IS528-ADD1
Novel diagnostic and therapeutic radionuclides for the development of innovative radiopharmaceuticals

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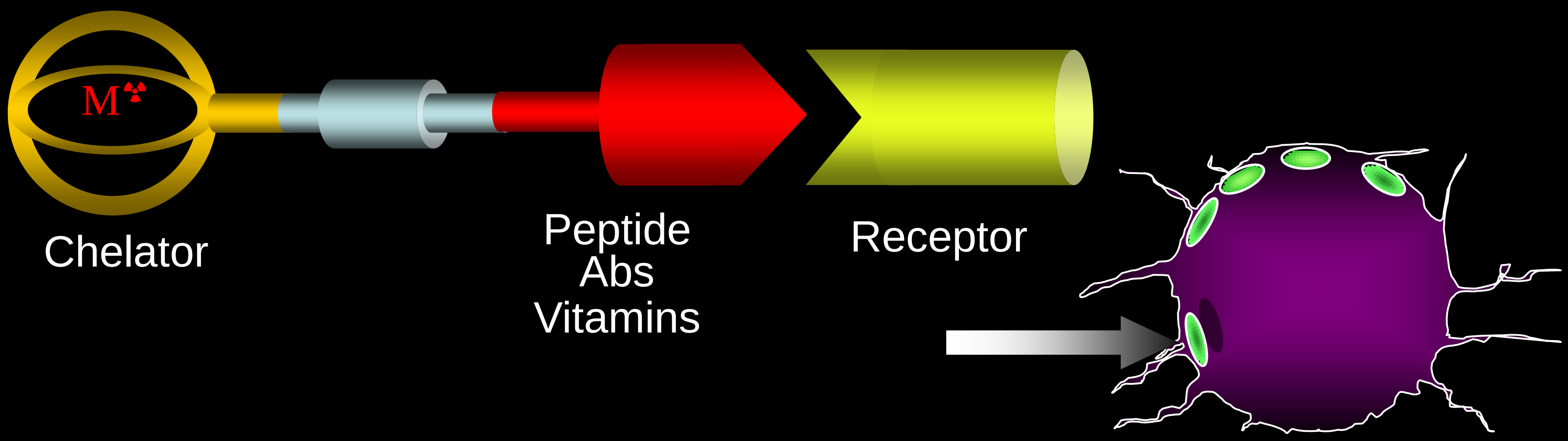
Radiometals for diagnostic imaging and therapy

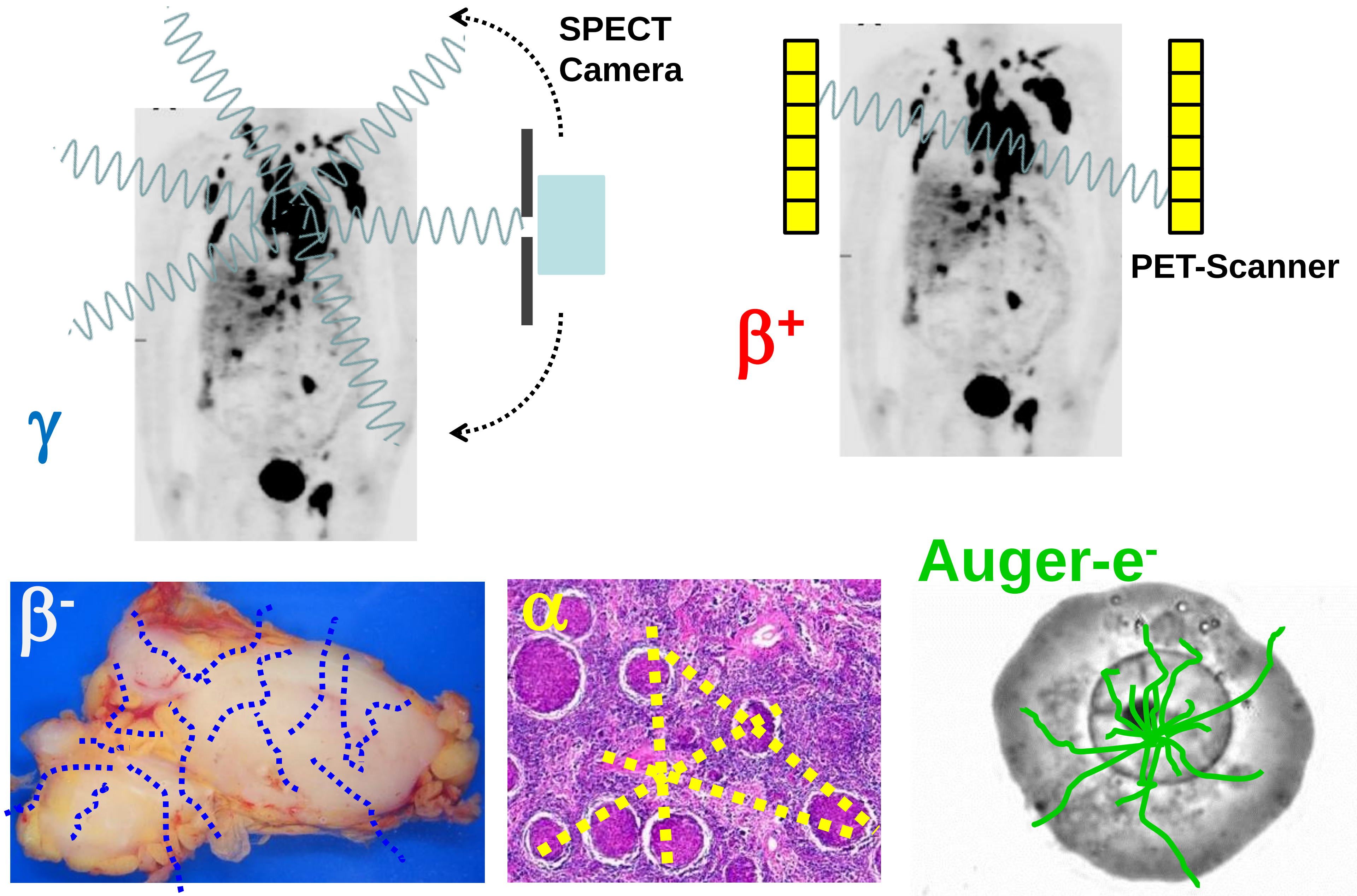


Photon or positron emitters ^{99m}Tc, ^{68}Ga, … for imaging

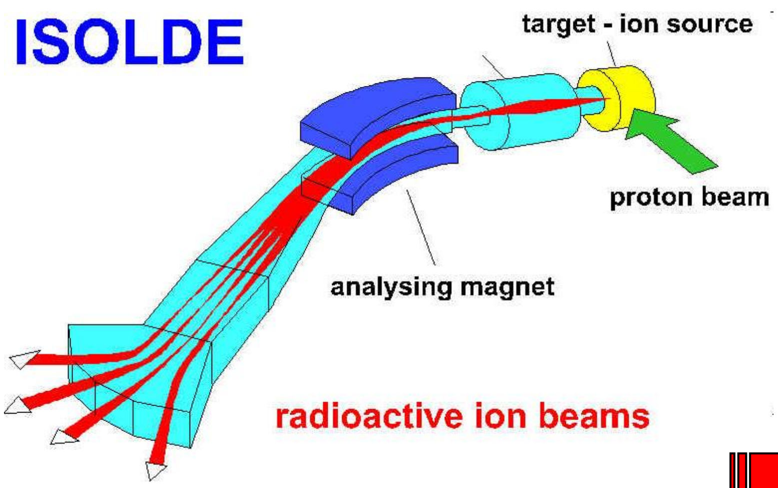
Particle emitters ^{90}Y, ^{177}Lu, … for radionuclide therapy

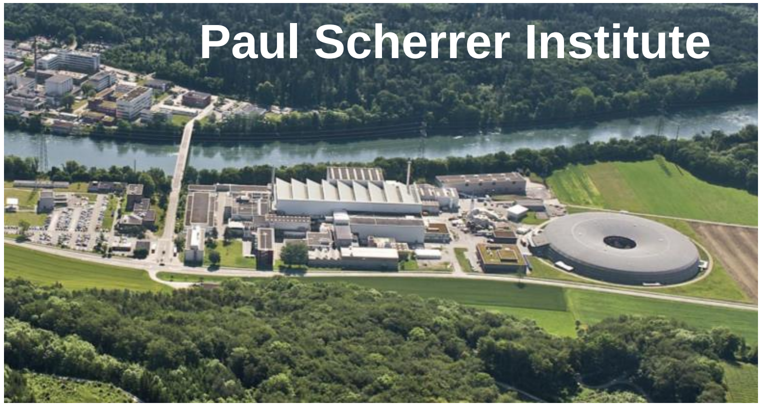
applicable only
with high specific activity and chemical purity

