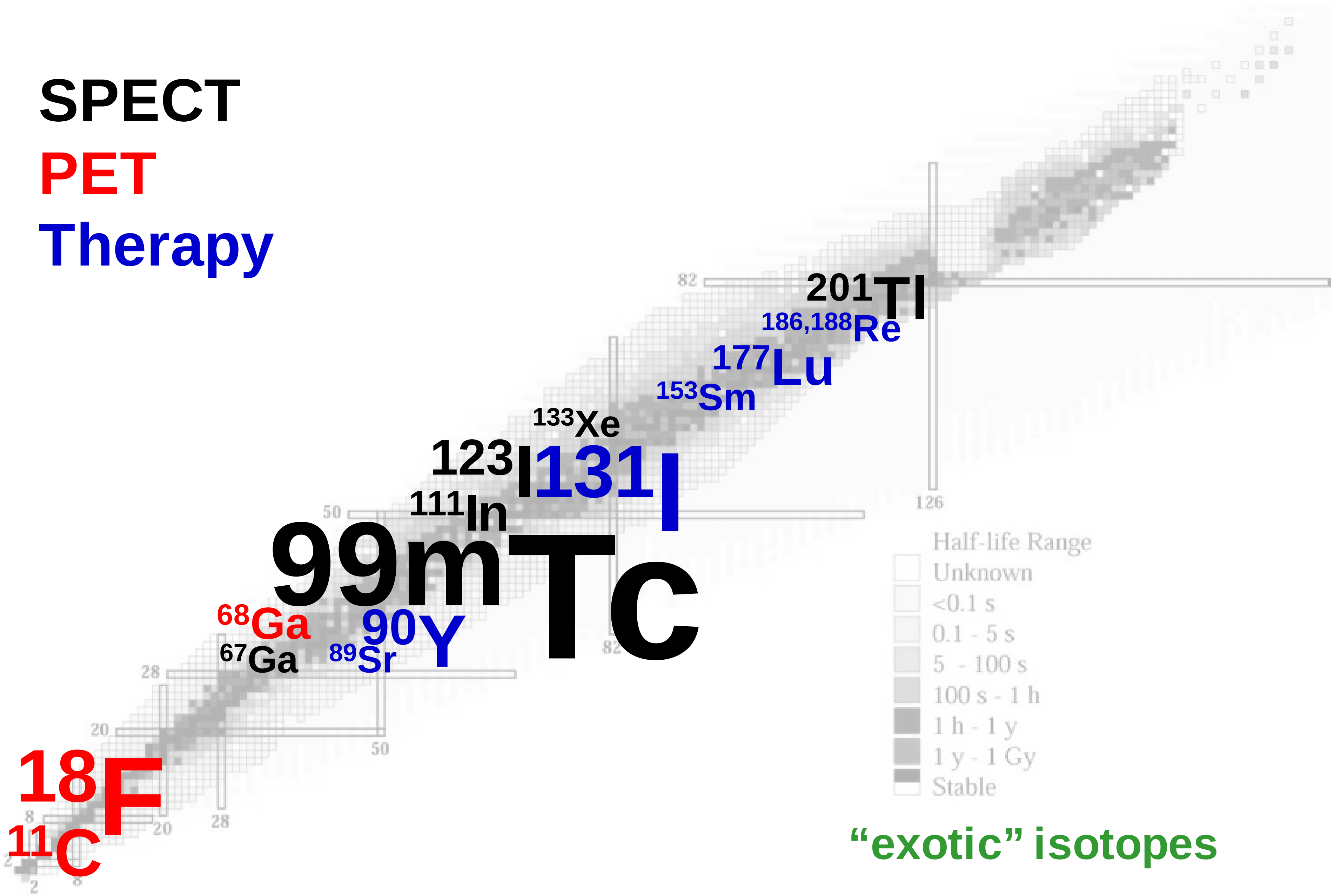


Radioimmunotherapy



The chart of nuclides – nuclear medicine perspective

SPECT
PET
Therapy

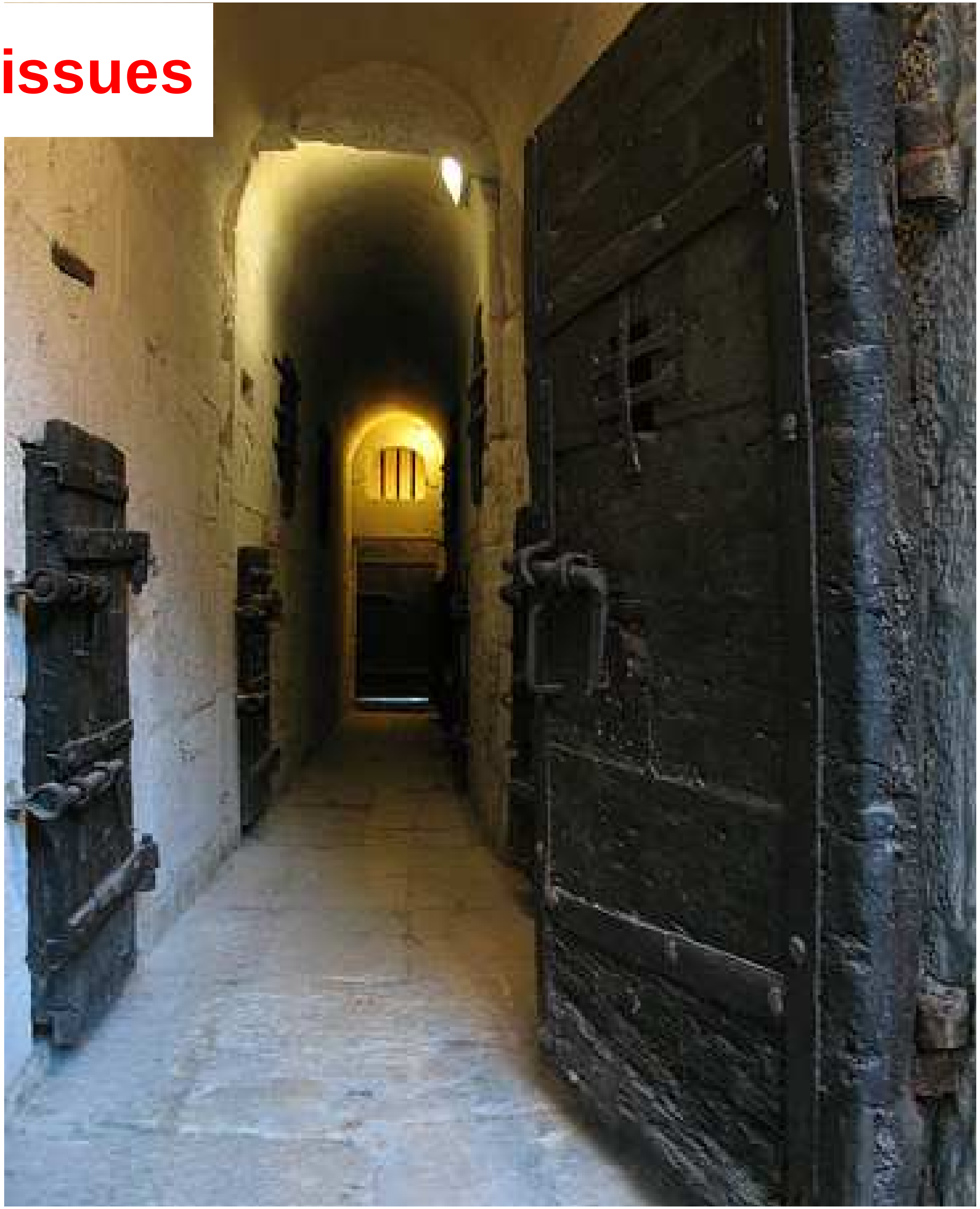


^{131}I: radioprotection issues

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

3.7 GBq patient dose $\Rightarrow$ 0.2 mSv/h at 1 m

requires dedicated shielded treatment rooms



