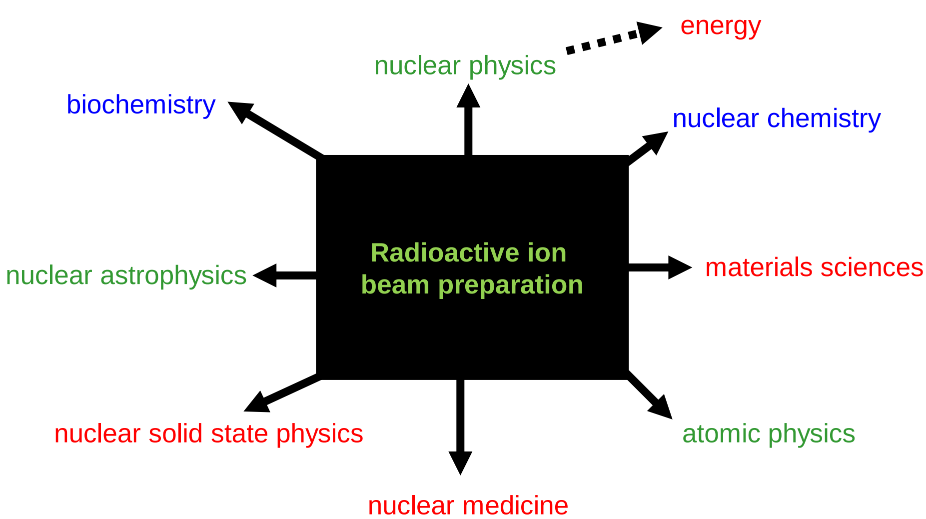
Applications of physics of unstable nuclei to energy, medicine, material science