The Nuclear Medicine Alphabet



Production of n.c.a. [$^{149/152/155}$Tb]-Terbium
ISOLDE CERN and PSI





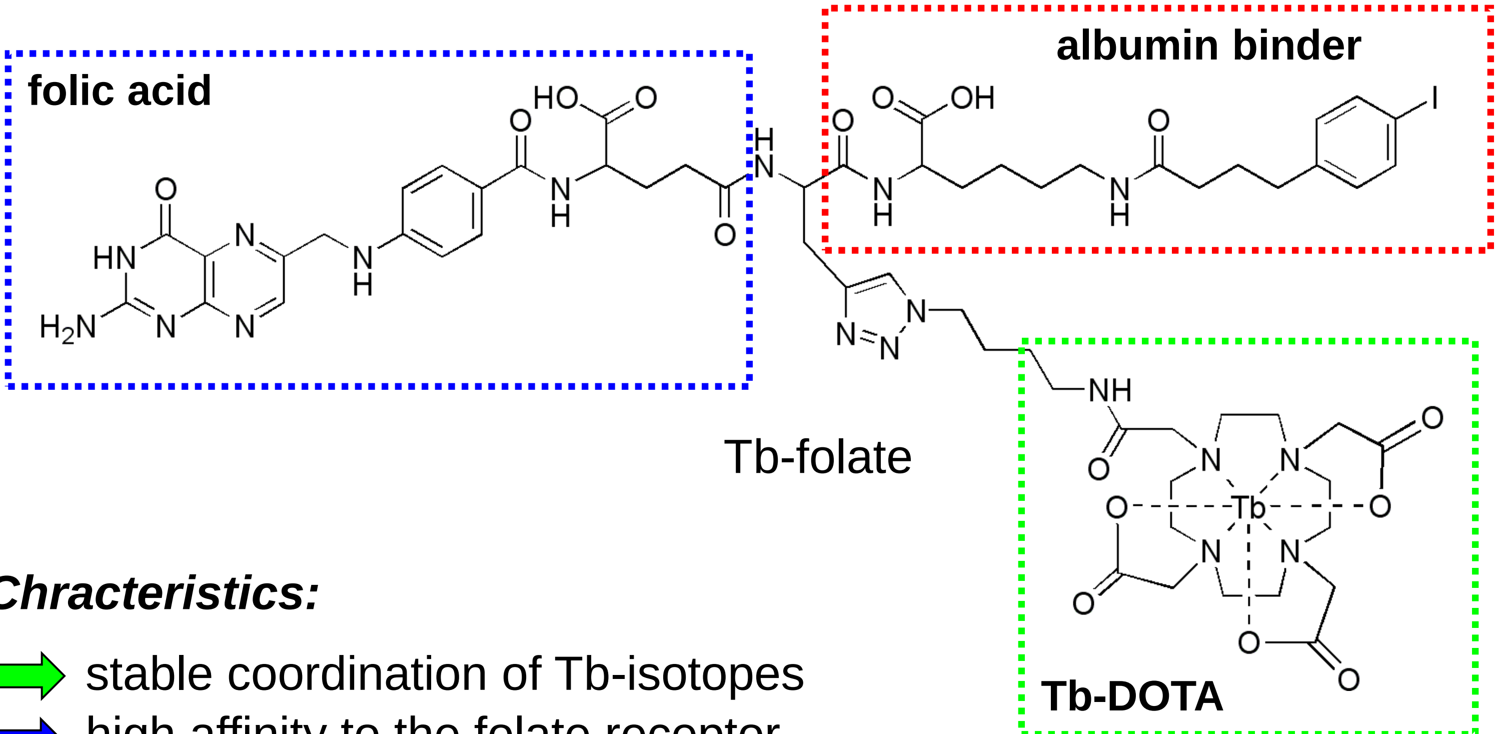
Separation by means of cation exchange chromatography

Spallation of tantalum targets followed by resonant laser ionization of Dy precursor and mass separation

$\Rightarrow$ ^{149,152,155}Tb with some oxide sidebands

Tumor Tageting Agent for Tb-Coordination

Chemical Structure with 3 Functionalities



Tb-folate

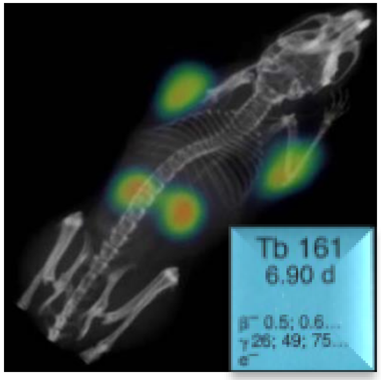
Chracteristics:

- stable coordination of Tb-isotopes
- high affinity to the folate receptor
- prolonged blood circulation time

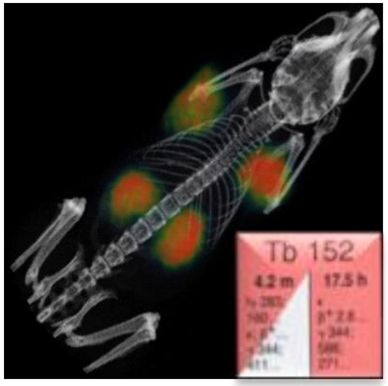
Terbium: the Swiss Army knife of Nuclear Medicine

^{149}Tb-therapy

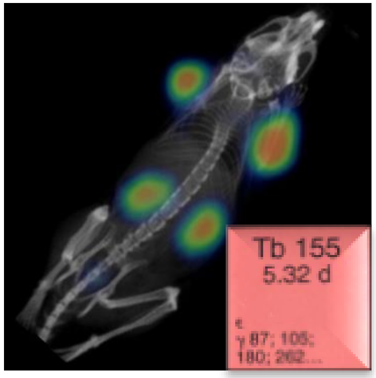
^{161}Tb-therapy & SPECT



^{152}Tb-PET



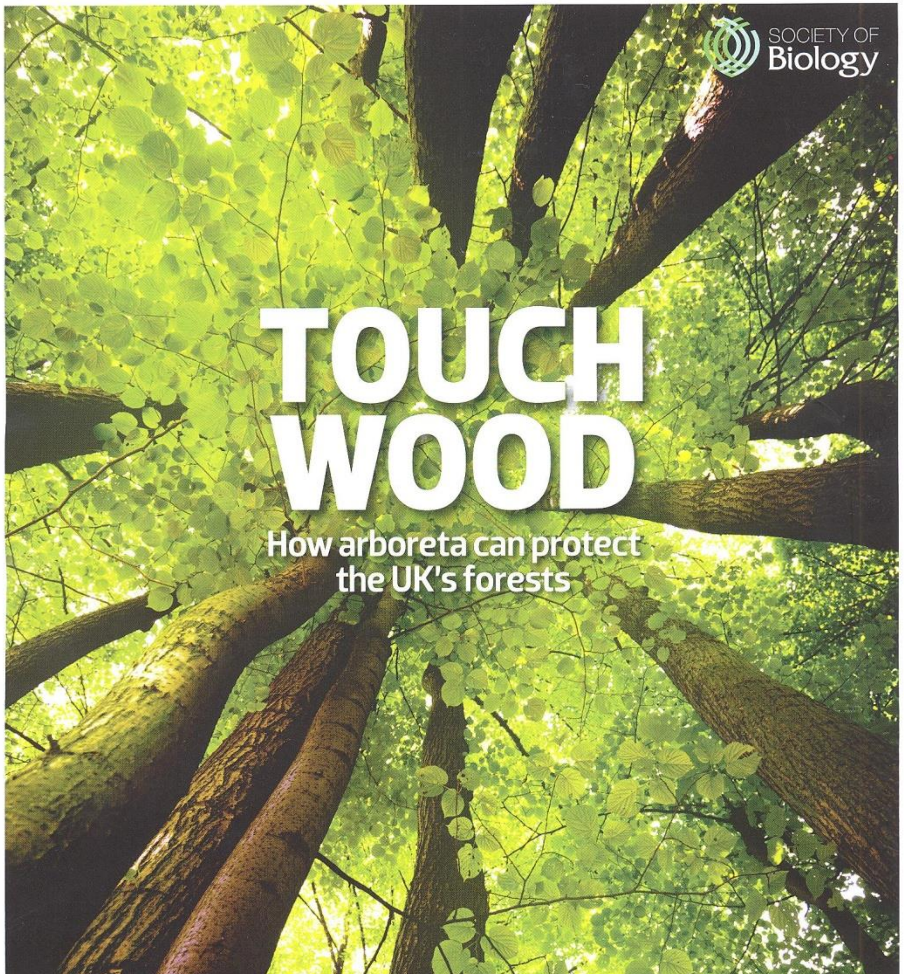
^{155}Tb-SPECT



Müller et al. **2012**, J Nucl Med 53:1951.

The Biologist

THE SOCIETY OF BIOLOGY MAGAZINE ▪ ISSN 0006-3347 ▪ SOCIETYOFBIOLOGY.ORG VOL 60 NO 3 ▪ JUNE/JULY 2013



TOUCH WOOD

How arboreta can protect the UK's forests

PHARMACOLOGY

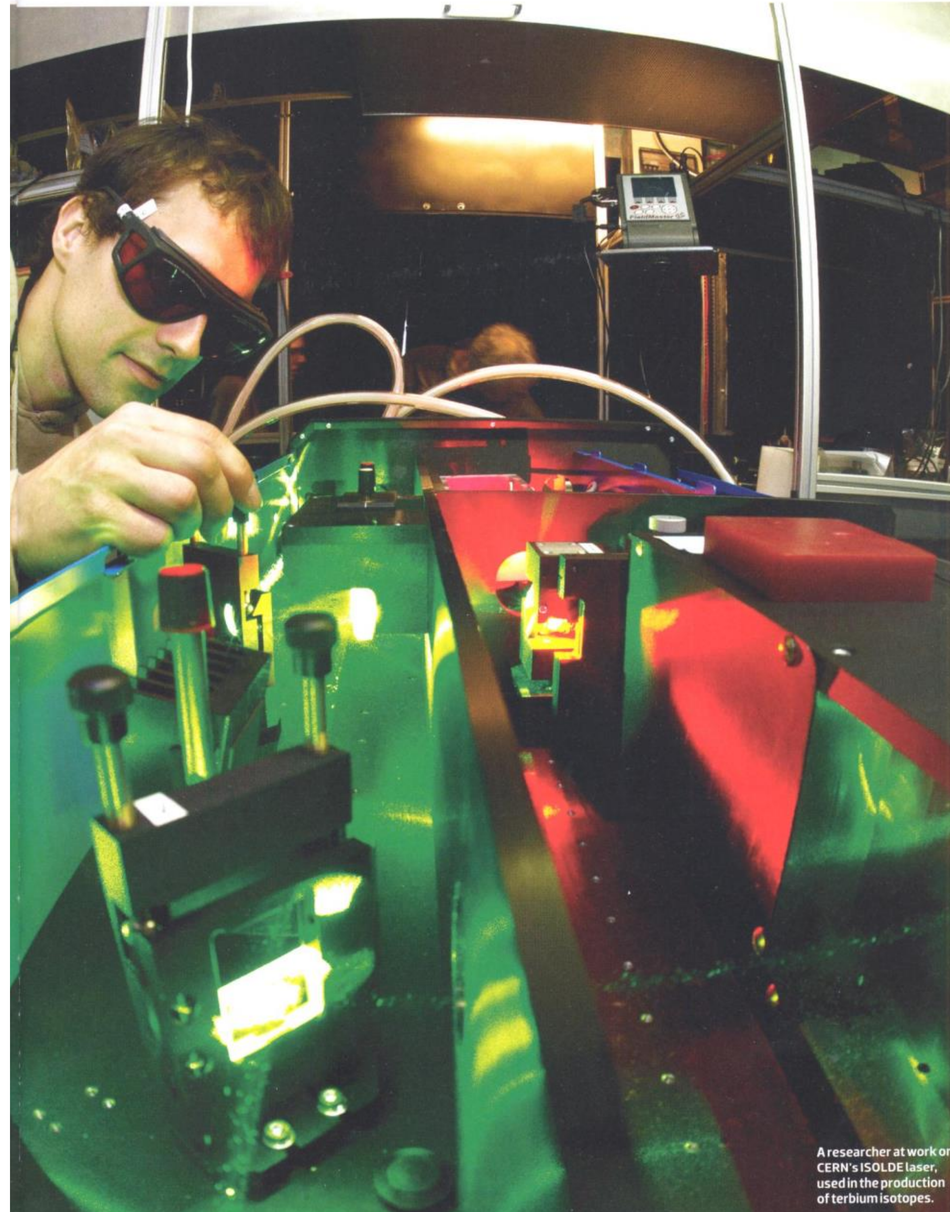
RADIOACTIVE REMEDIES
Fighting cancer with rare radioisotopes