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

Q_{β^-} = 2.28 MeV
up to 12 mm range

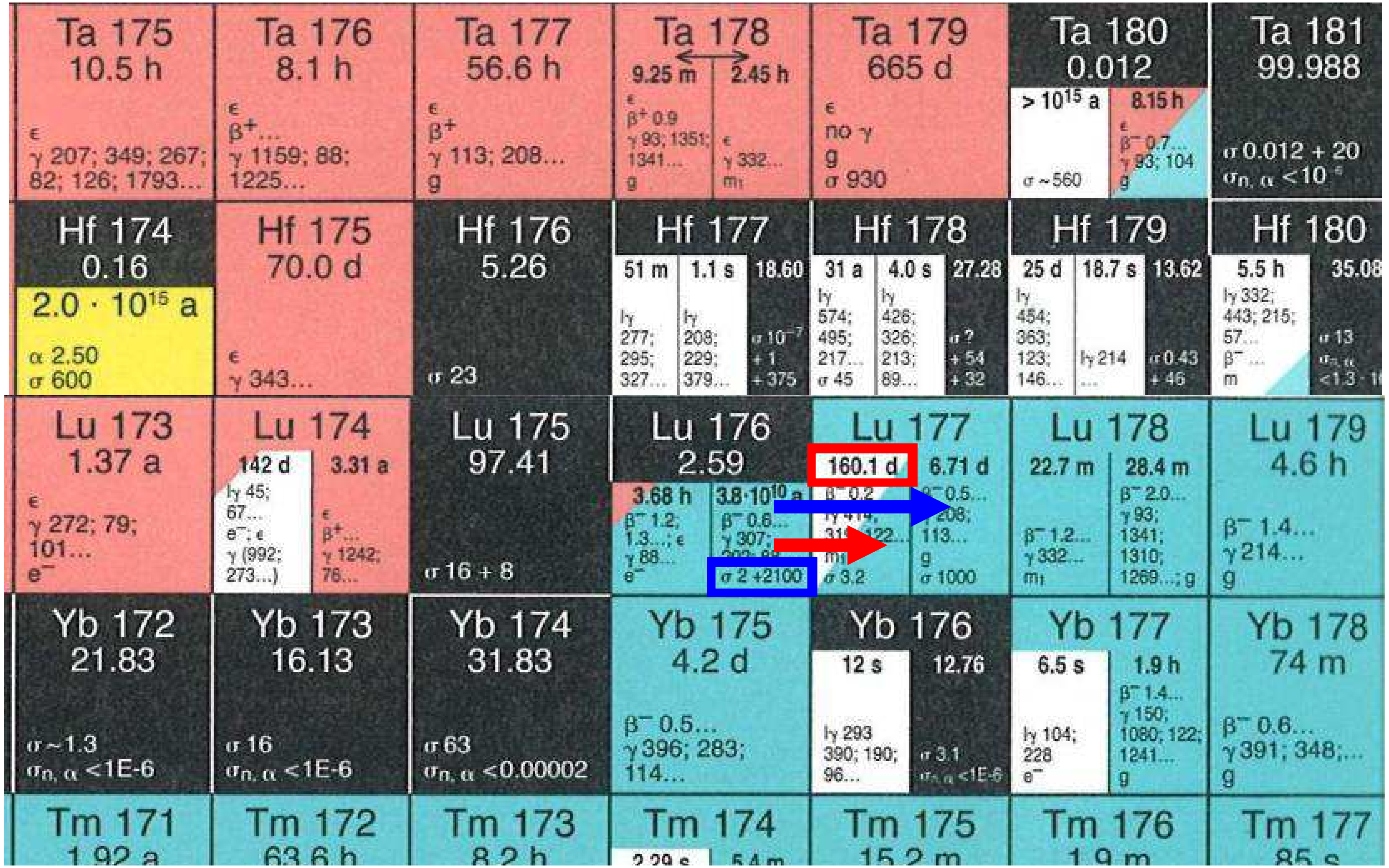
Radionuclides for RIT and PRRT

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

Established isotopes

Emerging isotope

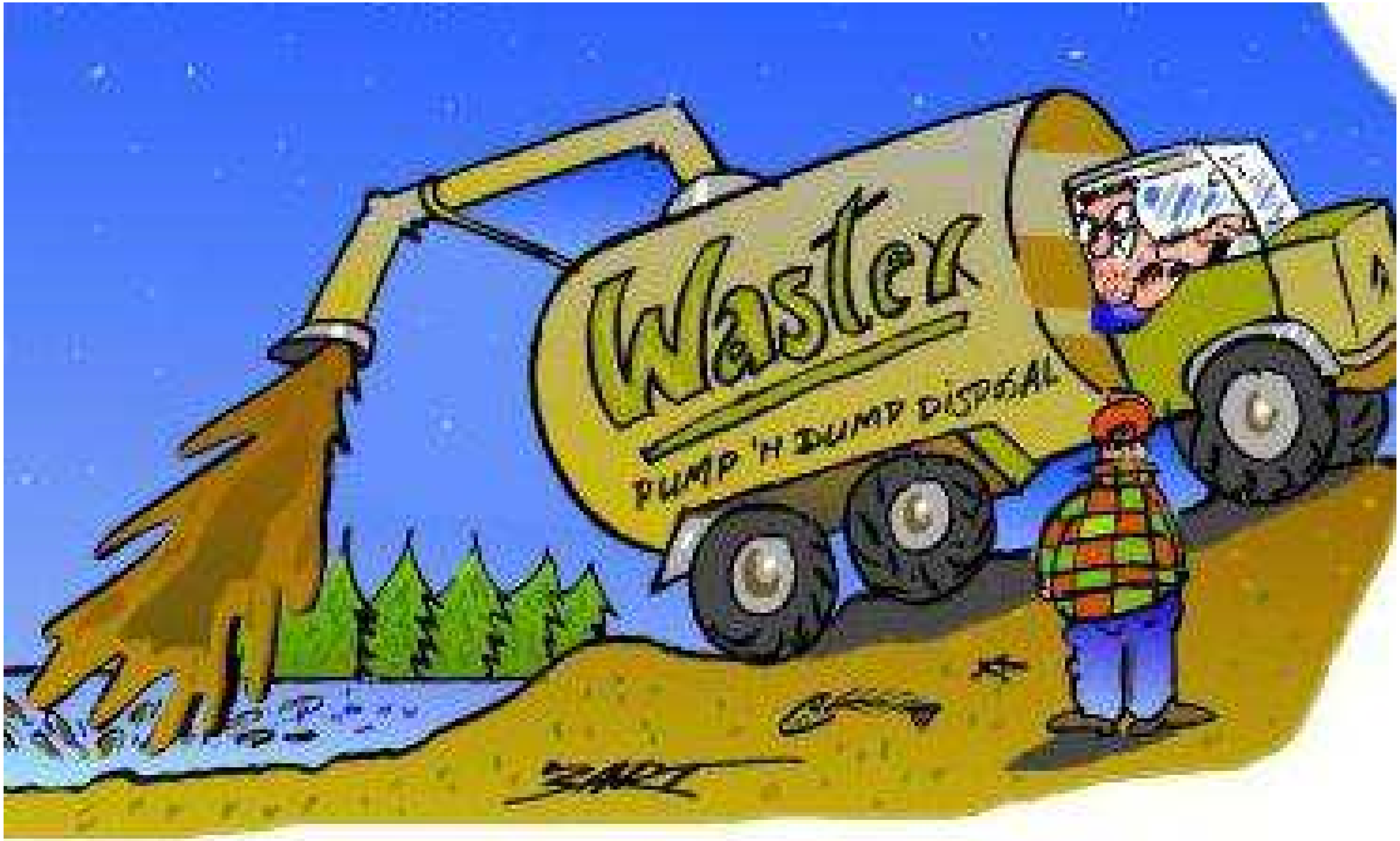
Production of ^{177}Lu



Waste problem for hospitals!