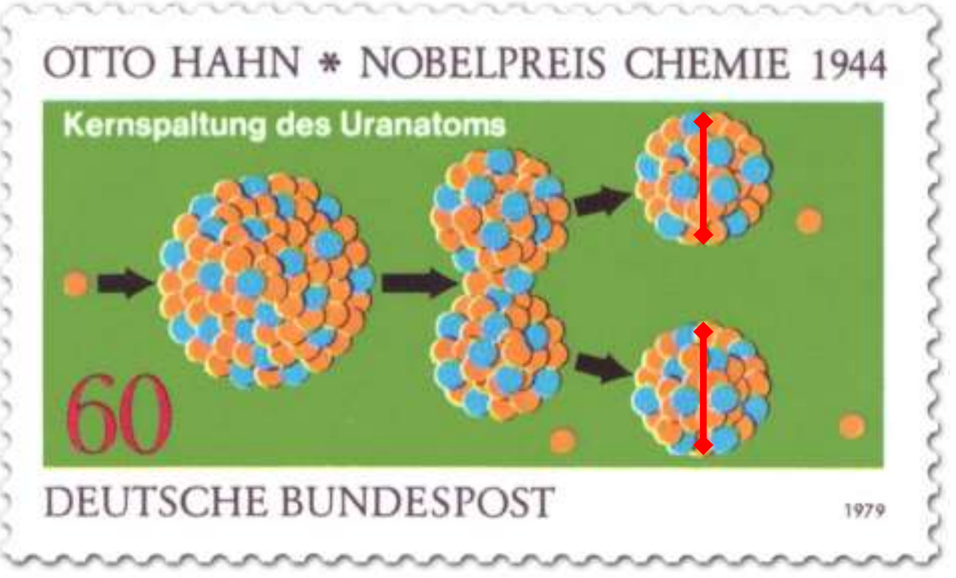
Ulli Köster

Institut Laue-Langevin

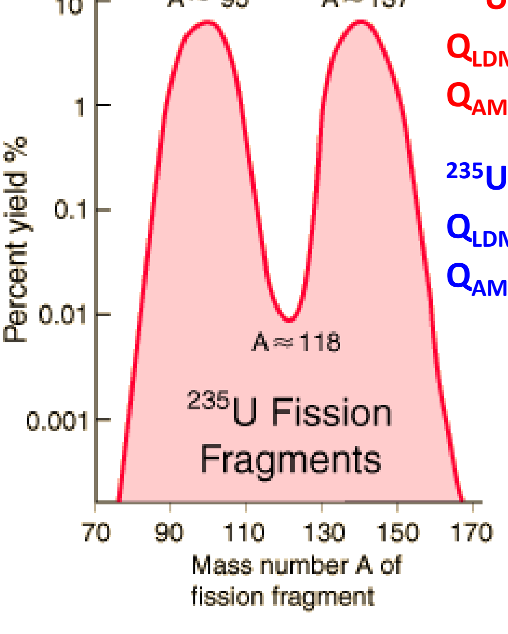
Grenoble, France

Applications





Mass yields of fission fragments



$^{235}U + n \rightarrow {}^{118}Pd + {}^{118}Pd$

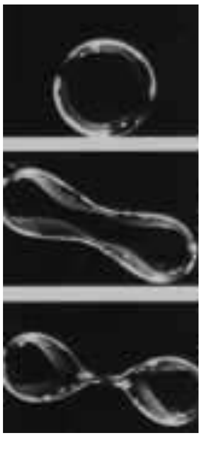
Q_{LDM} = +184 MeV

Q_{AME} = +200 MeV

$^{235}U + n \rightarrow {}^{138}Xe + {}^{98}Sr$

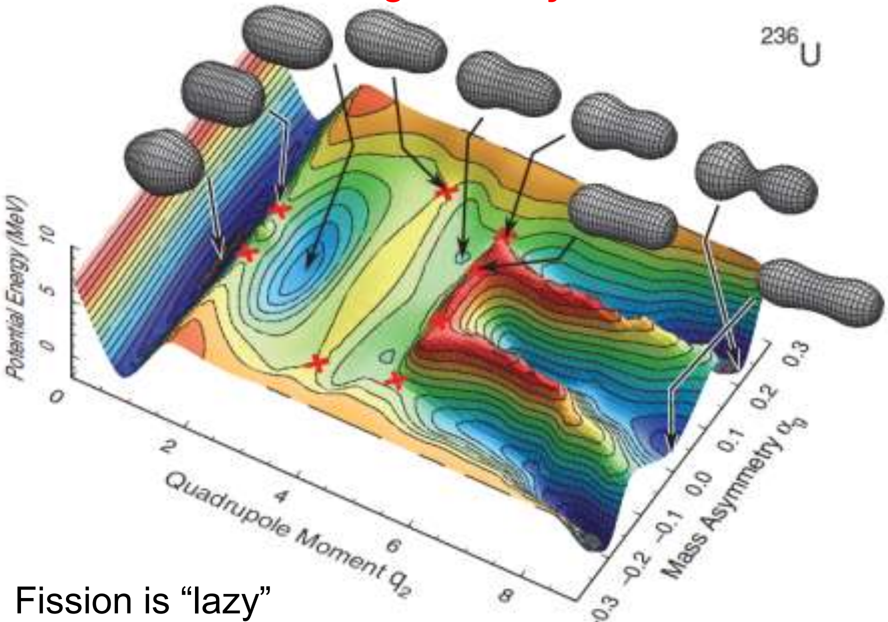
Q_{LDM} = +176 MeV

Q_{AME} = +196 MeV



T.G. Wang et al.
J Fluid Mech
354, 43 (1994)
STS-50 flight

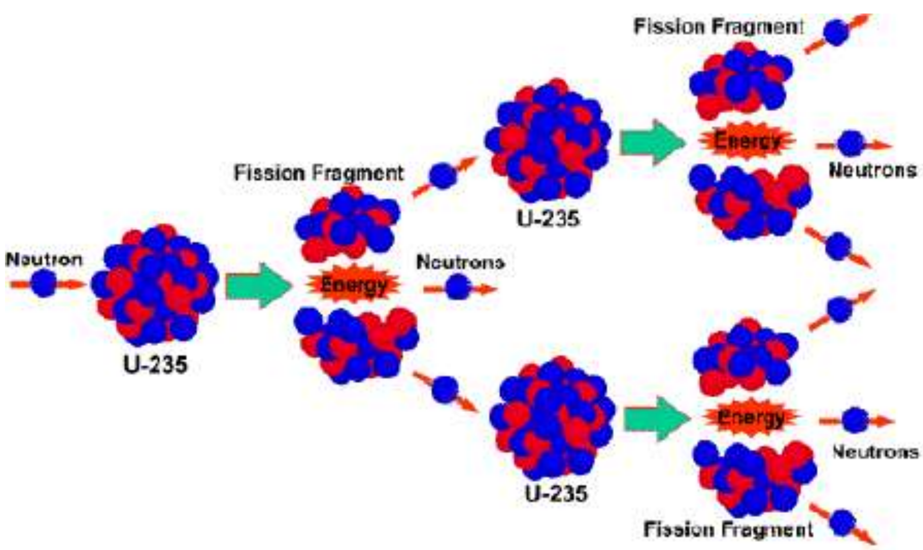
Understanding fission yields of ^{236}U



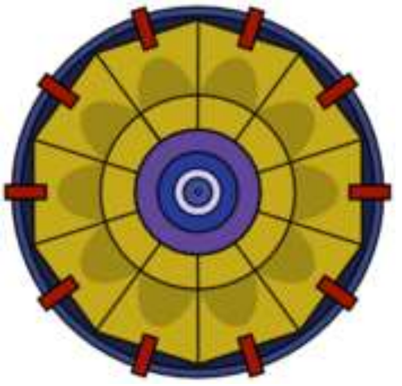
Fission is “lazy”

T. Ichikawa et al. PRC 86, 024610 (2012)

A nuclear chain reaction

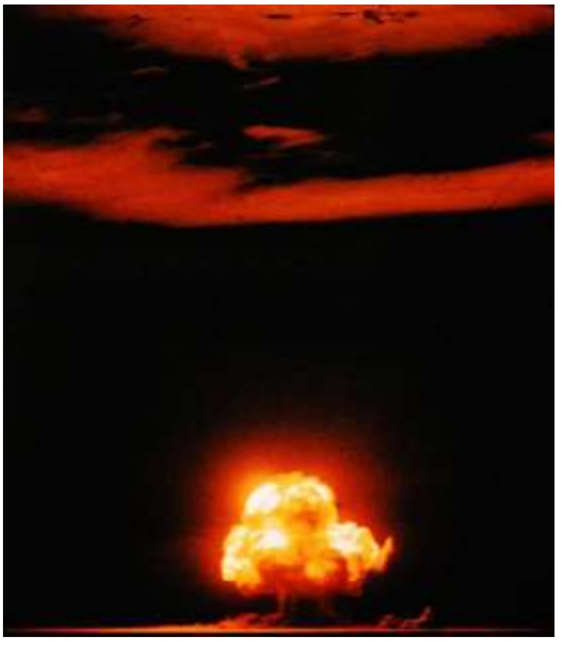


A single-pulse neutron source

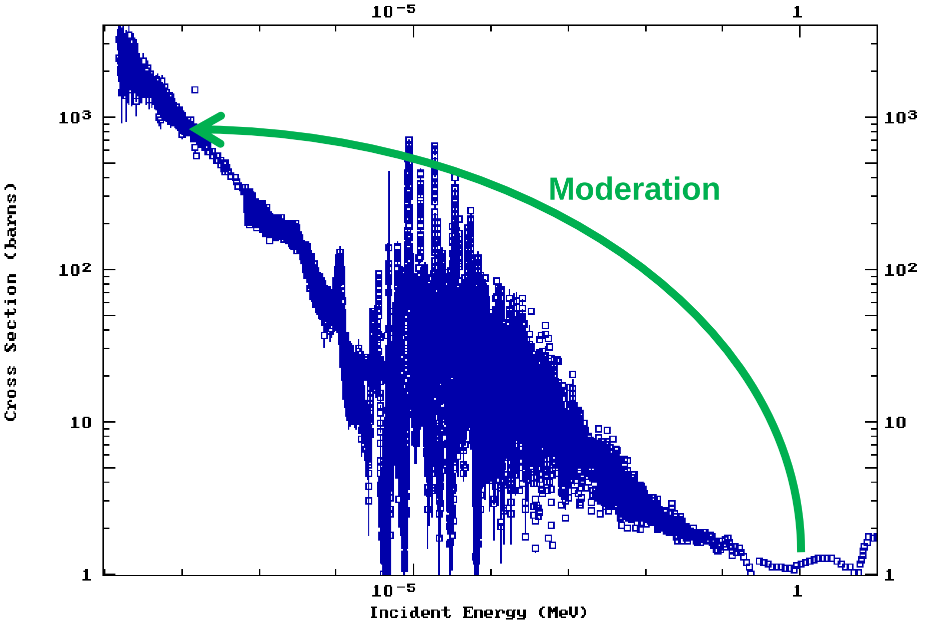


Uncontrolled chain reaction of fast-neutron induced fission

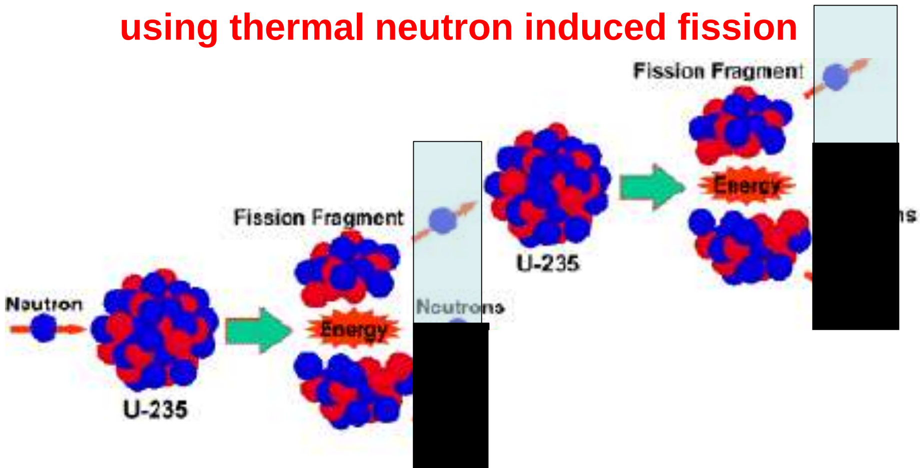
≈25 kg of 93% ^{235}U



^{235}U(n,f) cross-section as function of energy



A controlled nuclear chain reaction using thermal neutron induced fission



1. Moderate neutrons
2. Control neutron losses

k = multiplication factor = (neutrons produced in one generation) / (neutrons produced in previous generation)

Prompt neutron kinetics

Prompt neutron lifetime τ_p is the average time between the birth of prompt fission neutrons and their final absorption.

<u>Assumptions</u>:
-No delayed neutrons
-Infinite reactor, multiplication factor $k_\infty = k$

time	N(t)
0	n
τ_p	kn
$2\tau_p$	k^2n
$3\tau_p$	k^3n

$$\frac{dn}{dt} = \frac{k-1}{\tau_p} n \Rightarrow n(t) = n(0) e^{\frac{(k-1)}{\tau_p} t}$$

Time constant $T = \frac{\tau_p}{k-1}$

Exponential decrease (k<1) or exponential growth (k>1)

cf. demographic projections for Germany
Fertility: 1.5 child/women -> k=0.75
T=25 years / (1-0.75) =100 years

Prompt neutron kinetics

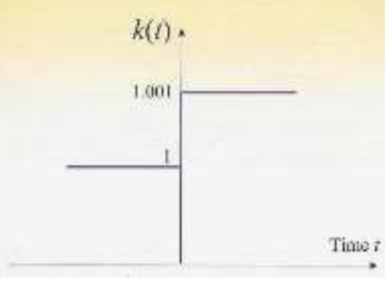
$\tau_p = \tau_s + \tau_d$ = slowing down time + diffusion time

In thermal reactors: $\tau_s << \tau_d$, i.e. $\tau_p \cong \tau_d$

$\tau_d \cong \lambda_a/v \cong 10$ cm / (2000m/s)

$\tau_p \cong \tau_d \cong 50$ μsec

Example: step of reactivity from k=1.000 to k=1.001



$$T = \frac{\tau_p}{k-1} = \frac{50.10^{-6}}{10^{-3}} = 0.05\text{sec}$$

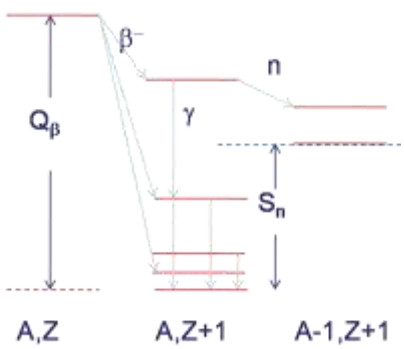
$$n(t) = n_0 e^{\frac{t}{0.05}}$$

$$\frac{n(1\text{sec})}{n_0} = e^{20} = 5E8$$

"Prompt" control is not possible!