RESEARCH

GET INVOLVED
The 10 best citizen science biology projects

INTERVIEW

BRUCE HOOD
Psychology, neuroscience and our sense of self

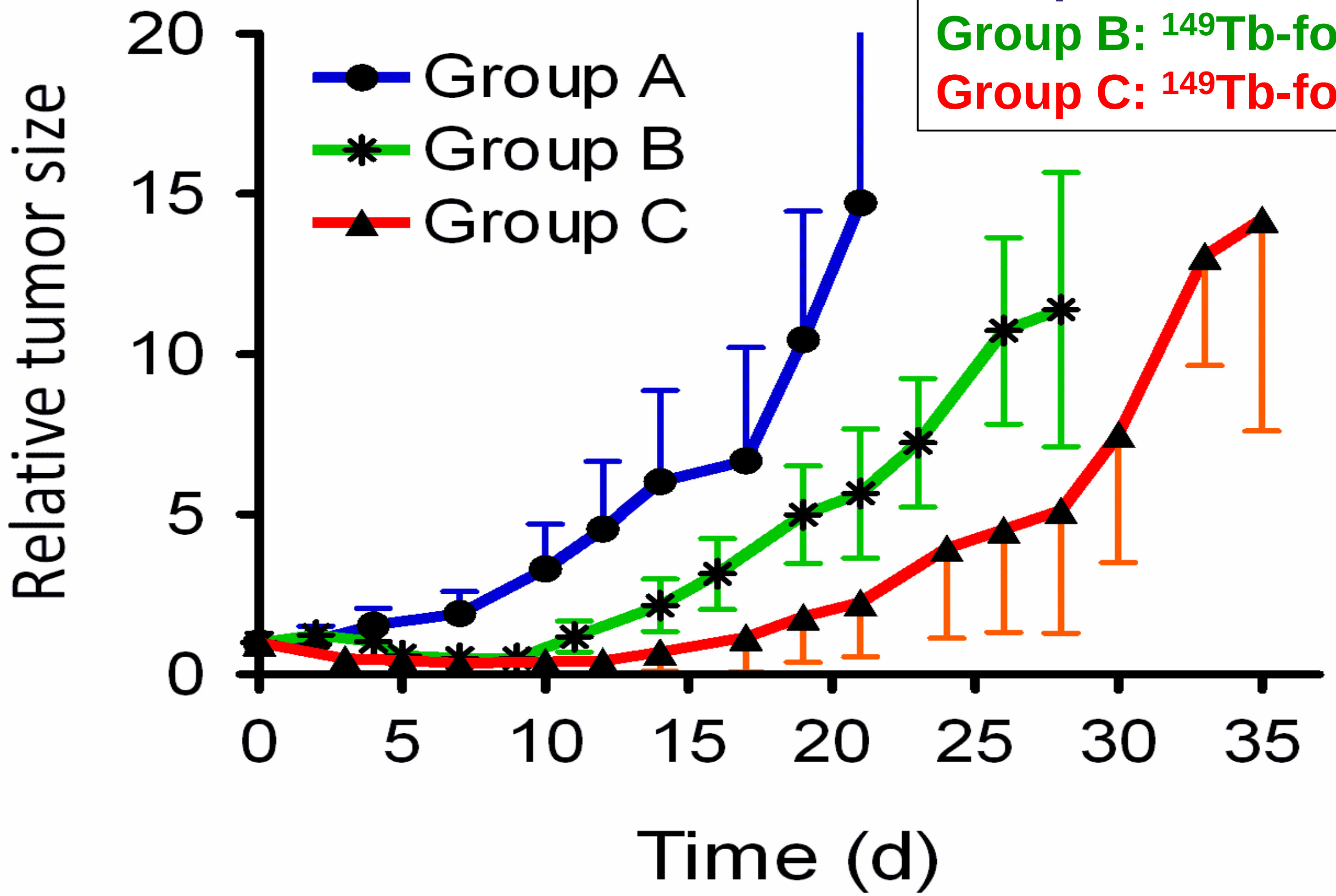


A researcher at work on CERN's ISOLDE laser, used in the production of terbium isotopes.

Terbium-149: alpha-Emitter

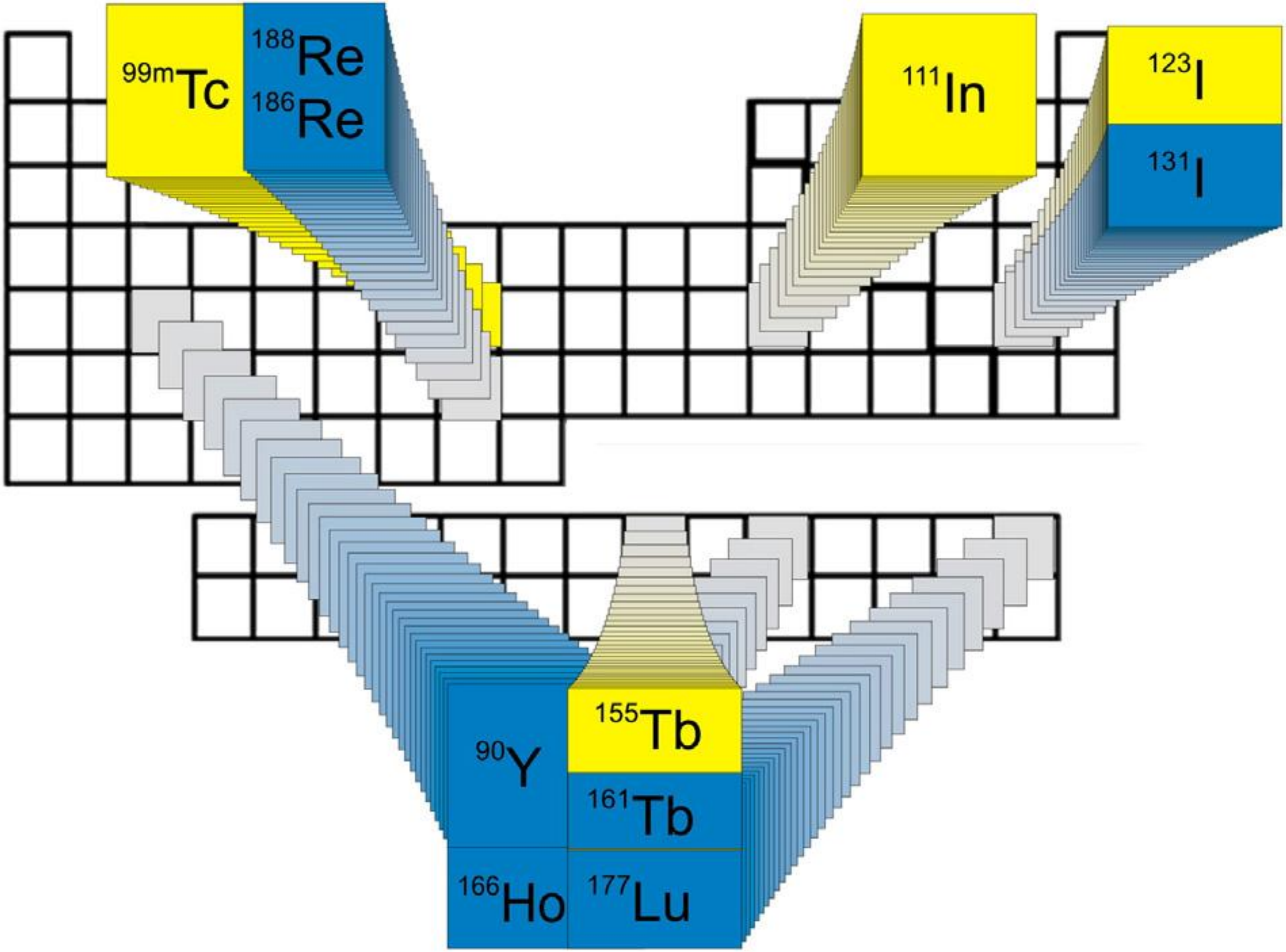
Folate Receptor Targeted α-Radionuclide Therapy

Group A: control
Group B: ^{149}Tb-folate 2.2 MBq
Group C: ^{149}Tb-folate 3.0 MBq