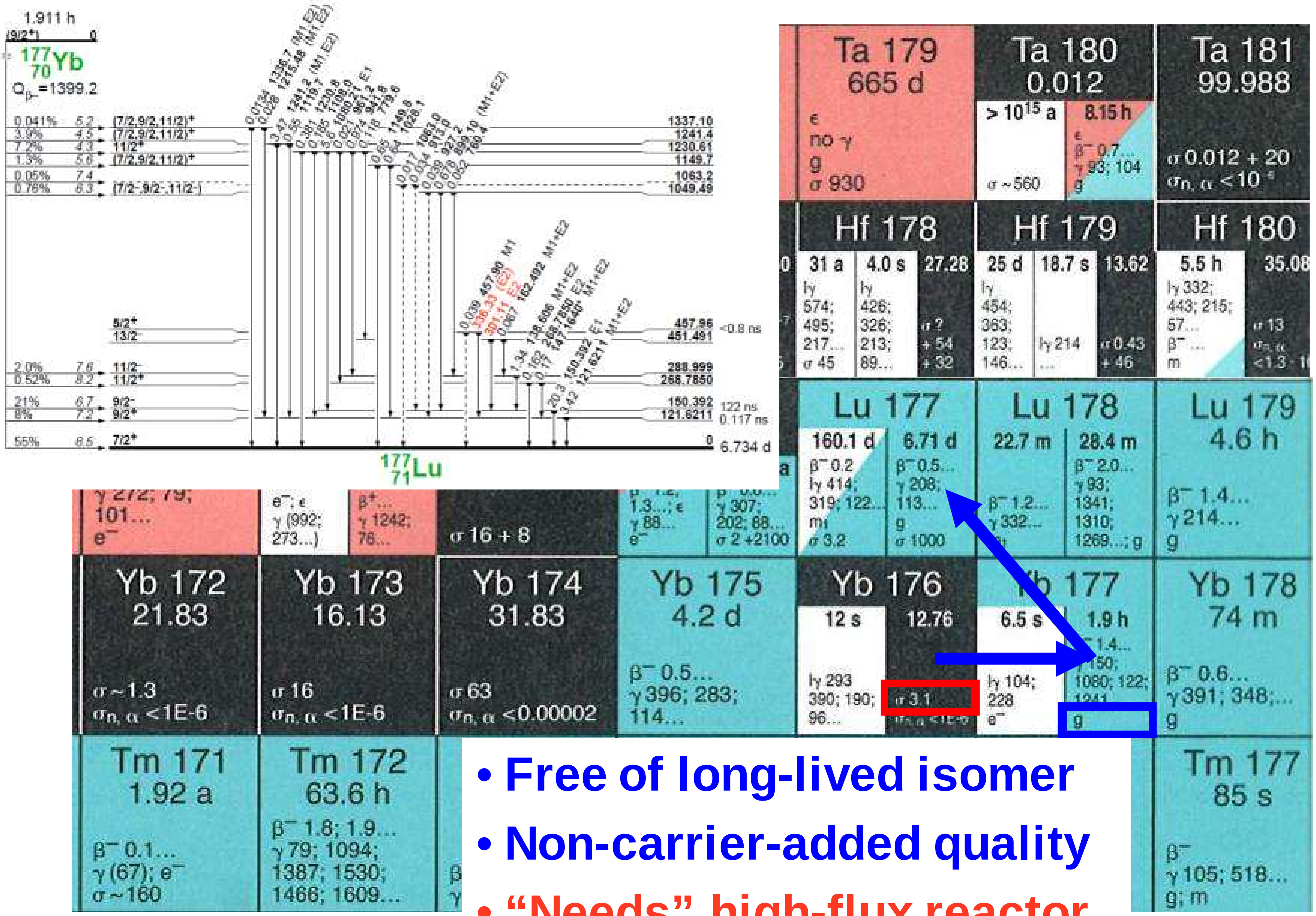
R. Henkelmann et al., Eur. J. Nucl. Med. Mol. Imag. 36 (2009) S260.

The curse of the *K*-isomer !



"So it'll pollute the lake. It will also make the fish glow in the dark when we go night-fishing !"

Alternative production route to ^{177}Lu



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

The rising star for therapy

Radionuclides for RIT and PRRT

Radio-nuclide	Half-life	E mean (keV)	Eγ (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

Estab-lished isotopes

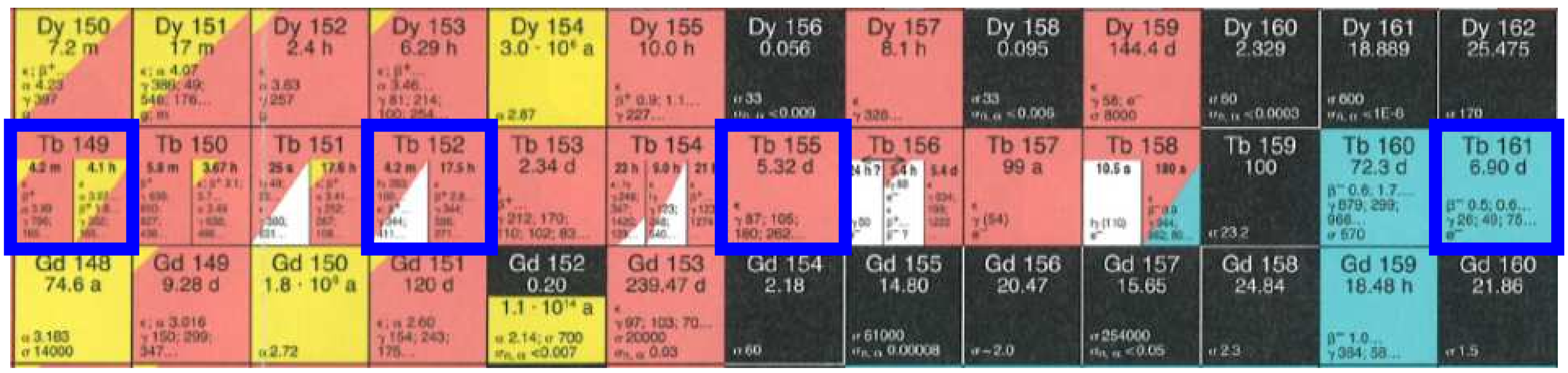
Emerging isotopes

R&D isotopes: supply-limited!