Chernobyl: a criticality accident

Delayed neutron emission from fission products



Possible precursors
^{87}Br
^{88}Br, ^{137}I, ^{136}Te, ^{134}Sb, ^{141}Cs
^{89}Br, ^{138}I, $^{92,93}Rb$, ^{147}La, ^{87}Se, ^{84}As
^{85}As, ^{90}Br, ^{135}Sb, ^{94}Rb, ^{139}I, $^{98,99}Y$, ^{142}Cs, ^{80}Ga
$^{86,87}As$, ^{136}Sb, $^{147,148}Ba$, $^{81,82}Ga$, $^{140,141}I$, ^{91}Br, ^{134}Sn, ^{145}Cs, ^{89}Se
^{83}Ga, $^{146,147}Cs$, $^{95,96,97,98,99}Rb$, ^{92}Br, ^{91}Se

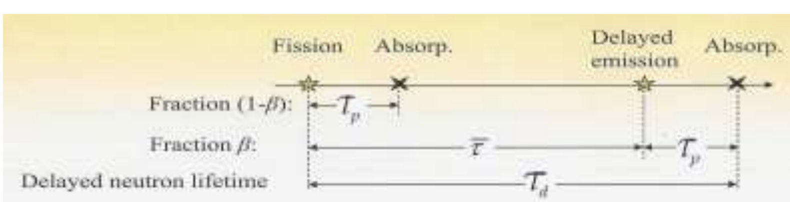
β= percentage of delayed neutrons

^{235}U	β	ν	ν_p	ν_d
Ther	0.0067	2.490	2.473	0.01668

average emission time

$$\tau_{delayed} = \frac{1}{\beta}\sum_i \beta_i \tau_i \approx 12\,\mathrm{sec}$$

Neutron lifetime, taking into account delayed neutrons



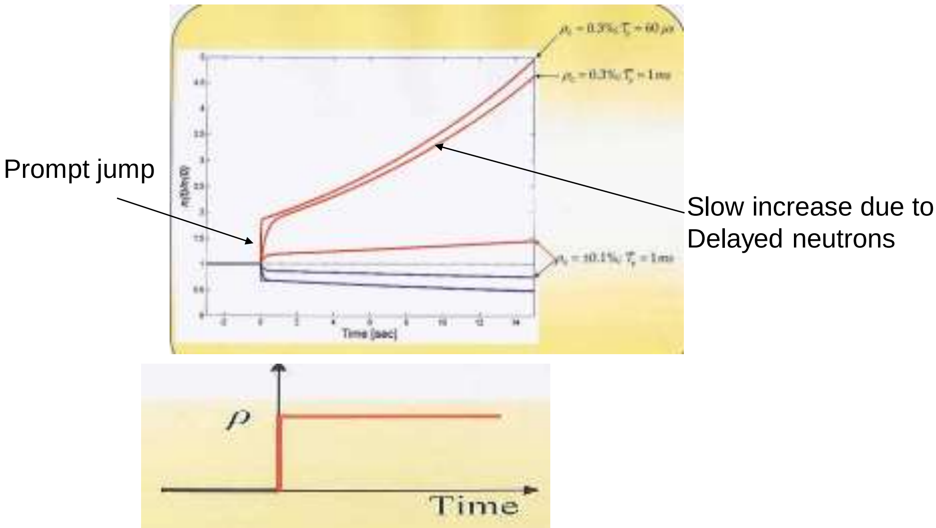
$$k = k_{prompt} + k_{delayed} = 1 = (1-\beta) + \beta$$

$$\tau = (1-\beta)\tau_p + \beta(\tau_{delayed} + \tau_p) \approx \beta\tau_{delayed} = 0.08\,\mathrm{sec}$$