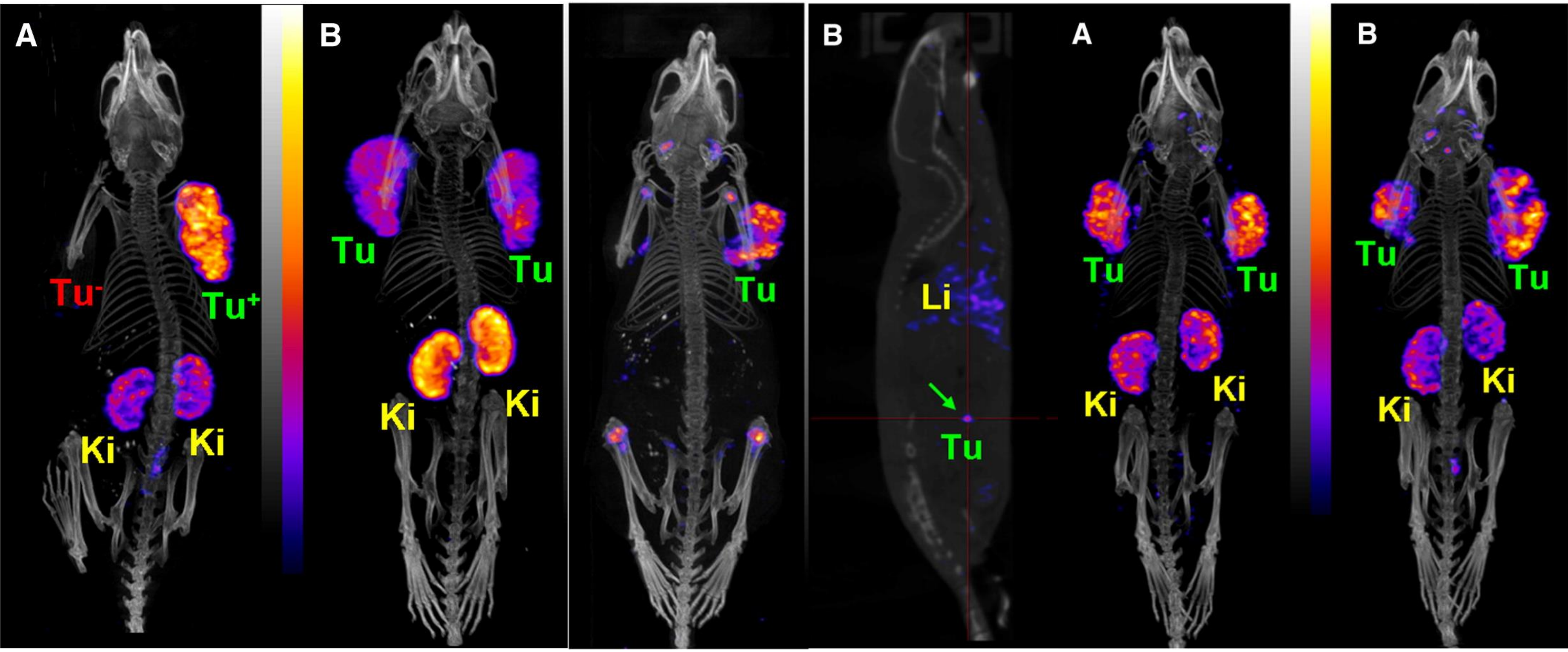
Müller et al. **2013**, Pharmaceuticals, submitted

^{155}Tb: low-dose SPECT prior to therapy



Müller et al. **2013**, Nucl Med Biol, in press: doi:10.1016/j.nucmedbio.2013.11.002

in vivo validation with peptides, mAbs and vitamins



Peptides		monoclonal antibody		folate	
MD	DOTATATE	chCE7	chCE7	cm09	cm09

Müller et al. **2013**, Nucl Med Biol, in press: doi:10.1016/j.nucmedbio.2013.11.002

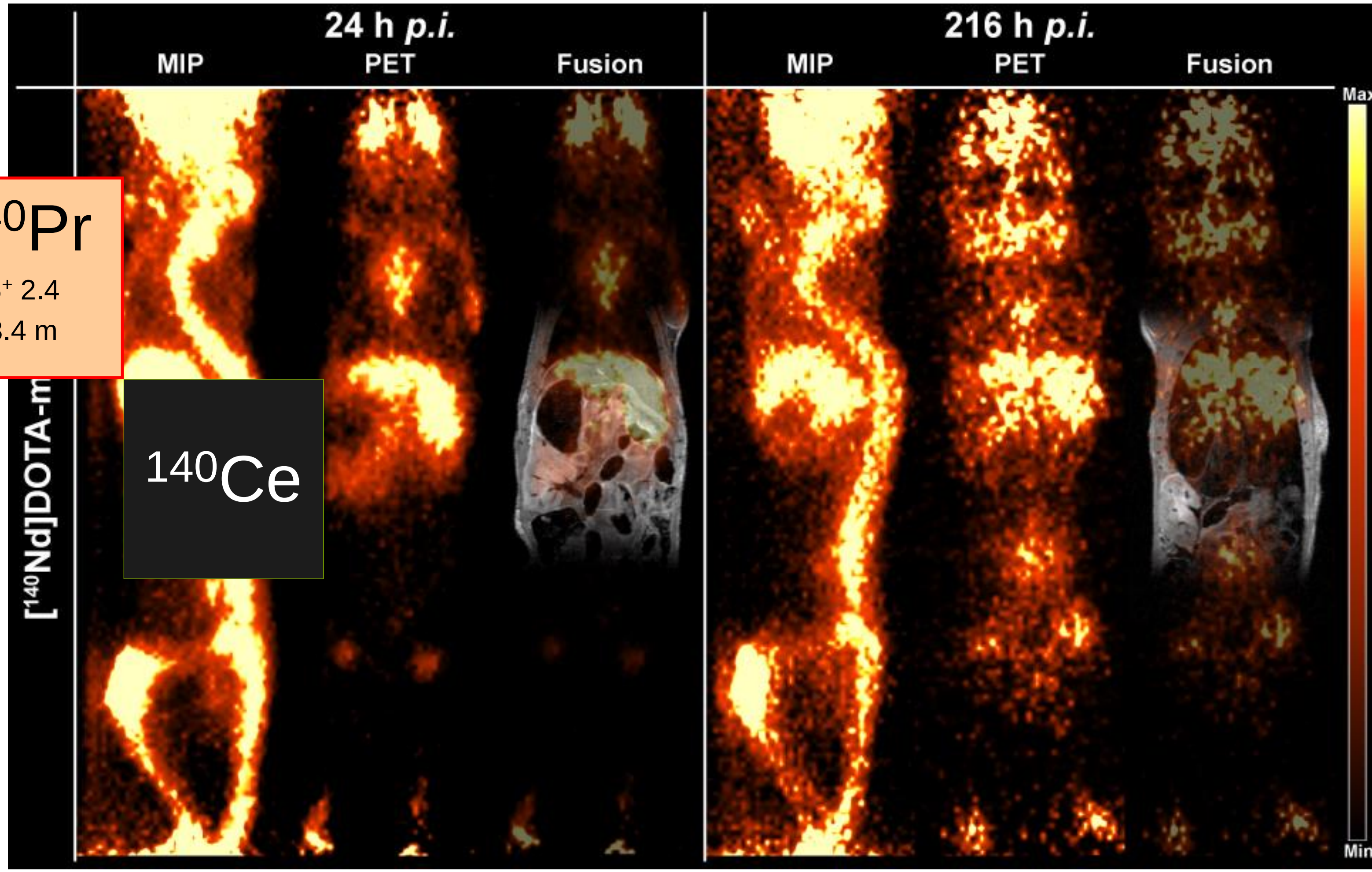
Efficient parallel operation

^{140}Nd/^{140}Pr: an *in vivo* PET generator

^{140}Nd
ε
3.37 d

^{140}Pr
$β^+$ 2.4
3.4 m

^{140}Ce



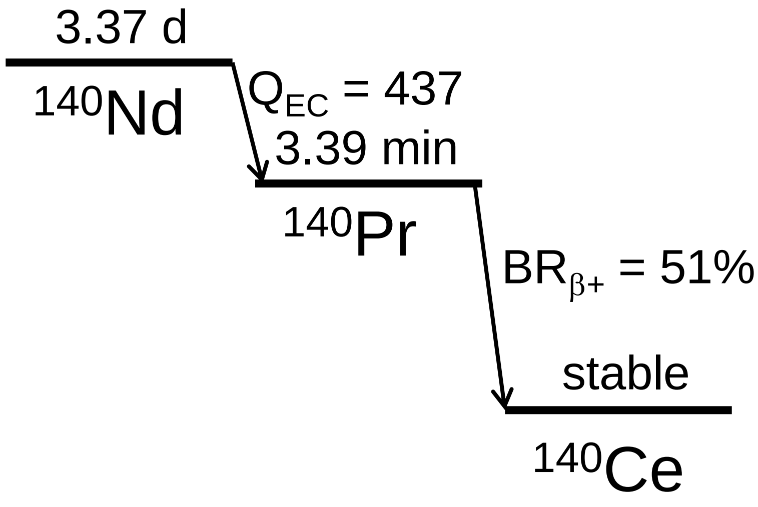
UNIVERSITÄTS KLINIKUM TÜBINGEN

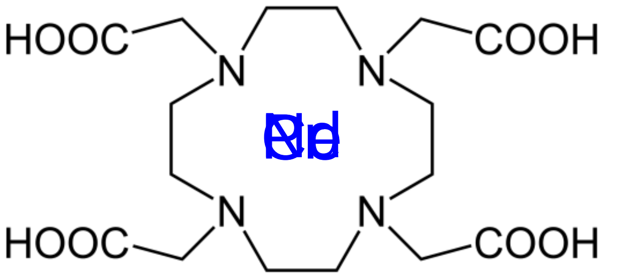
Werner Siemens Imaging Center

EBERHARD KARLS UNIVERSITÄT TÜBINGEN

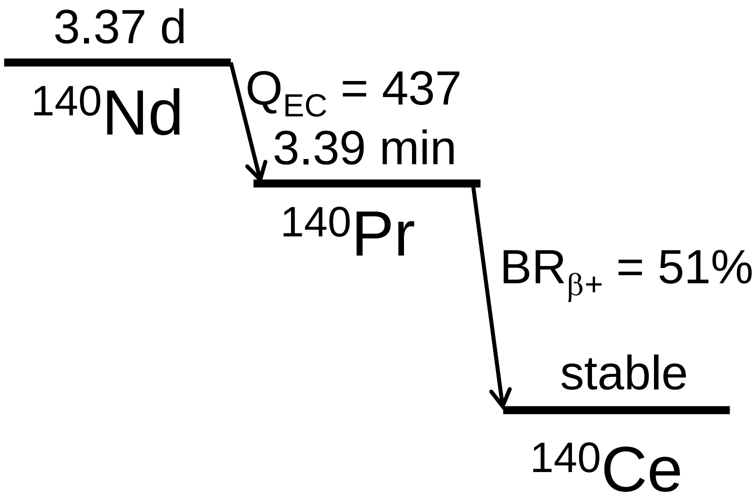
Köster et al. **2014**, Nucl Med Biol, submitted.