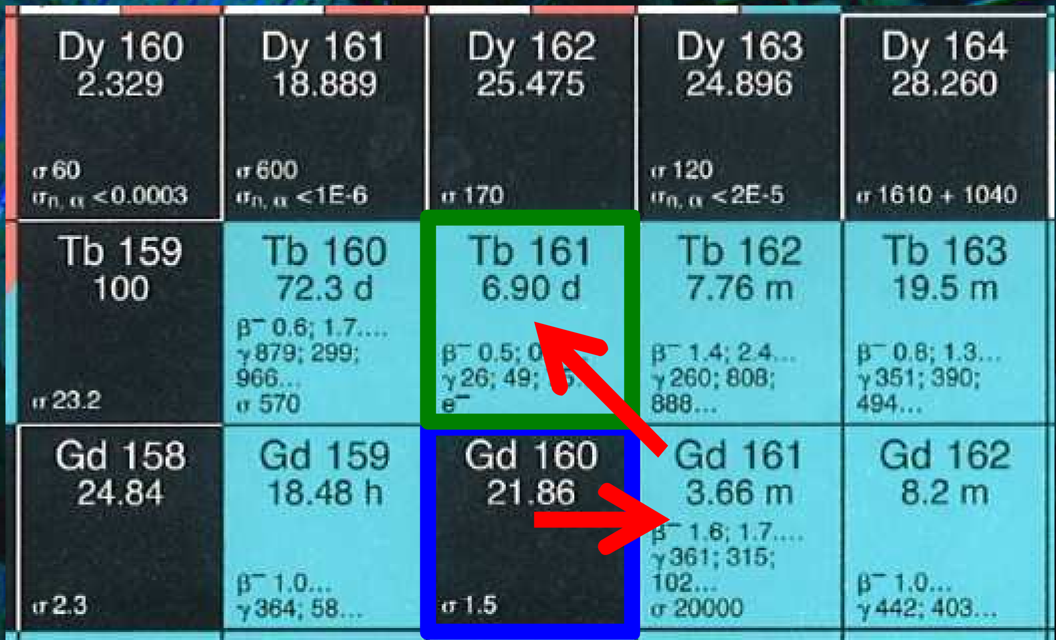
localized

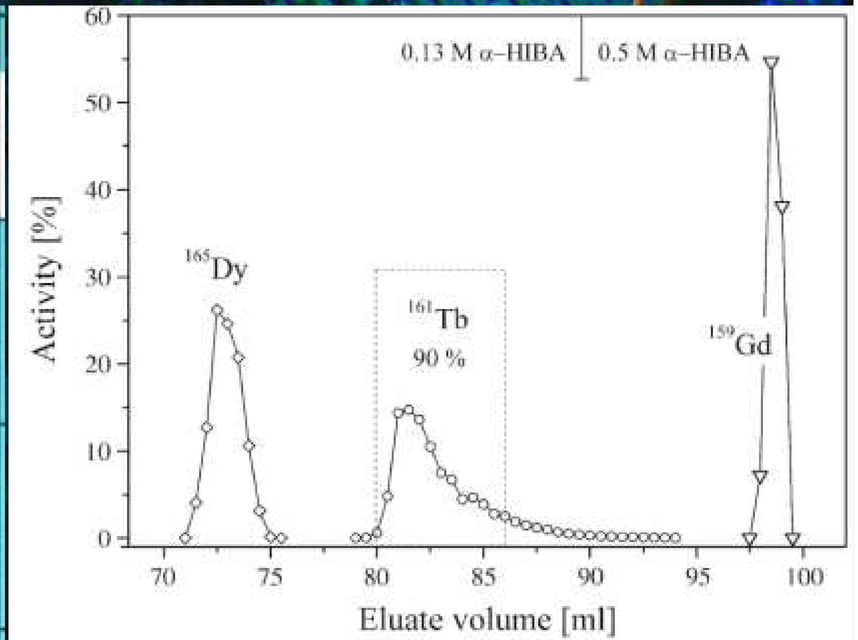
Modern, better targeted bioconjugates require shorter-range radiation $\Rightarrow$ need for adequate (R&D) radioisotope supply.