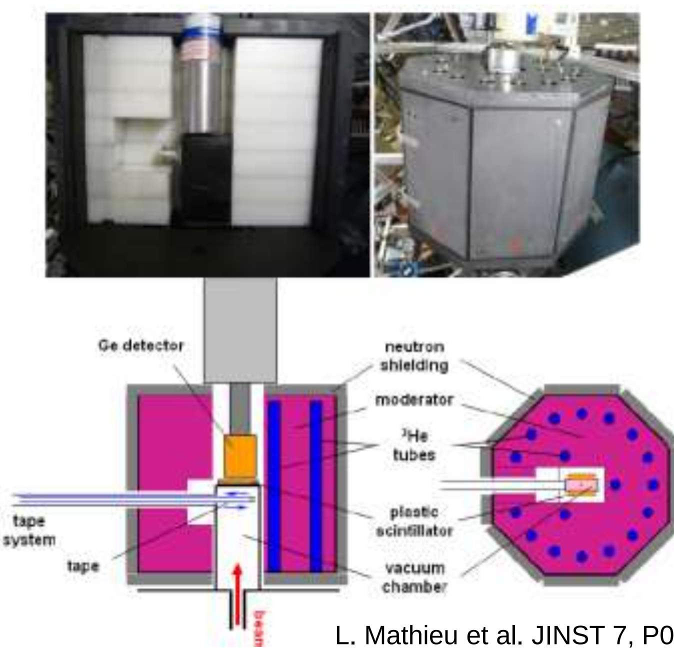
Now for step from k=1.000 to k=1.001

$T = \beta\tau_{delayed}/(k-1) = 80$ seconds

Reactor response to a step of reactivity

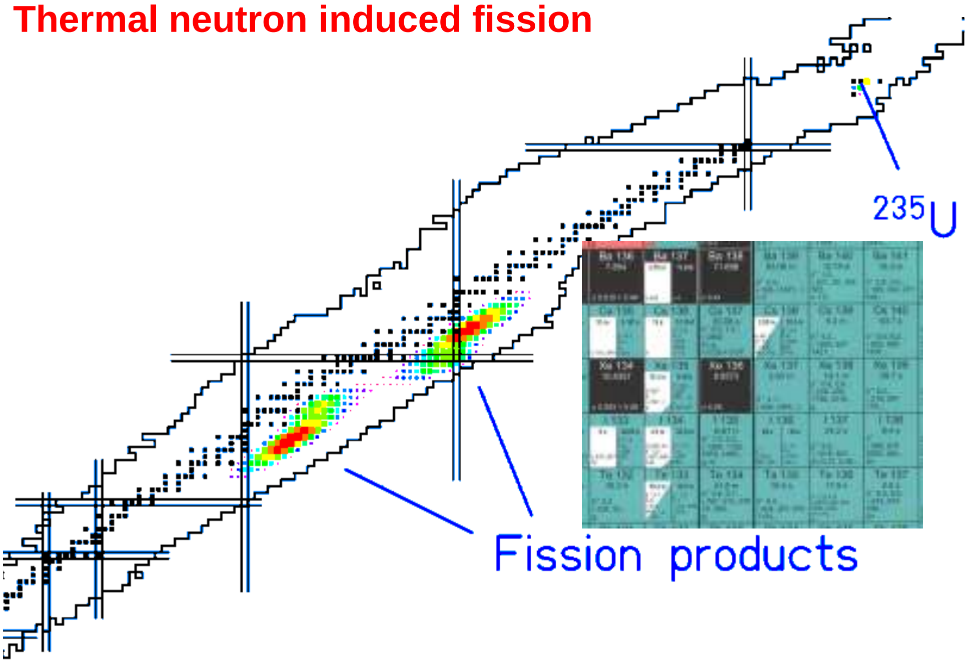


Study of delayed neutron emitters



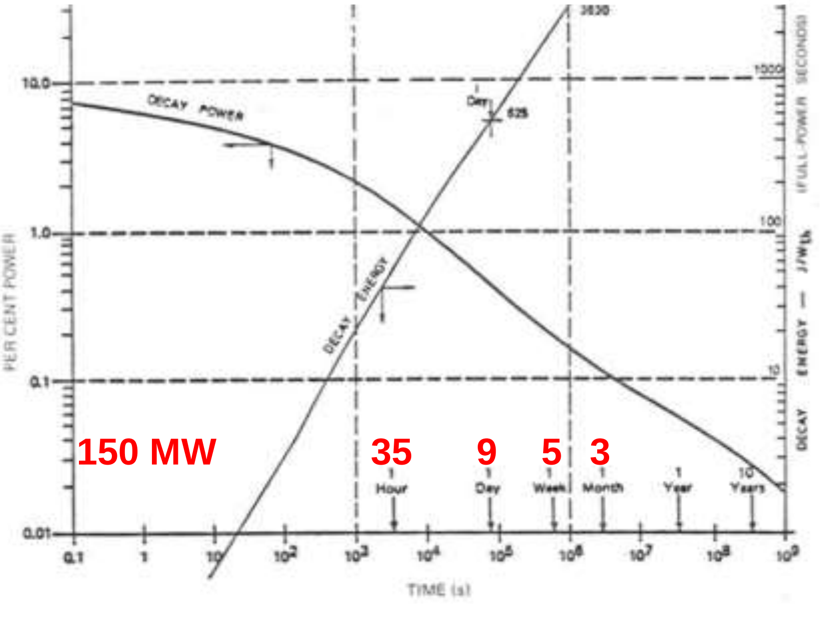
L. Mathieu et al. JINST 7, P08029 (2012).

Thermal neutron induced fission



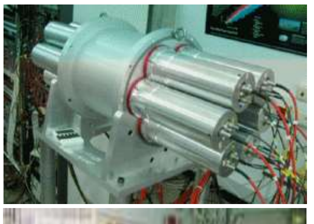
Nuclear decay heat

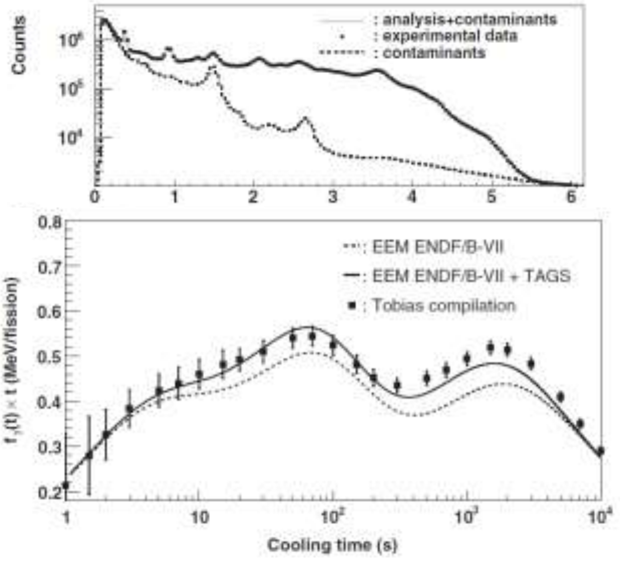
Fukushima 2 and 3: 784 MWe, 2300 MWth



Fukushima: a loss-of-coolant accident

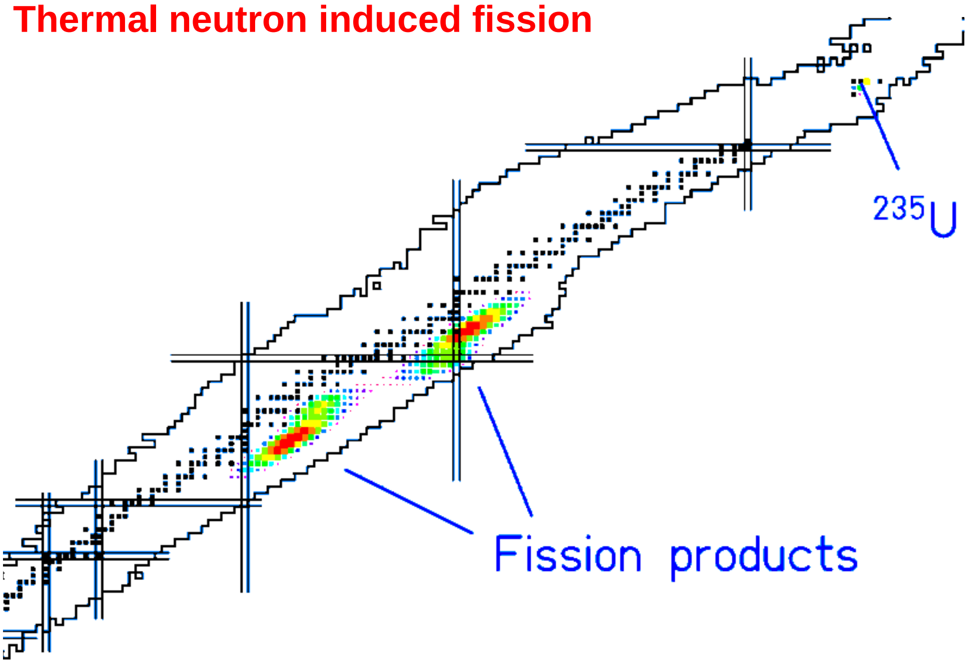
TAGS measurements to understand decay heat





A. Algora et al. PRL 105, 202501 (2010).

Thermal neutron induced fission



Thomson 1910: parabola mass spectrograph

Electric field parallel to magnetic field

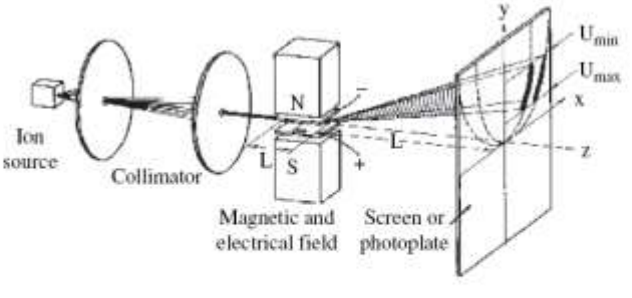


Figure 1.5 Parabola mass spectrograph constructed by J. J. Thomson (1910) with a discharge tube as ion source, a superimposed electrical field and a magnetic field oriented parallel to it for ion separation, and a photoplate for ion detection. (H. Kienitz (ed.), Massenspektrometrie (1968), Verlag Chemie, Weinheim. Reproduced by permission of Wiley-VCH.)

1912: Neon consists of two isotopes with mass 20 and 22

The LOHENGRIN fission fragment separator

mass-separated fission fragments,

up to 10^5 per second, $T_{1/2} \geq$ microsec.