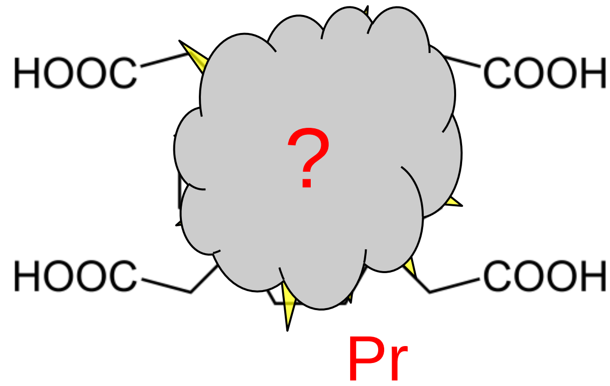
Understanding the Auger release from chelators



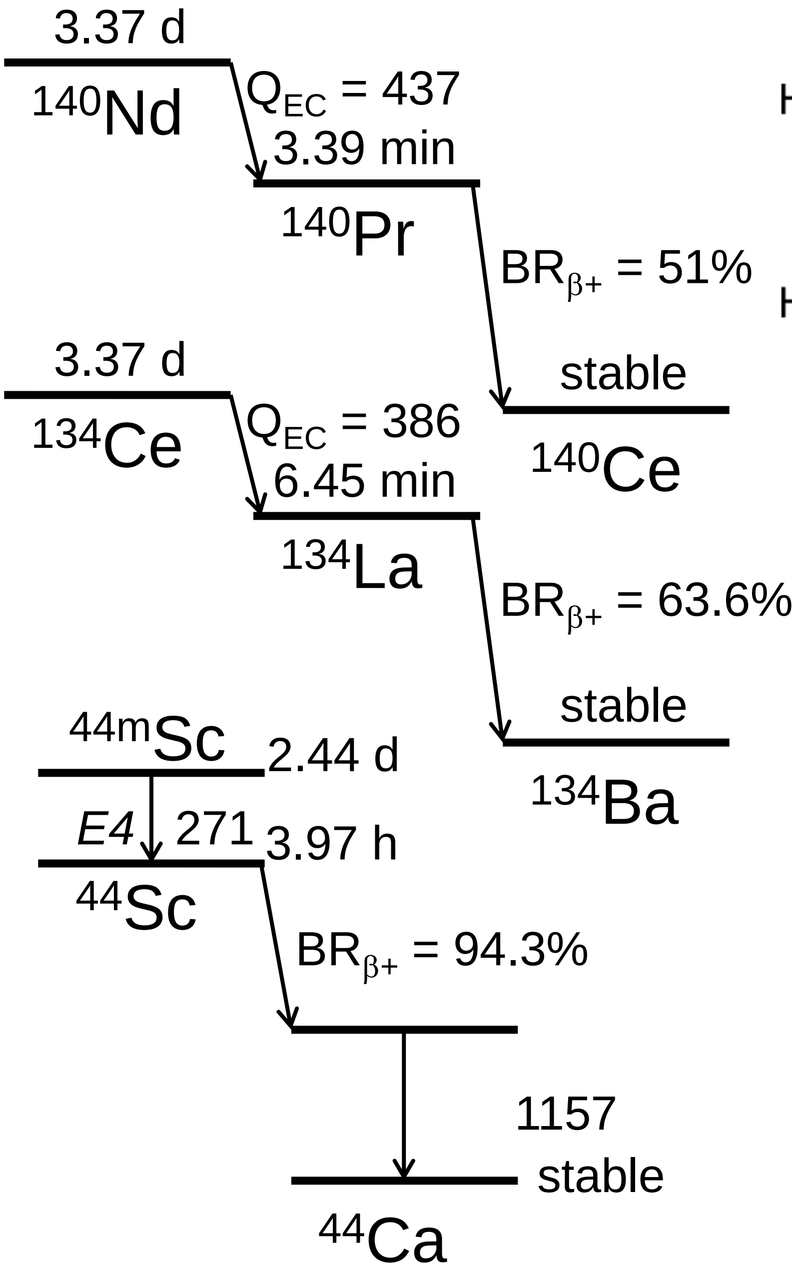


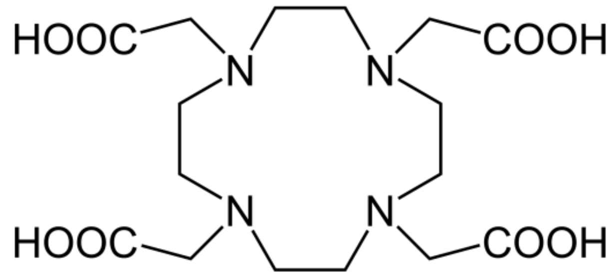
Understanding the Auger release from chelators

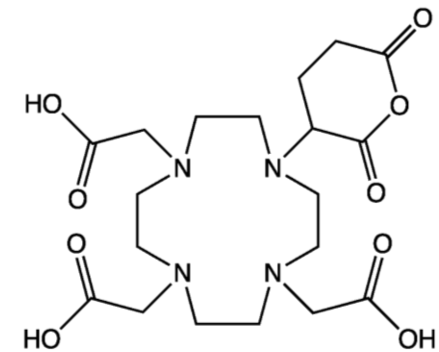


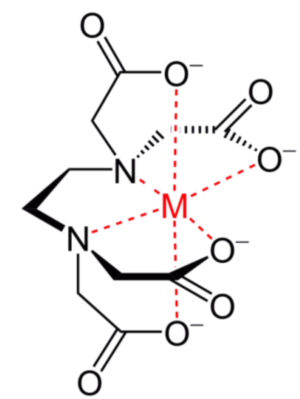


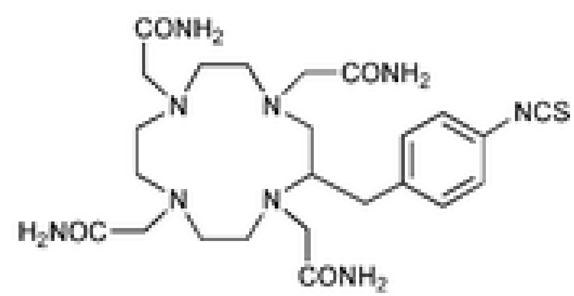
Understanding the Auger release from chelators











Risø DTU

Theranostic of Invasive Aspergillosis and Echinococcus Multilocularis

MATHIAS

New Molecular-Functional Imaging Technologies and Therapeutic Strategies for Theranostic of Invasive Aspergillosis

SEVENTH FRAMEWORK PROGRAMME

- HOME
- CONSORTIUM
- WORKPACKAGES
- MANAGEMENT
- NEWS
- PUBLICATIONS
- MEETINGS
- LINKS

Welcome to the MATHIAS project

The MATHIAS project is funded by the European Union in the 7th Framework Programme under the theme: HEALTH.2013.12-1 - Development of imaging technologies for therapeutic interventions in rare diseases.

The project started on 1st October 2013, the project duration is five years.