Terbium: a unique element for nuclear medicine



Production of non-carrier-added ^{161}Tb

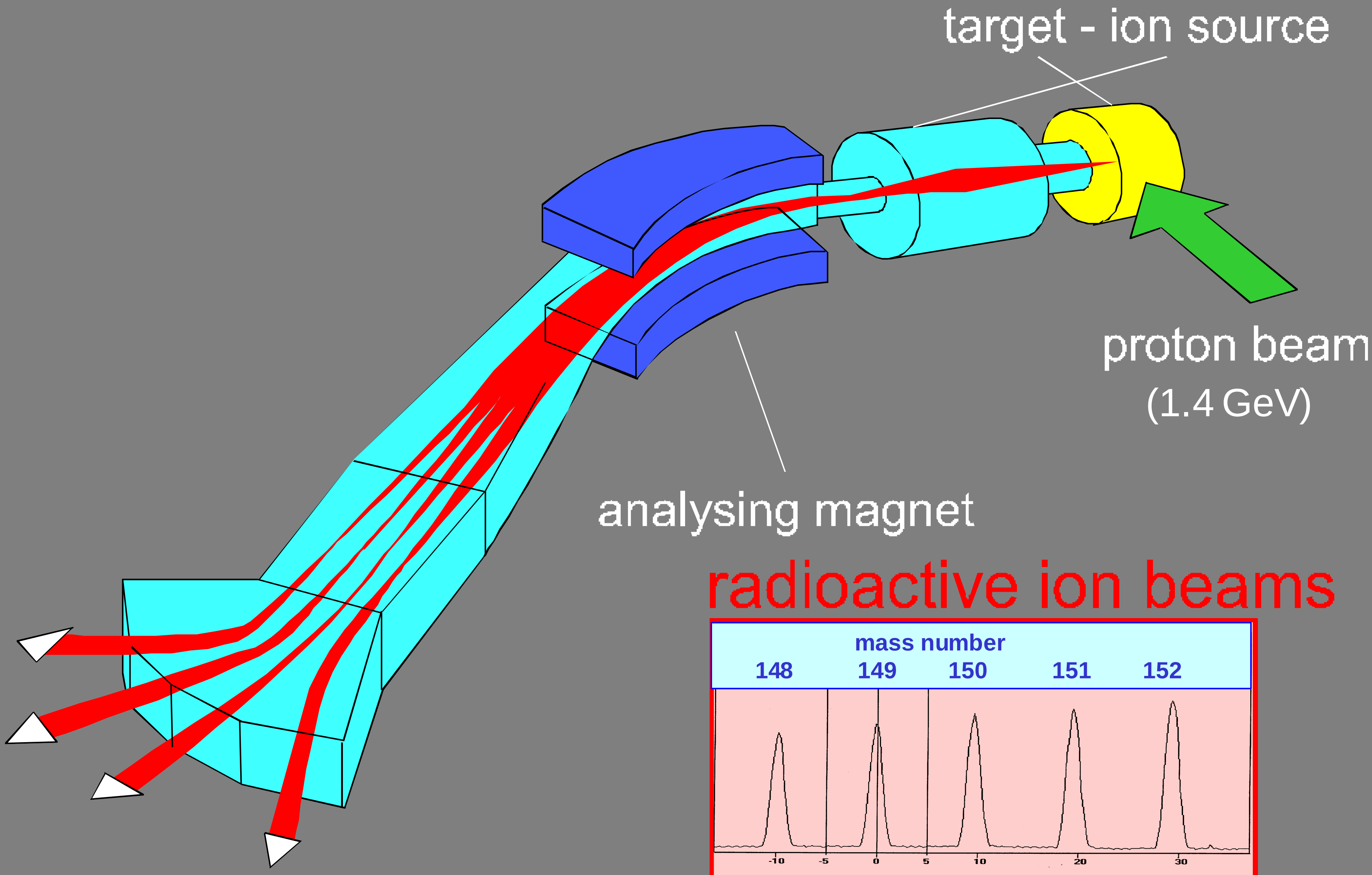


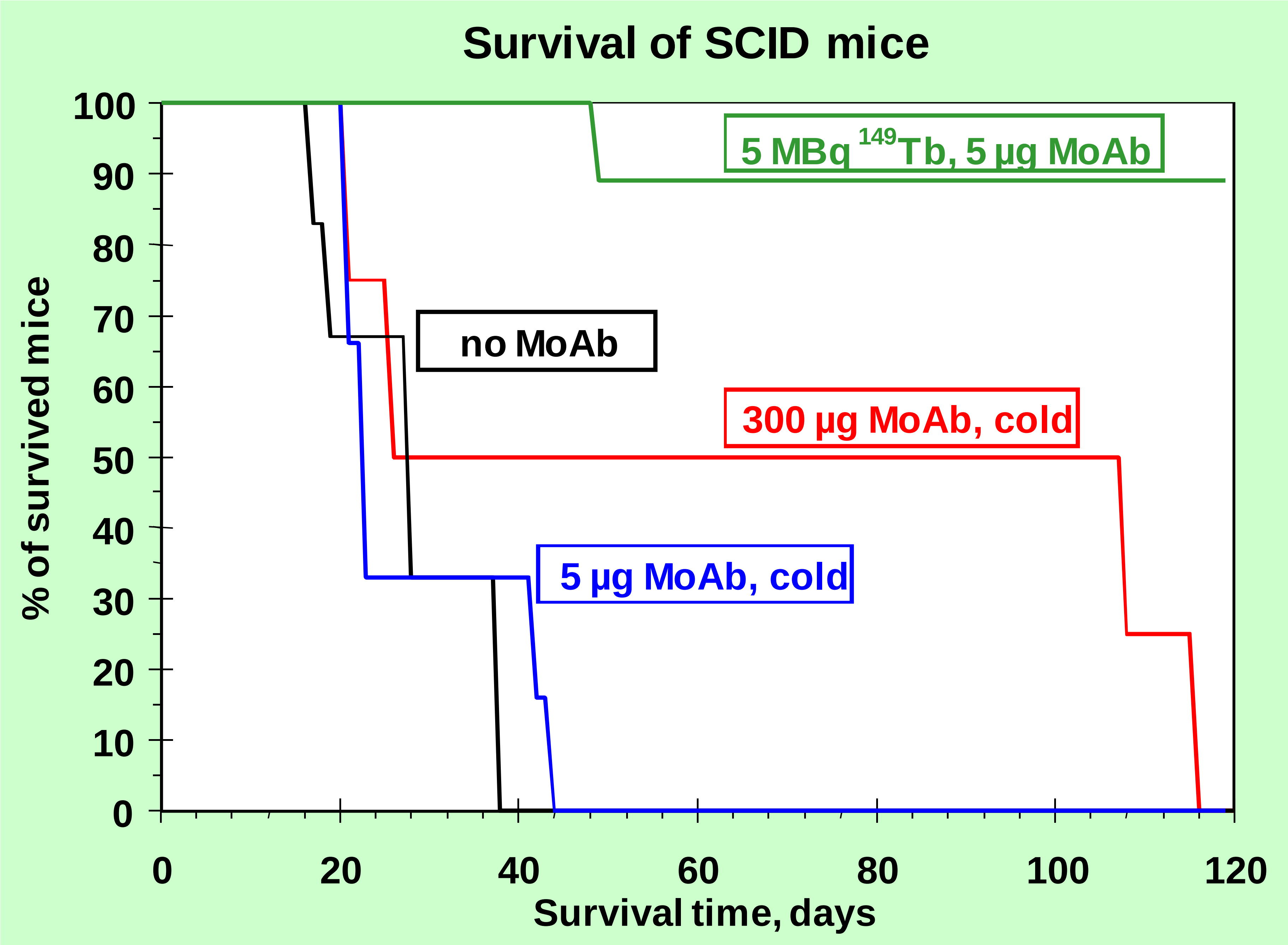


Irradiation in high flux reactor, then chemical separation

S. Lehenberger et al., Nucl. Med. Biol. 38 (2011) 917.

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

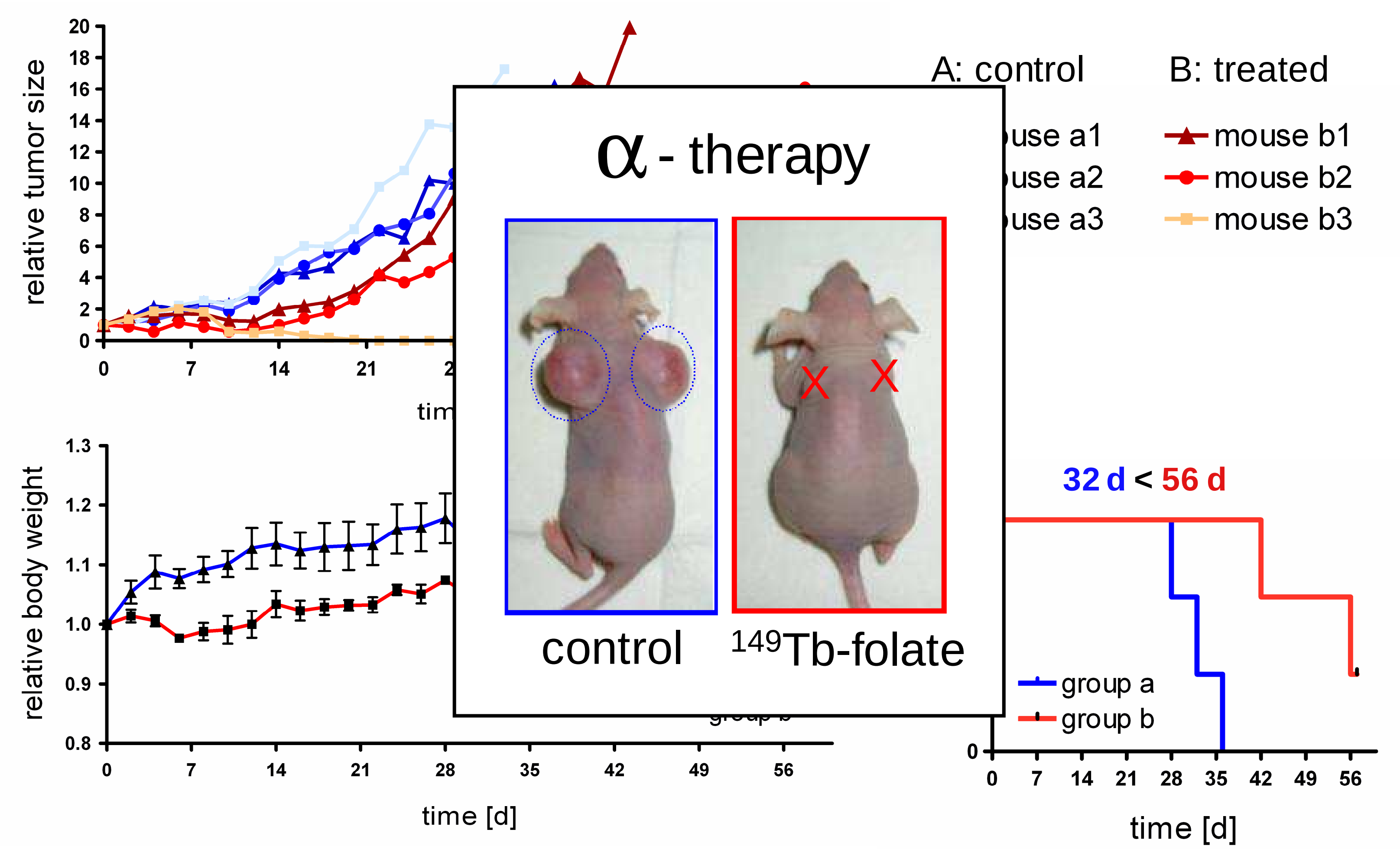




G.J. Beyer et al., Eur. J. Nucl. Med. Molec. Imaging ***31*** *(2004) 547.*