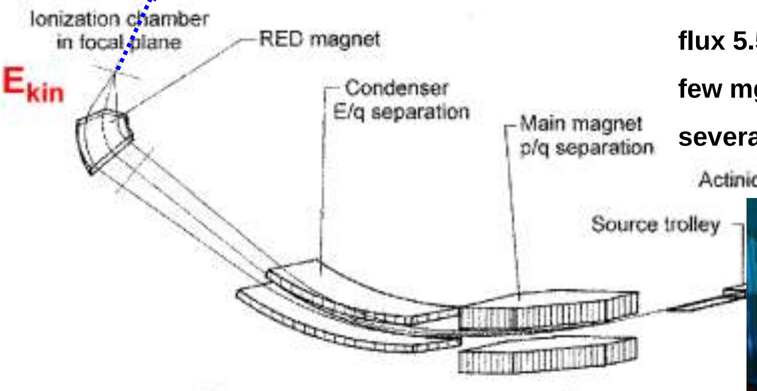
$\Delta A/A$ = 3E-4 – 3E-3

$\Delta E/E$ = 1E-3 – 1E-2

flux $5.5 \cdot 10^{14}$ n./cm^2/s

few mg fission target

several 10^{12} fissions/s



$$m v^2 / r_{el} = q E \qquad m v^2 / r_{magn} = q v B$$

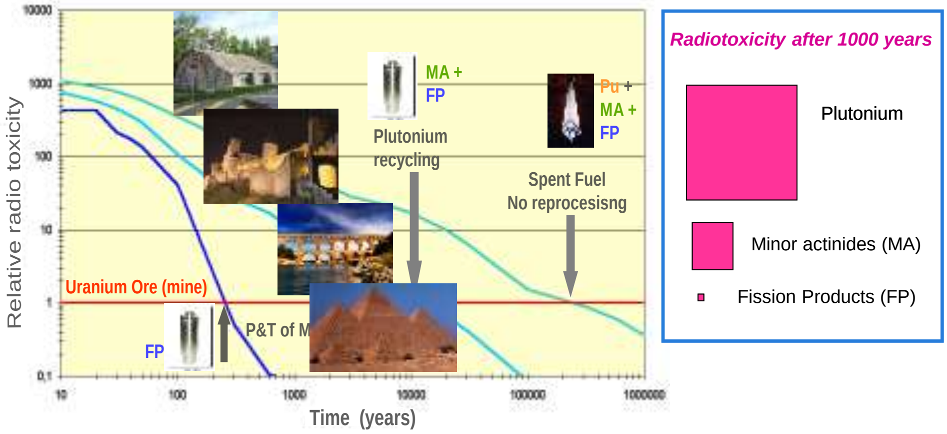
$$E_{kin} / q = E / 2 r_{el} \qquad m v / q = B r_{magn}$$

P. Armbruster et al., Nucl. Instr. Meth. 139 (1976) 213.

The LOHENGRIN fission fragment spectrometer

Nuclear waste transmutation

Not fission is responsible for the nuclear waste problem, but neutron capture (producing Pu + MA) !



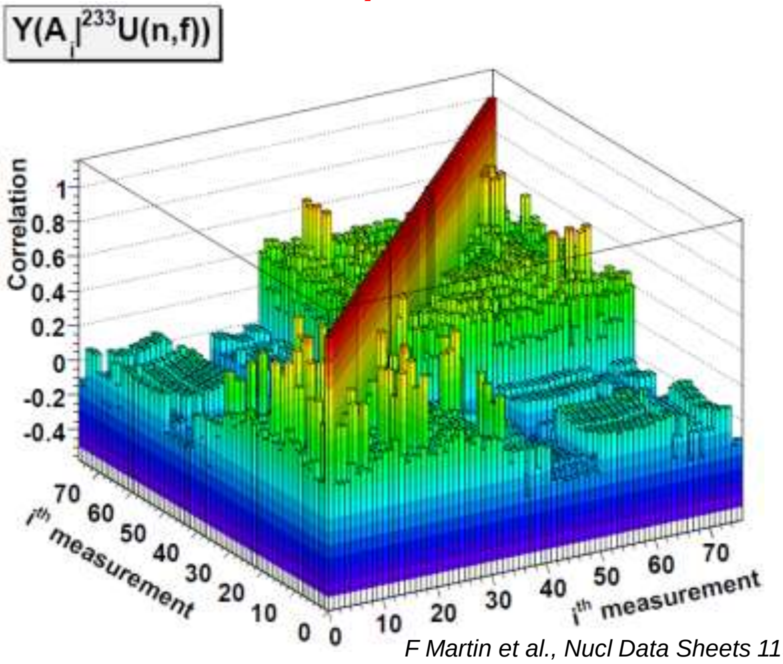
Pu has a high energetic potential.

Nuclear data for "energy"

- **Fission cross-sections**
- **Absorption cross-sections**
- **Scattering cross-sections**
- **Fission yields**
- **Beta-delayed neutron emitters**
- **Neutron poisons**
- **Prompt gamma ray emission**
- **Delayed gamma ray emission**
- **Beta spectra**
- **etc.**

Nuclear data for applications require moderately exotic beams and medium precision (~1%) but excellent accuracy and reliability.

Fission yield measurements



F Martin et al., Nucl Data Sheets 119, 328 (2014).

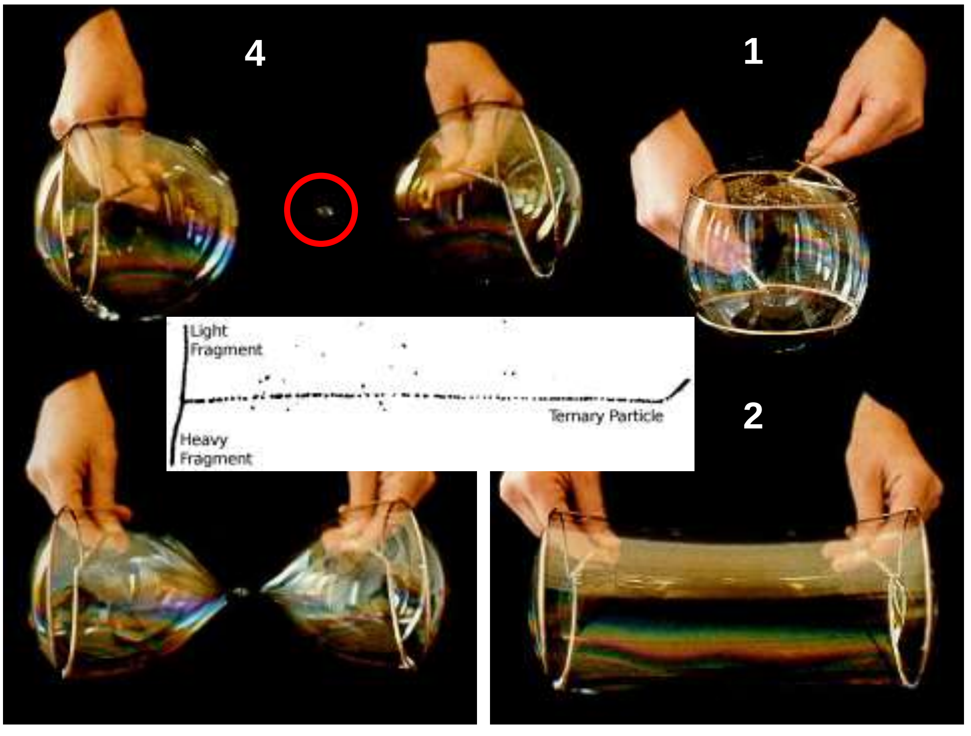
The importance of error correlations

^{11}Li production in thermal neutron induced fission?

$$^{235}U + n \Rightarrow {}^{11}Li + {}^{225}Ac$$

A	235	+	1	=	11	+	225
Z	92	+	0	=	3	+	89
ΔM (MeV)	40.919		8.071		40.728		21.639

Q (MeV) = (40.919 + 8.071) – (40.728 + 21.639) = -13.4

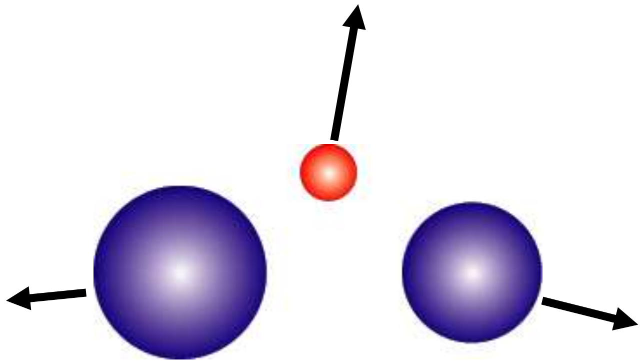


^{11}Li production in thermal neutron induced fission?