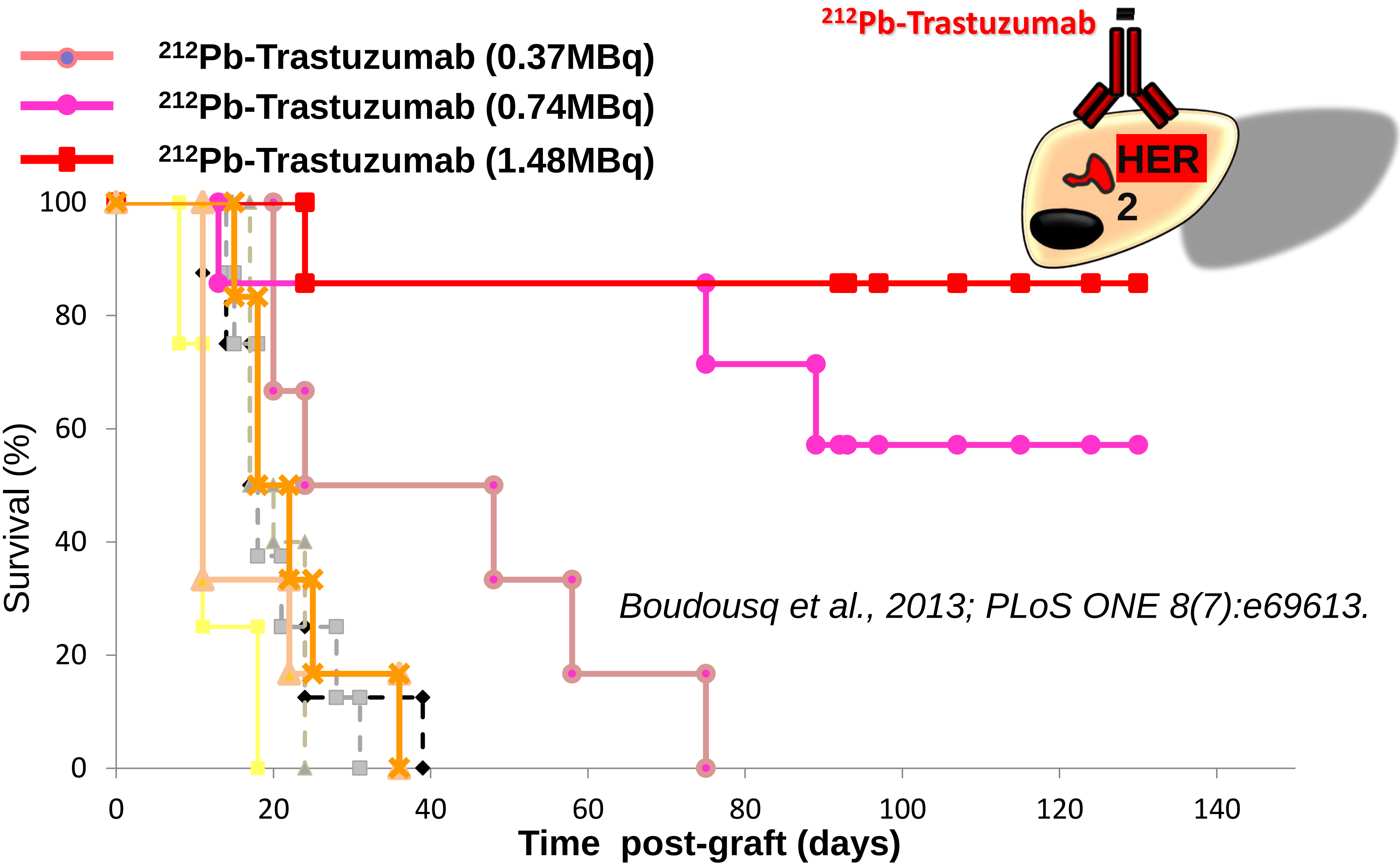
Scope of the project

The development of novel technologies to diagnose and clinically treat invasive Aspergillus fumigatus infections is the scope of this research consortium.

A. fumigatus is a ubiquitous mould whose spores are airborne and thus frequently inhaled. Humans with impaired immunity, e.g. those with haematological malignancies or bone marrow transplant recipients, are at a dramatically increased risk of severe, invasive A. fumigatus infection known as invasive aspergillosis (IA). IA is a rare disease in Europe but causes tremendous costs to the public health sector.

Currently definitive diagnosis of IA is only obtained at autopsy or relies on invasive biopsy, an extremely unpleasant procedure which is not always applicable in suffering patients. Thus, a convenient, fast and specific diagnosis of IA is not available forcing clinicians to administer antifungal drugs, if a standard antibiotic treatment failed to reduce fever in risk patients. It would be of high financial benefit for clinics and has the potential to increase the survival rates of immuno-compromised patients, if a definitive diagnosis of IA could be obtained early and its response to treatment be monitored. This would allow applying the correct therapy at a dose and duration exactly tailored to patient needs. Equally important is the development of new treatment

Survival with anti-HER2 ^{212}Pb-mABS



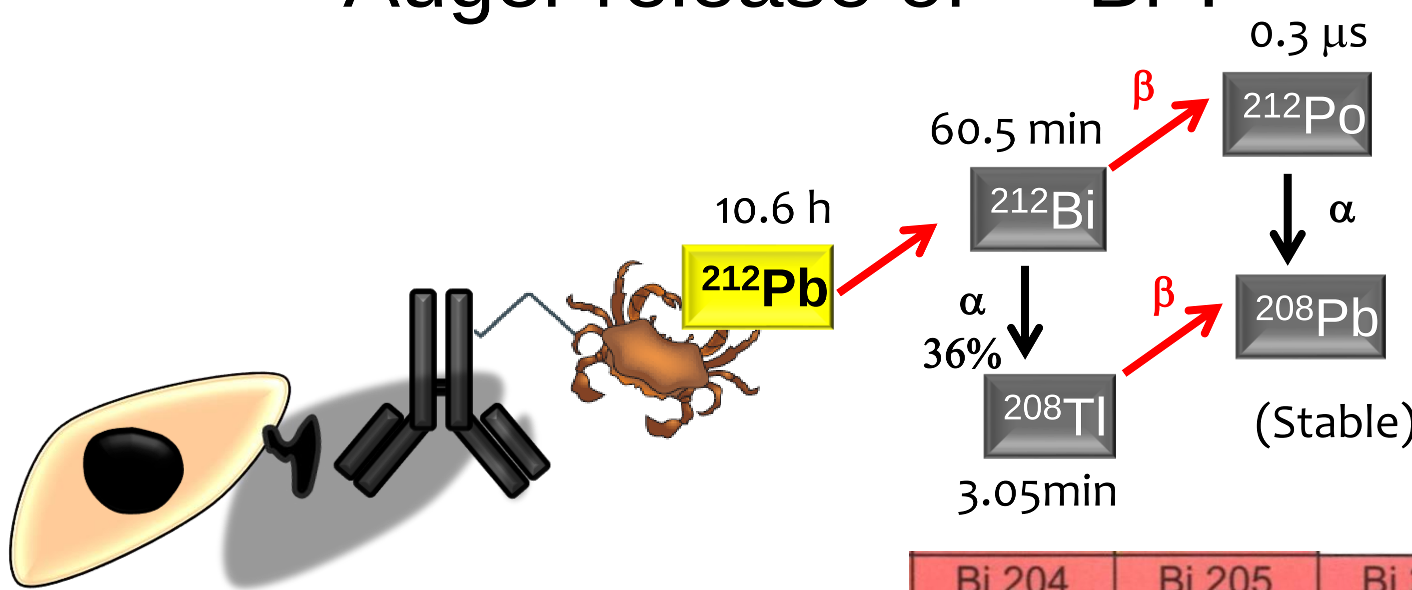
Boudousq et al., 2013; PLoS ONE 8(7):e69613.

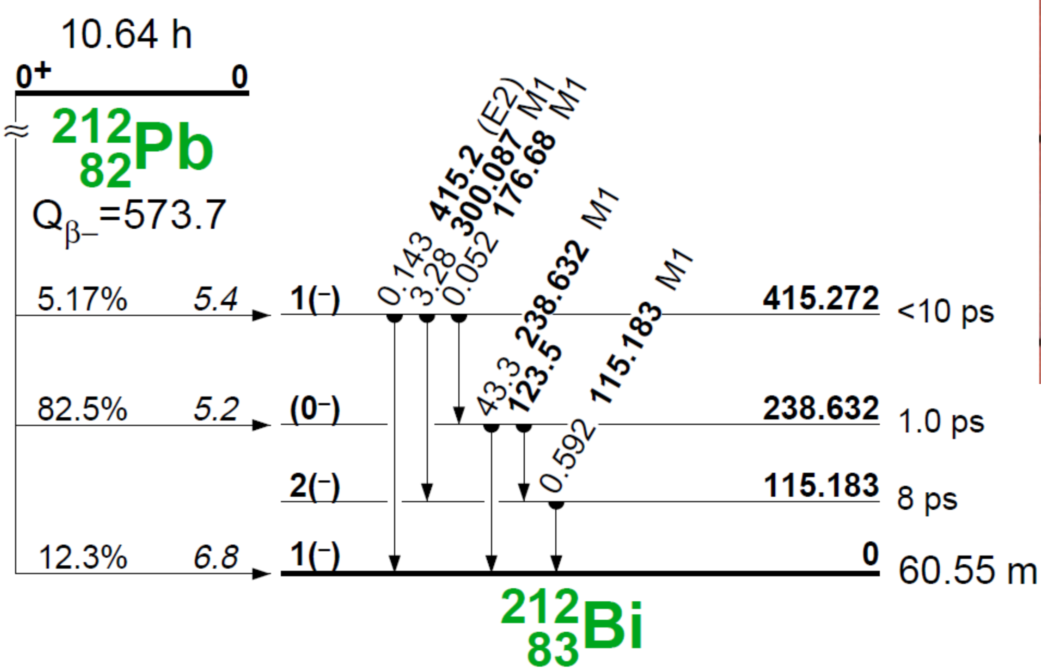
Inserm
Institut national de la santé et de la recherche médicale

Institut de Recherche en Cancérologie
I R C Montpellier

AREVA Med
^{212}Pb for Powerful Targeted Therapies

Auger release of ^{212}Bi ?



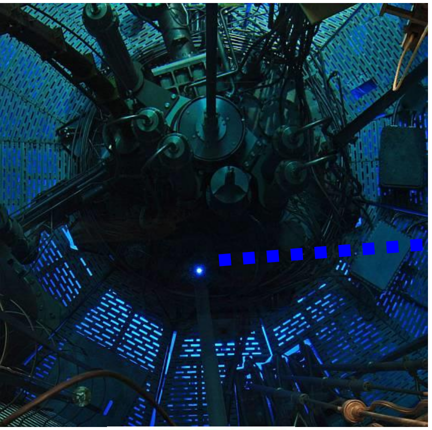


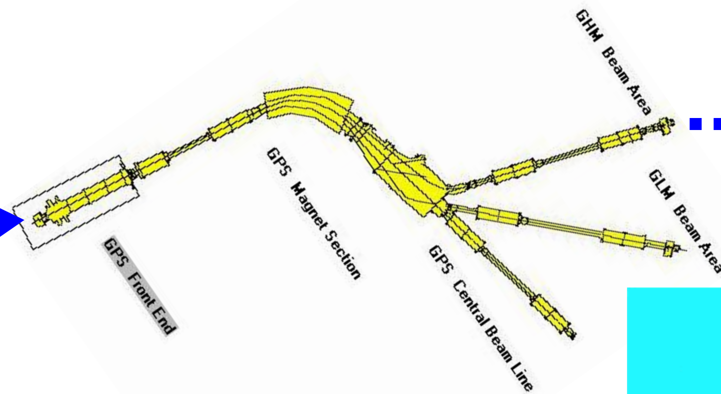
45.1% conversion electrons

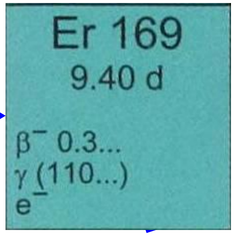
⇒ Auger cascades

⇒ partial delabeling?