Targeted Alpha Radionuclide Therapy

KB Tumor-Bearing Mice Treated with ^{149}Tb-Folate

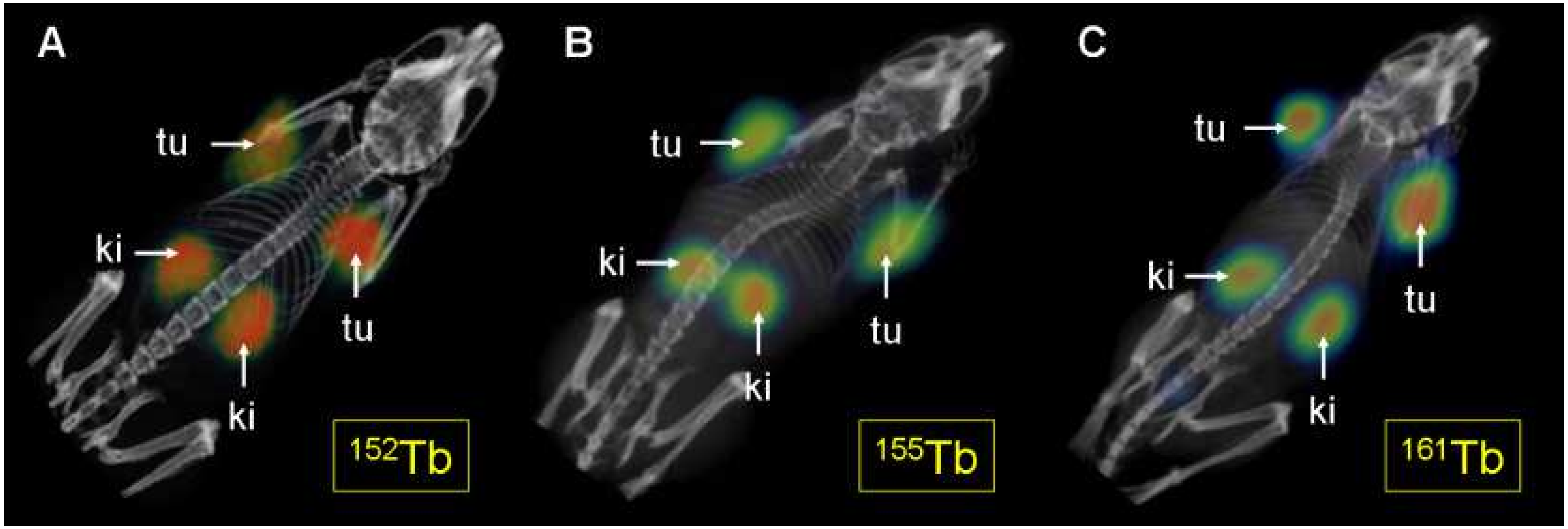


C. Müller et al., subm. to J. Nucl. Med.

Imaging Studies Using PET and SPECT

KB Tumor-Bearing Nude Mice

PET *SPECT* *SPECT*



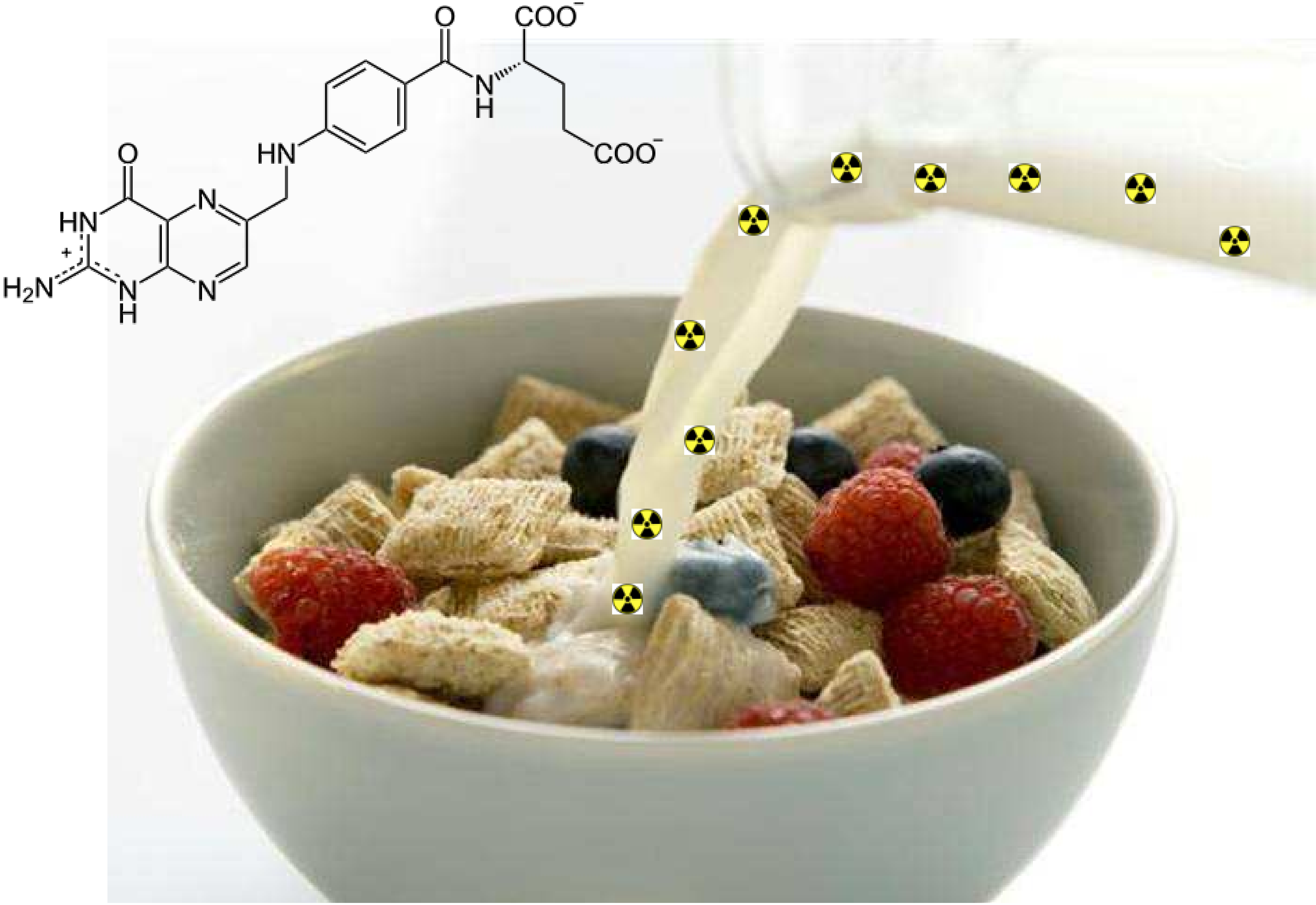
^{152}Tb-folate: 9 MBq	^{155}Tb-folate: 4 MBq	^{161}Tb-folate: 30 MBq
Scan Start: 24 h p.i.	Scan Start: 24 h p.i.	Scan Start: 24 h p.i.
Scan Time: 4 h	Scan Time: 1 h	Scan Time: 20 min