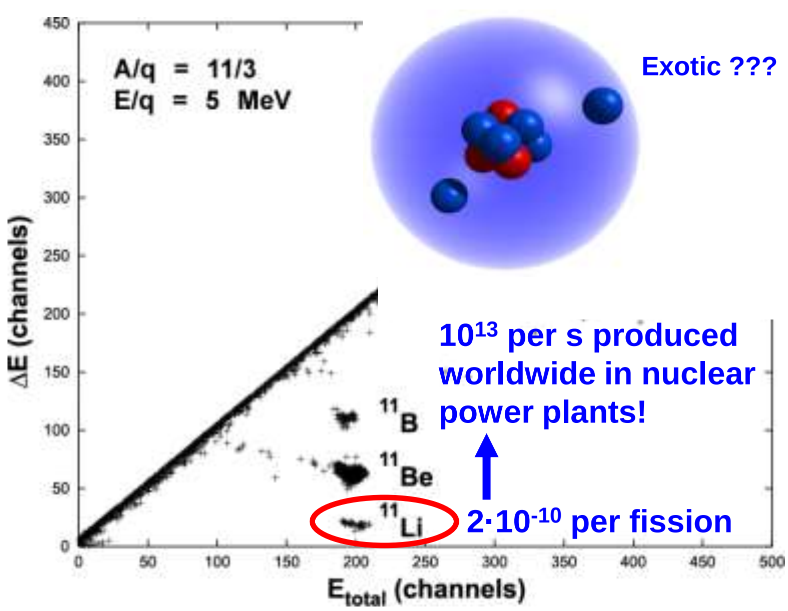
$$^{235}\mathrm{U} + \mathrm{n} \Rightarrow {}^{11}\mathrm{Li} + {}^{134}\mathrm{Te} + {}^{91}\mathrm{Rb}$$

A	235	+	1	=	11	+	134	+	91
Z	92	+	0	=	3	+	52	+	37
ΔM (MeV)	40.919		8.071		40.728		-82.536		-77.745

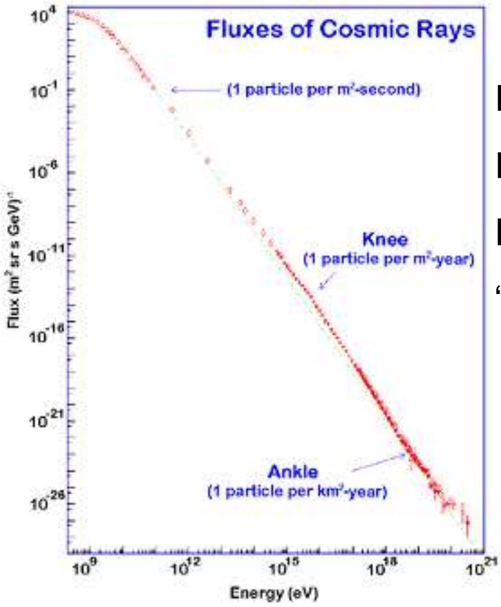
Q (MeV) = (40.919 + 8.071) – (40.728 – 82.536 – 77.745) = **+168.5**



Detection of rare ternary particles



Particle accelerators in the Universe



Flux 10^{4} protons m^{-2}s^{-1}

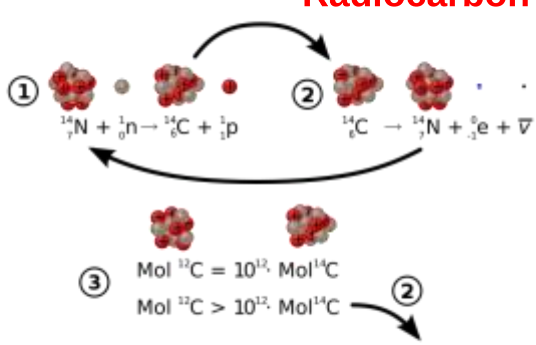
Energy ~GeV = 1.6·10^{-13} J

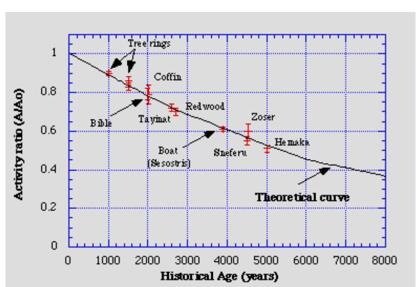
Earth's surface 10^{25} m^{2}

"Beam" power ~10^{15} W

(=1 PW)

Radiocarbon dating





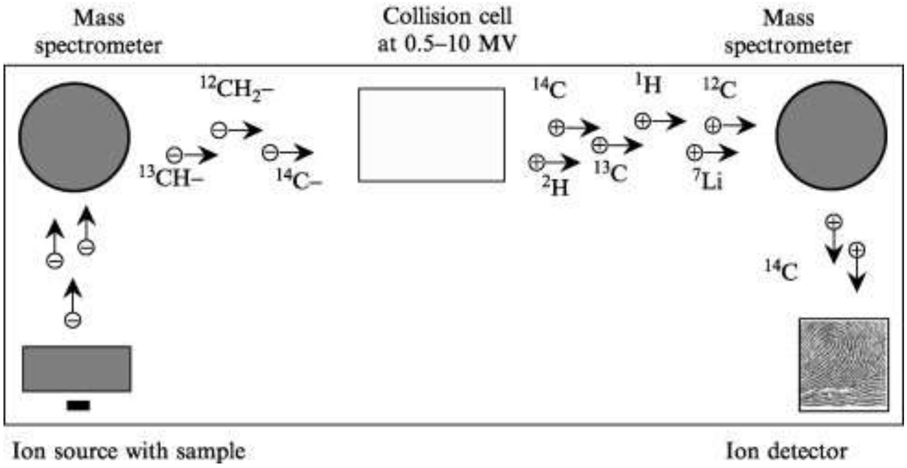
- **Cosmic radiation > spallation neutrons > ^{14}N(n,p)^{14}C reactions**
- **Living organisms: equilibrium with atmospheric ^{14}C/^{12}C ratio**
- **After death: ^{14}C/^{12}C decreases due to ^{14}C decay ($T_{1/2}$=5370 y)**

Problem: measure $^{14}C^{+}$ at ppt level without interference from

$^{14}N^{+}$, $^{12}CH_2^{+}$, $^{13}CH^{+}$, $^{28}Si^{++}$, $^{12}C^{16}O^{++}$, $^{42}Ca^{+++}$, $^{56}Fe^{++++}$,…

Multistep-Separation in Accelerator Mass Spectrometry

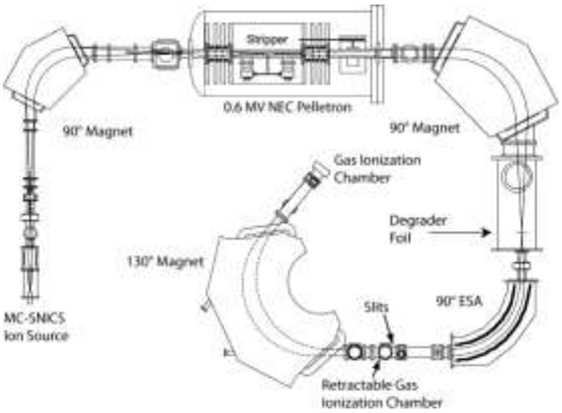
1. **Negative ion formation** — **$^{14}N^-$ anions do not exist**
2. **Acceleration and stripping** — **breakup of molecules**
3. **Z-selective ion detector** — $\frac{dE}{dx} \sim \frac{Z^2}{E}$