^{169}Er (beta$^-$) vs. ^{165}Er (Auger) radiobiology

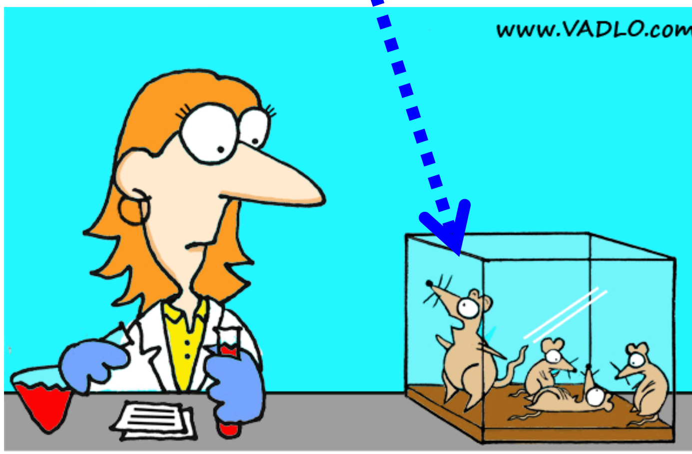




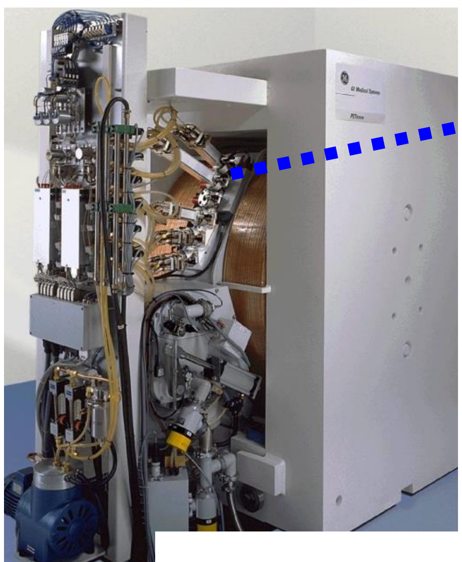


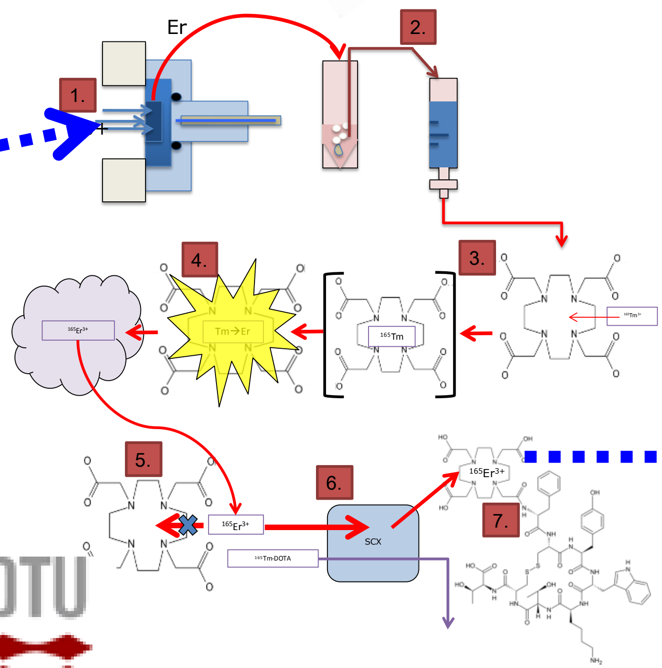
NEUTRONS FOR SCIENCE

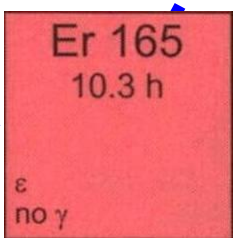
ISOLDE



"Hey, my pup is sick. Are you a real doctor or just PhD?"







Risø DTU

DTU

Beam request

		Shifts
A)	^{149}Tb-cm09 dose escalation study	8
B)	^{149}Tb-PRRT pilot study	3
C)	^{152}Tb/^{155}Tb companion diagnostics	incl.
D)	^{140}Nd/^{134}Ce chelator optimization	6
	^{140}Nd/^{134}Ce immuno-PET	6
E)	exploratory experiments (Pb, Bi,…)	3
F)	mass separation of ^{169}Er/^{168}Er	6 (offline)
Total		26 + 6
Available		-10
New request		**16 + 6** (offline)

Off-line separation of ^{169}Er

- Therapy study with 6 mice, 70 MBq ^{169}Er-DOTATOC per mouse
- factor 2 for decay losses and labeling yield
- 850 MBq needed (1E15 atoms collected)
- LA[^{169}Er]=5 MBq $\Rightarrow$ up to 500 MBq can be handled in “class C” bat. 170

  $\Rightarrow$ collect and ship two separate samples of 425 MBq each

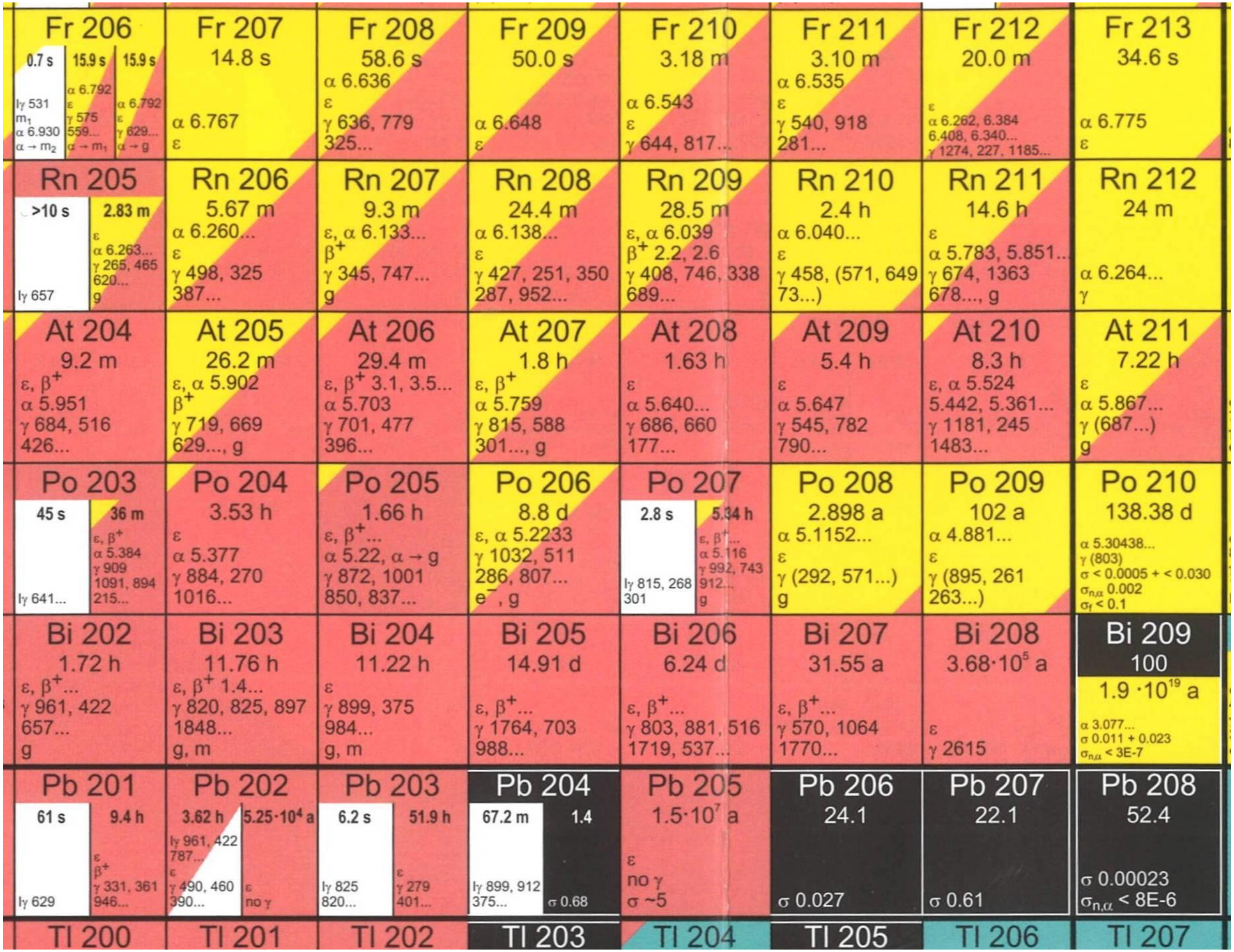
  $\Rightarrow$ ship as UN2910 (“excepted package”)
- implantation current ~1 nA of ^{169}Er for 24 h (3 shifts per sample)
- total current ~1 μA Er (^{168}Er + ^{169}Er) [cf. ^{7}Be collections]

- ionization potential 6.11 eV > ~0.5% thermal ionization efficiency
- RILIS efficiency >5%? (to be tested!)
- ship ~20 GBq from ILL (2% of A2 limit > “type A” transport)

- Note: ^{169}Er is a low-energy beta emitter, with very low emission of γ rays:
  0.16% 8 keV, 0.01% 110 keV

  $\Rightarrow$ very low dose rate: <1 μGy/h at 1 m from unshielded 1 GBq sample.