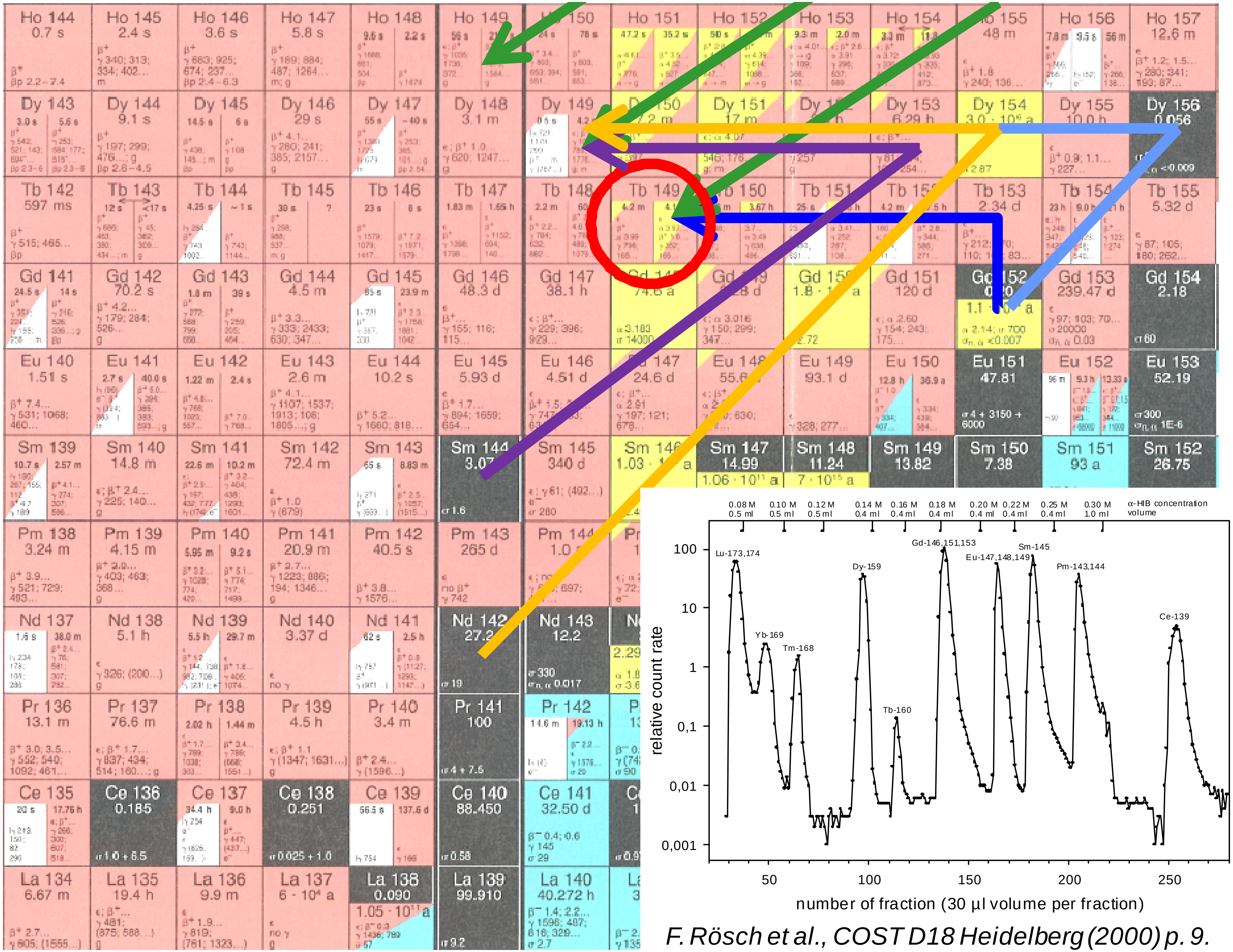
PAUL SCHERRER INSTITUT

NEUTRONS FOR SCIENCE

C. Müller et al., subm. to J. Nucl. Med.

Folic acid





F. Rösch et al., COST D18 Heidelberg (2000) p. 9.

Production of ^{149g}Tb

1. **spallation of Ta** (or Hg) target coupled to ISOL (possibly off-line)
   (**HIE-)Isolde, ISAC,** LAMPF, SNS, J-PARC, ESS, ISOL@MYRRHA,…
   needs ≈GeV protons + mass separation

2. ^{152}Gd(p,4n) with 55 MeV protons + chemical separation
   Arronax, PSI, KVI, JYFL, LLN, SPES,…
   needs grams of enriched ^{152}Gd, unknown C.S. & purity

3. ^{152}Gd($^{3/4}$He,6/7n)^{149}Dy with 120 MeV ^{4}He (or 100 MeV ^{3}He) + chem. sep.
   KVI, LLN, Karlsruhe,…
   needs grams of enriched ^{152}Gd, unknown C.S. & purity

4. ^{144}Sm(^{9}Be,4n)^{149}Dy with 65 MeV ^{9}Be + chem. sep.
   needs intense ^{9}Be beam, unknown C.S. & purity

5. ^{142}Nd(^{12}C,5n) with 120 MeV ^{12}C + chem. sep.
   SPIRAL2, CSS1, KVI, JYFL,…
   needs target design for high current, optimization of yield vs. purity

Radionuclides for RIT and PRRT

Radio-nuclide	Half-life	E mean (keV)	Eγ (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

Estab-lished isotopes

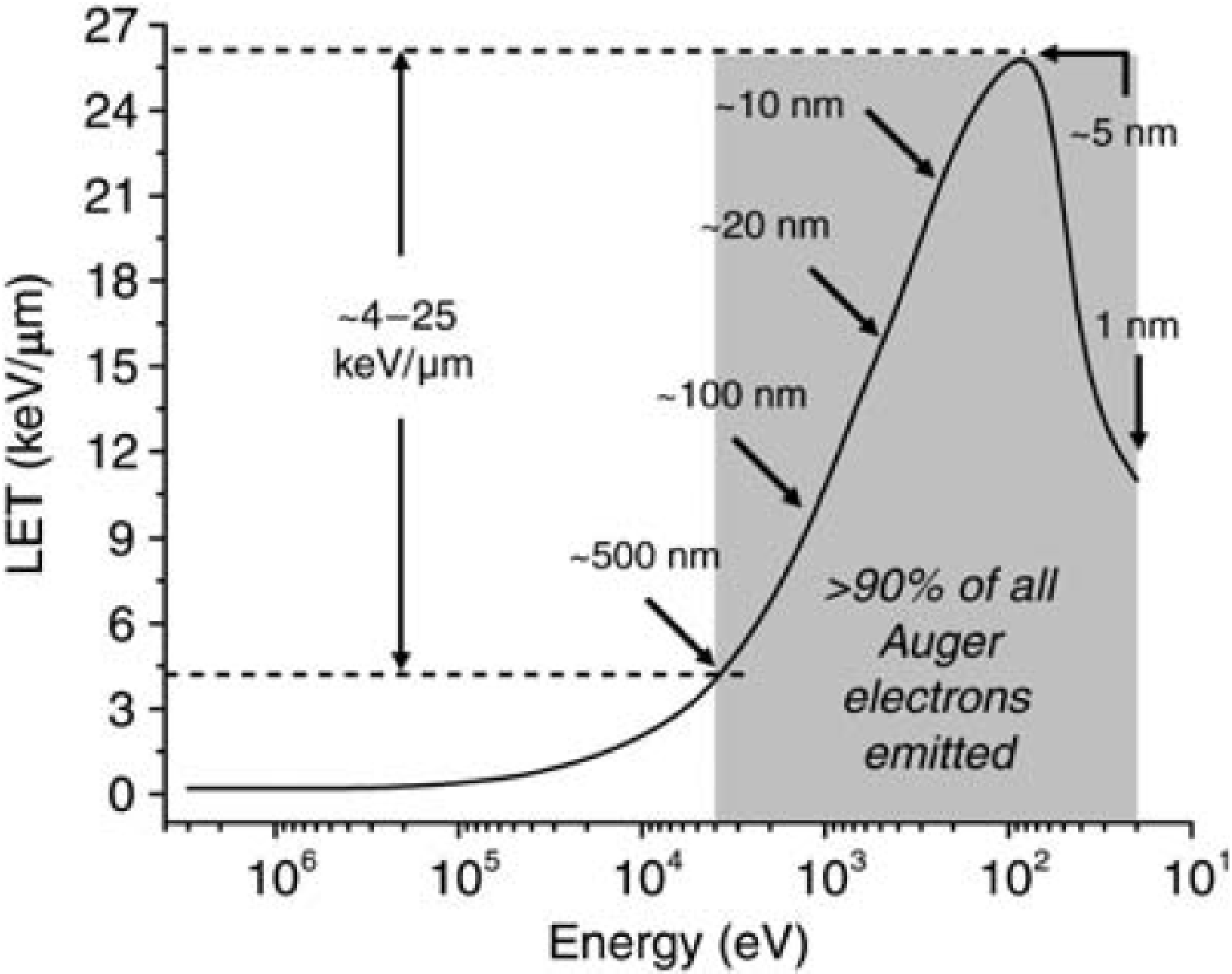
Emerging isotopes

R&D isotopes: supply-limited!