6 MV tandem: the “working horse” for AMS

ETH Zürich, Laboratory for Ion Beam Physics

0.6 MV TANDY: the “working pony” for AMS



Routine measurements of: ^{10}Be, ^{41}Ca, ^{129}I, ^{236}U, Pu, etc.
longer-lived than ^{14}C: geology, cosmochronology,…

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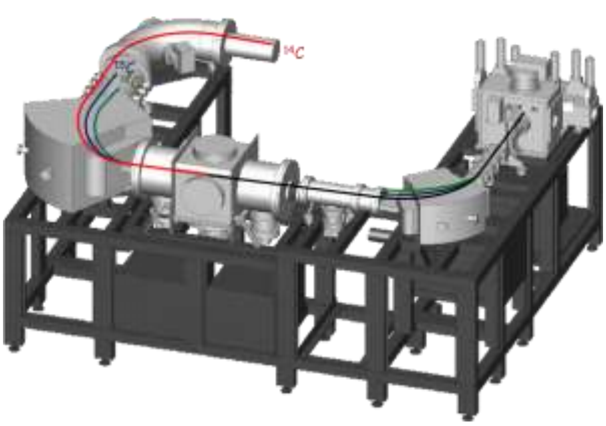
MICADAS (Mini-radioCArbon-DAting-System): 0.2 MV AMS



2.3 x 3 m^2 “tabletop”

Routine measurements of: ^{14}C

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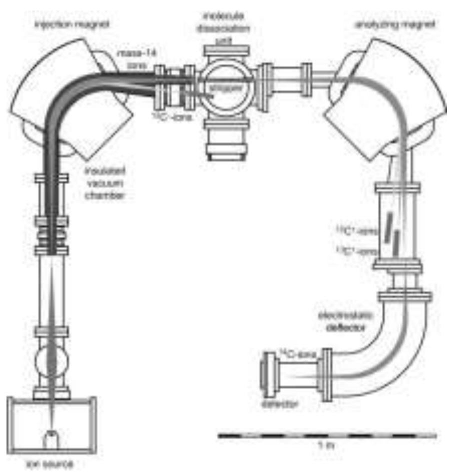
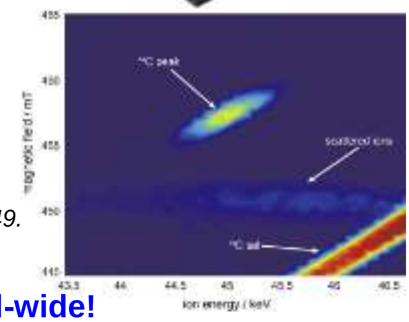
MUCADAS (MICRO-radioCArbon-DAting-System): 45 kV AMS



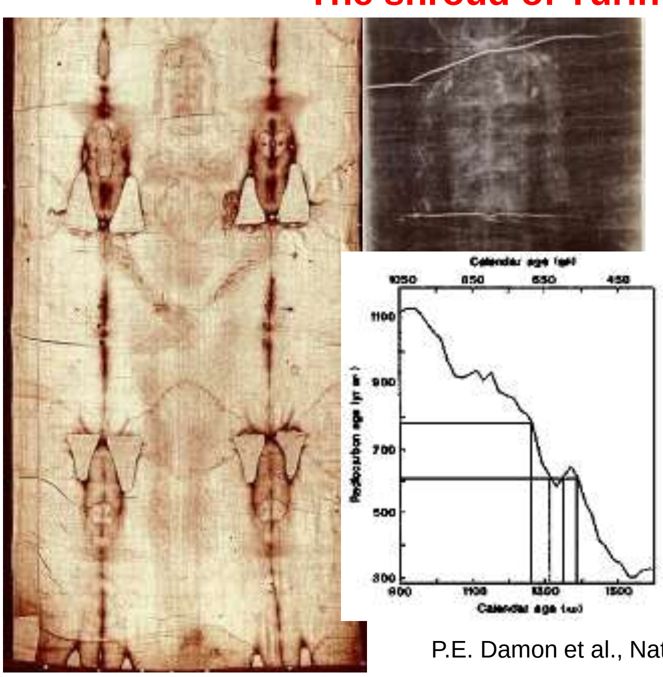


H.A. Synal et al., Nucl. Instr. Meth. B294 (2013) 349.

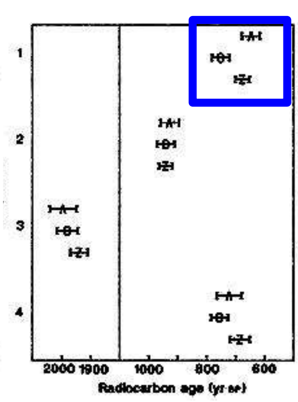
Today over 100 AMS facilities world-wide!

ETH Zürich, Laboratory for Ion Beam Physics

The shroud of Turin AD 1260-1390



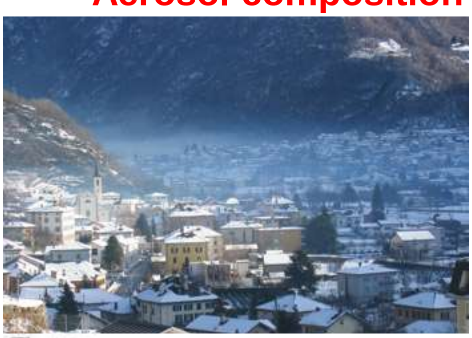
AMS measurements at Arizona, Oxford and Zurich.

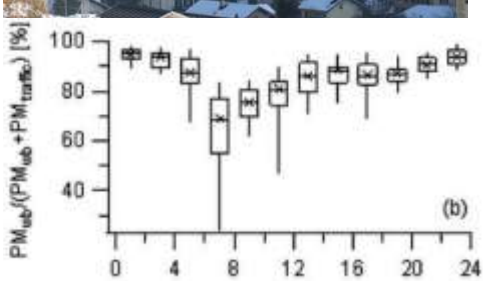


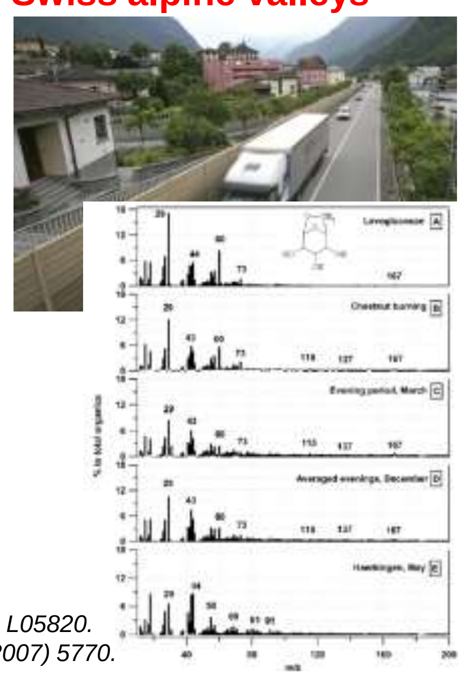
P.E. Damon et al., Nature 337 (1989) 611.

Winter smog

Aerosol composition in Swiss alpine valleys

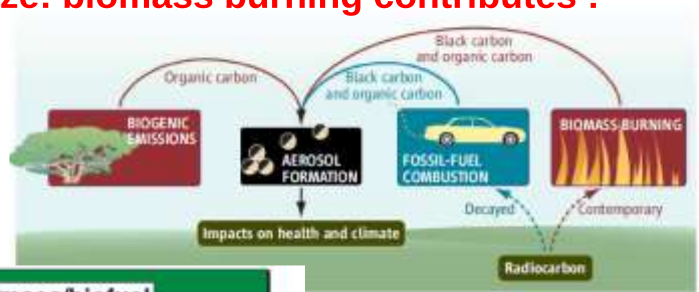


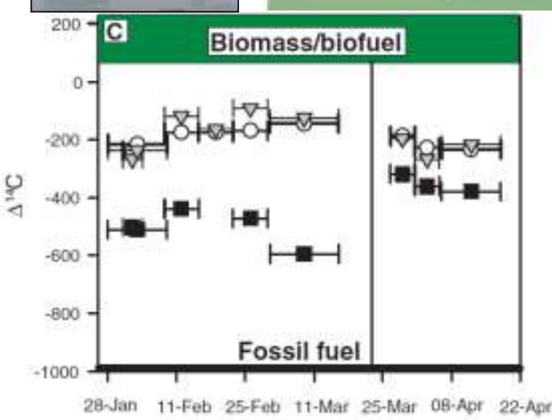




S. Szidat et al., Geophys. Res. Lett. 34 (2007) L05820.
M.R. Alfarra et al., Environ. Sci. Technol. 41 (2007) 5770.

Asian haze: biomass burning contributes !