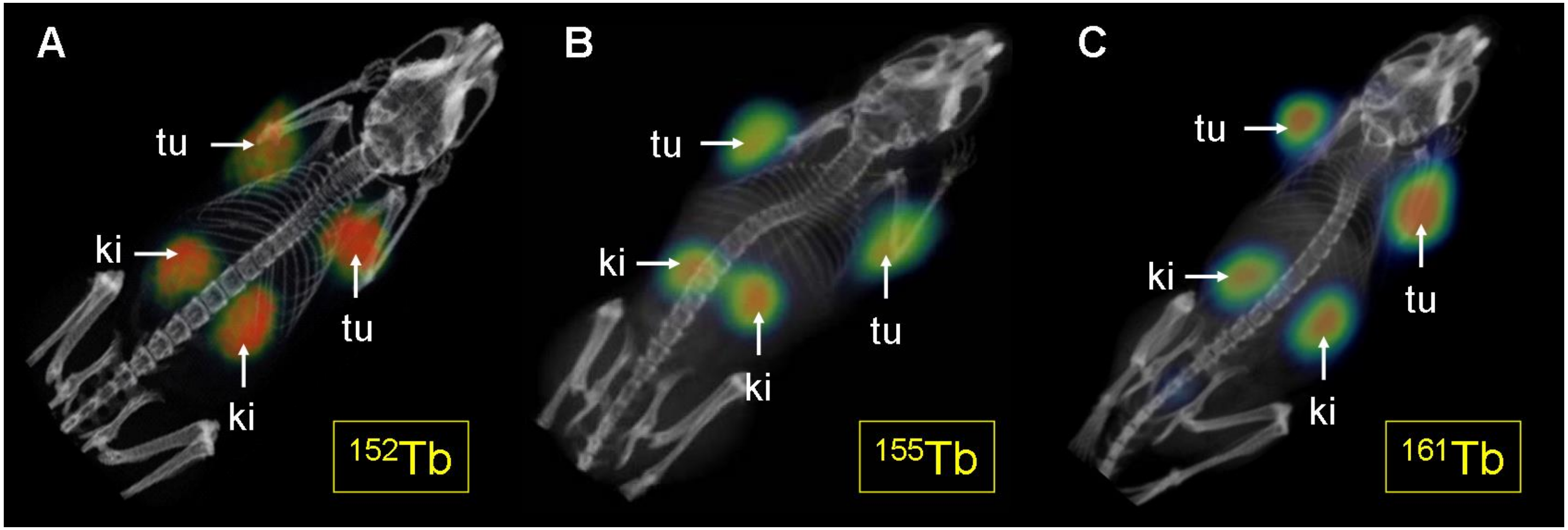
Indirect production of ^{203}Pb, ^{205}Bi



Imaging Studies Using PET and SPECT

KB Tumor-Bearing Nude Mice

PET *SPECT* *SPECT*



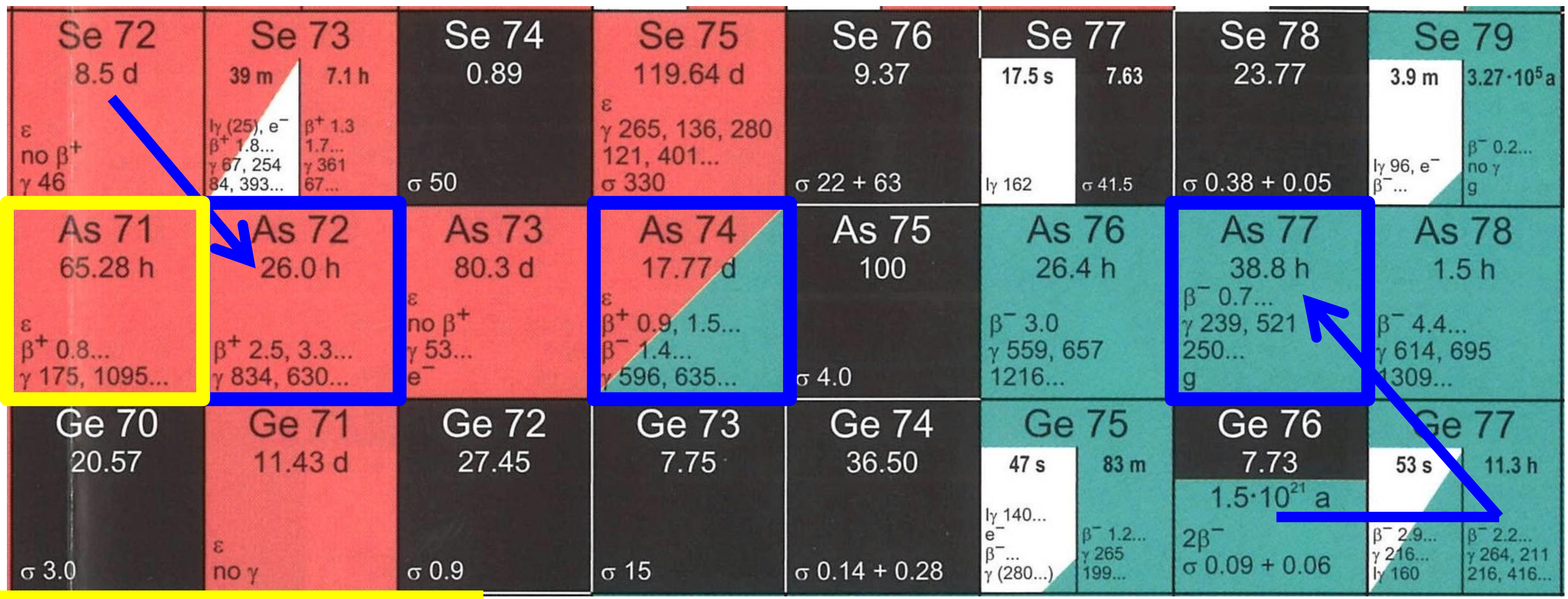
^{152}Tb-folate: 9 MBq
Scan Start: 24 h p.i.
Scan Time: 4 h

^{155}Tb-folate: 4 MBq
Scan Start: 24 h p.i.
Scan Time: 1 h

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

Müller et al. **2012**, J Nucl Med 53:1951.

Arsenic: another theranostic multiplet



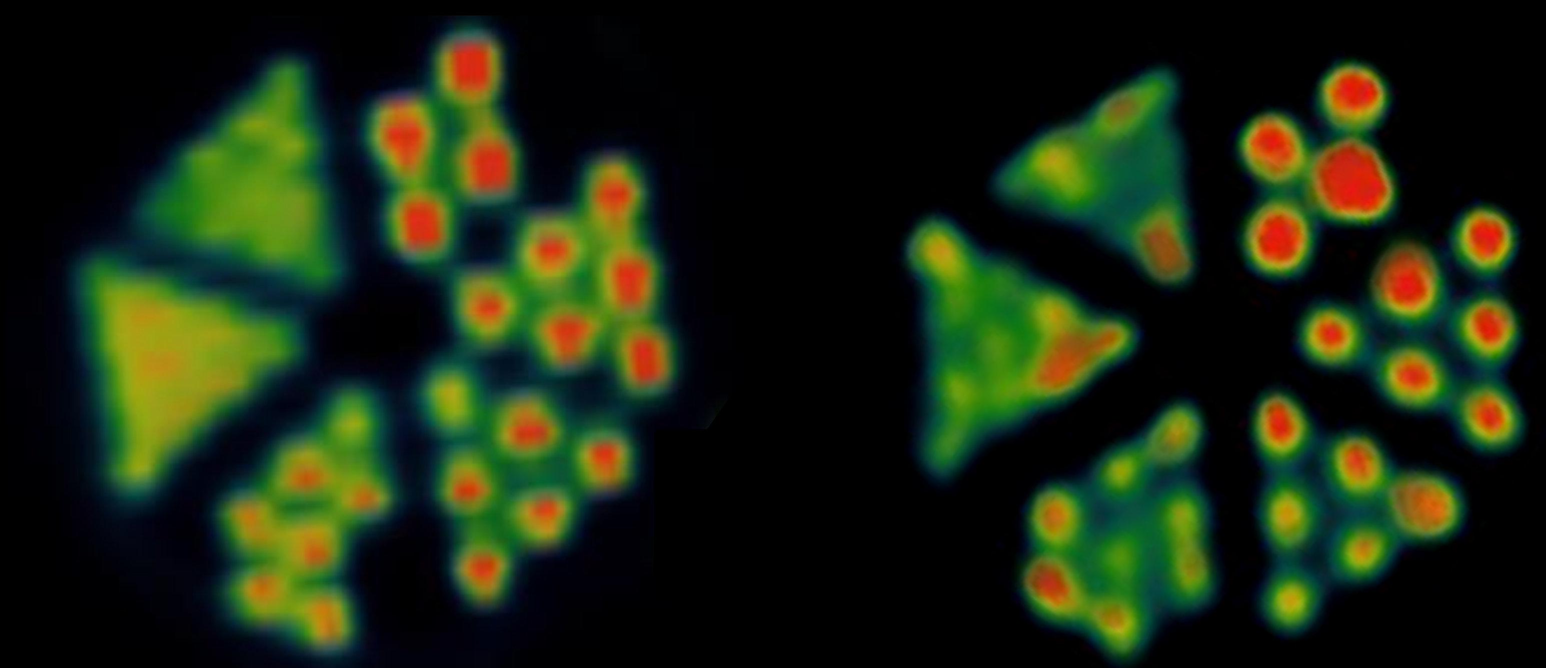
^{71}As:
low-energy β^+ emitter for high-resolution PET ?

^{74}As:
long-lived β^+ emitter for longitudinal PET studies

^{77}As:
reactor-produced β^- emitter for therapy

^{72}As:
generator-produced β^+ emitter for PET

Excellent resolution with Derenzo phantom



^{18}F $E_{\beta^+} = 0.25$ MeV

^{71}As $E_{\beta^+} = 0.35$ MeV

Köster et al. **2014**, Nucl Med Biol, submitted.