localized

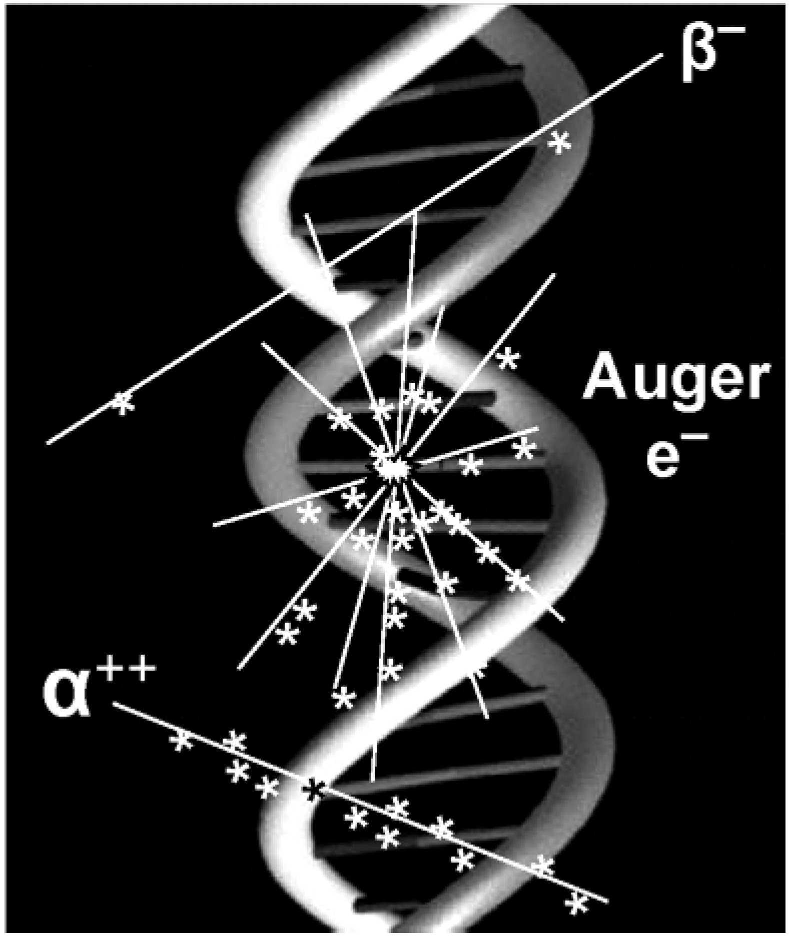
Modern, better targeted bioconjugates require shorter-range radiation ⇒ need for adequate (R&D) radioisotope supply.

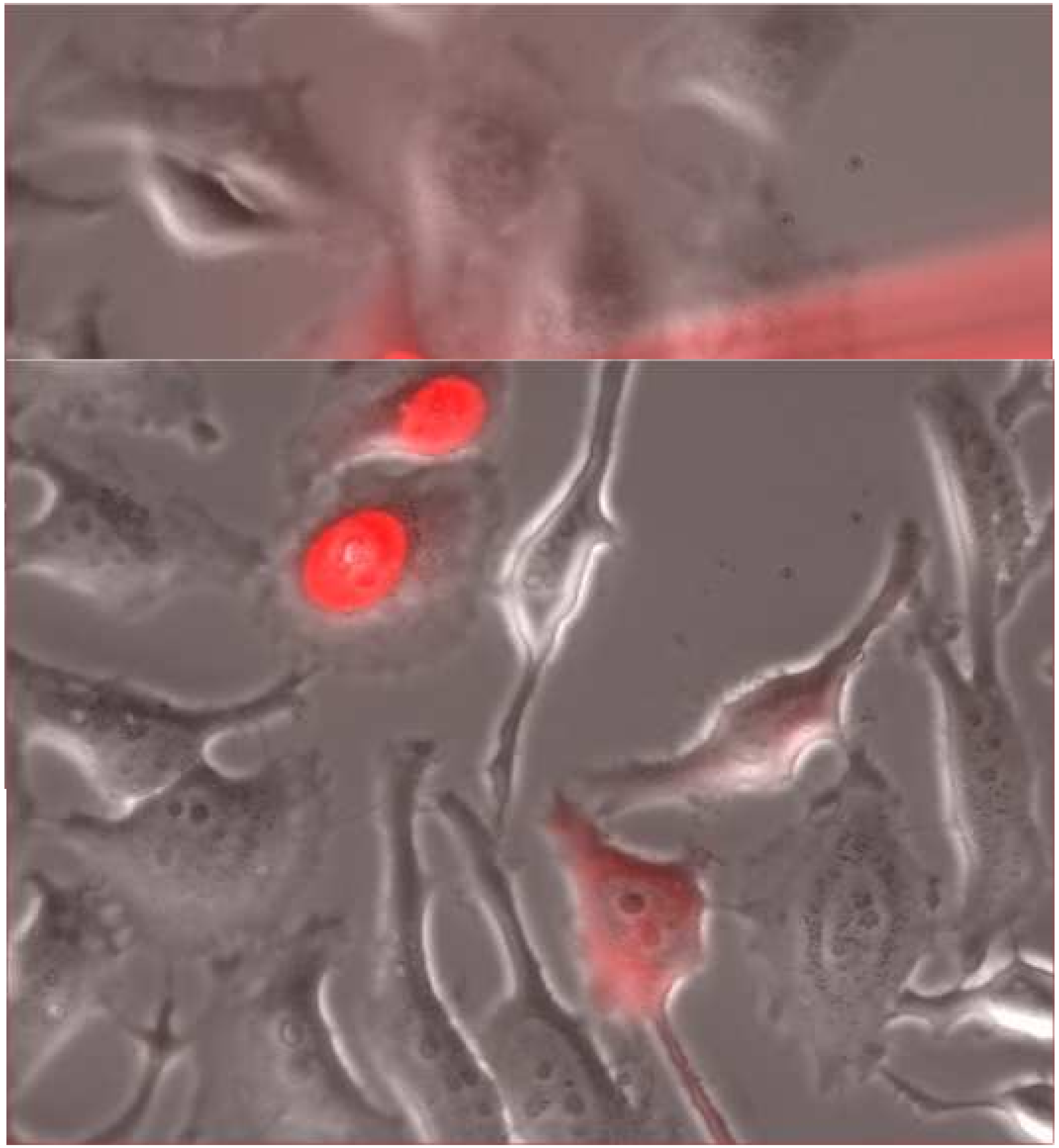
LET of Auger electrons



A.I. Kassis, Rad. Prot. Dosimetry 143 (2011) 241.

Radiobiology of Auger electron emitters ?





M. Jensen et al., DTU Risø

Outlook

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 1 (**1927**) 95.*
Translation : A.I. Kassis, Int. J. Radiat. Biol. 80 (2004) 789.

Today we are closer than ever to reach this goal !

What can nuclear physics facilities do ?

1. **provide now R&D isotopes for preclinical studies**
2. **facilitate facility access for remote “mail-out-users” from biochemical/medical research groups**
3. **clever design of beam dumps, collimators, etc. enabling isotope harvesting**
4. **get more radiochemists involved**