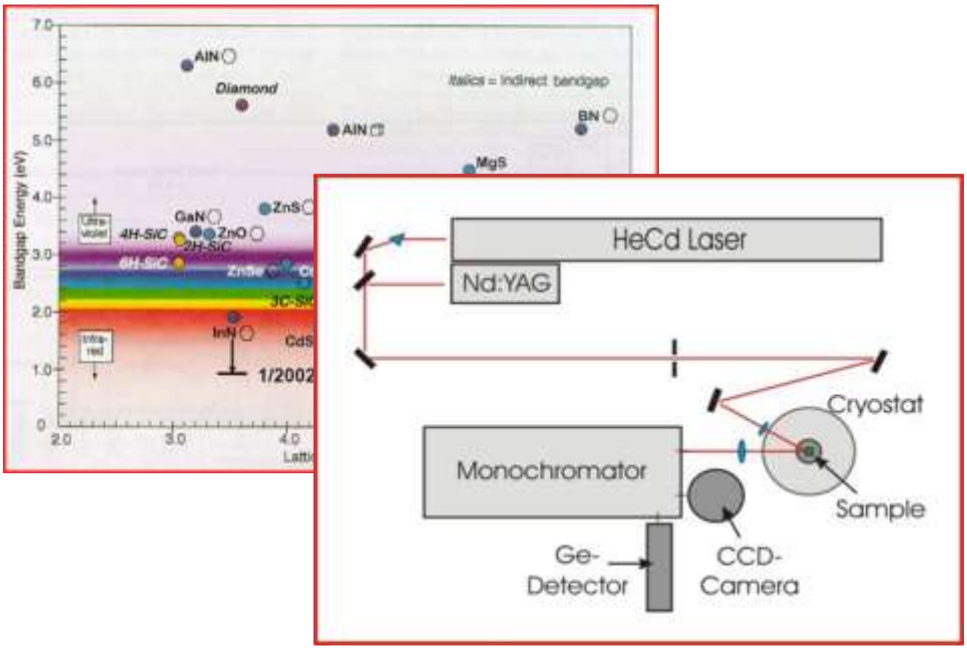


S. Szidat,
Science 323 (2009) 470.
Ö. Gustafsson et al.,
Science 323 (2009) 495.

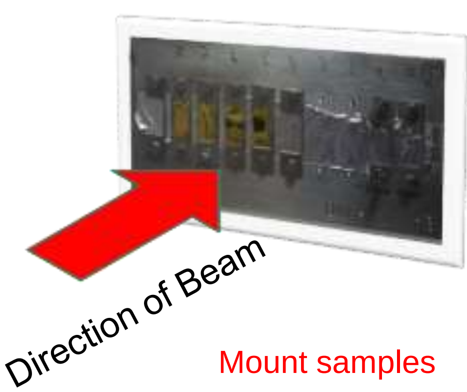
Questions in solid state physics
(in particular semiconductors)

- **How does a dopant modify the properties (optical, electrical, magnetic)?**
- **What is the preferred lattice position of a dopant, depending on implantation, annealing, etc.?**
- **What is the local electrical and magnetic environment at this position?**

Photoluminescence spectroscopy



Collection physics



Mount samples

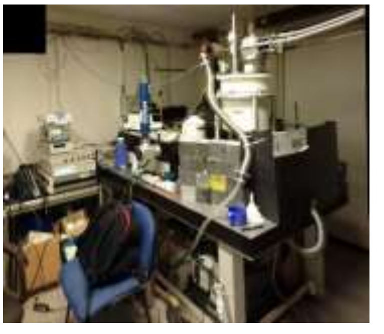
Collection chamber

Post-collection processing and spectroscopy

Transport to offline labs..

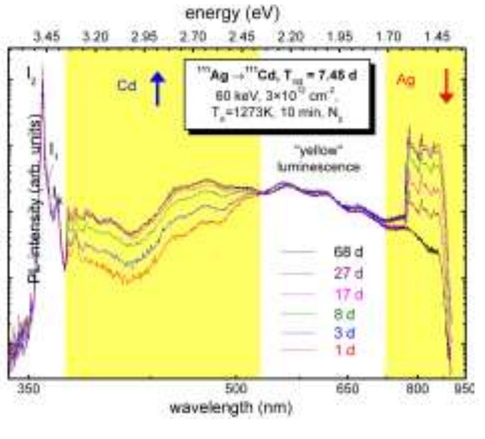
Ovens to repair crystal damage

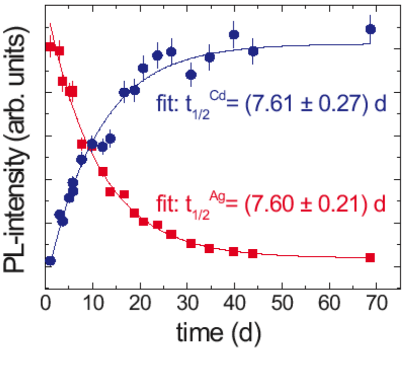
Chemistry (especially for biophysics)



PL measurements of ^{111}Ag>^{111}Cd implanted in GaN

direct identification of the Cd and Ag PL bands in GaN

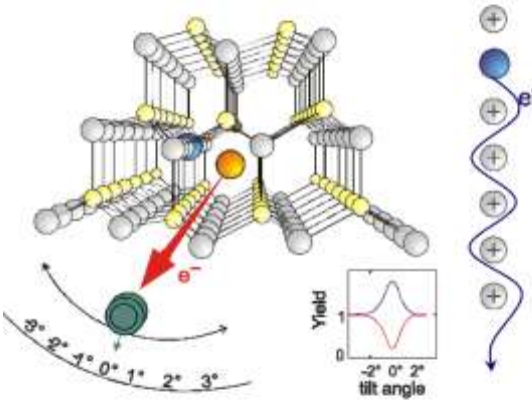


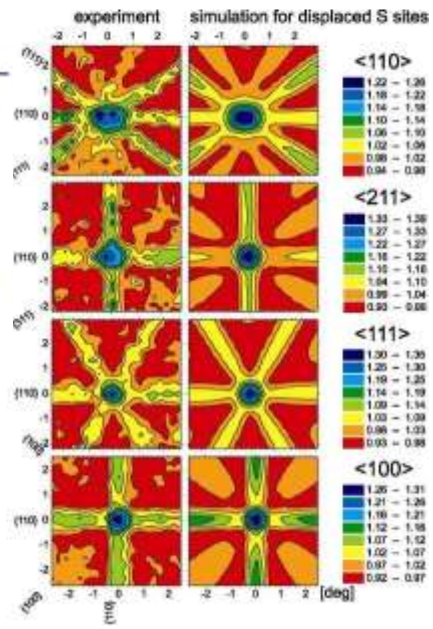


ONLY ONE Ag or Cd atoms are involved

A. Stötzler et al., Physica B **273/274** (1999) 144

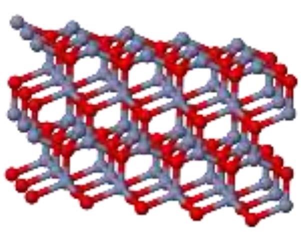
^{67}Cu for nuclear solid state physics





- Lattice location of Cu in Si studied by emission channeling
- 5 samples with each 5 min implantation of ^{67}Cu (ca. 100 ppm doping)

U. Wahl et al., Phys. Rev. Lett. 84 (2000) 1495.



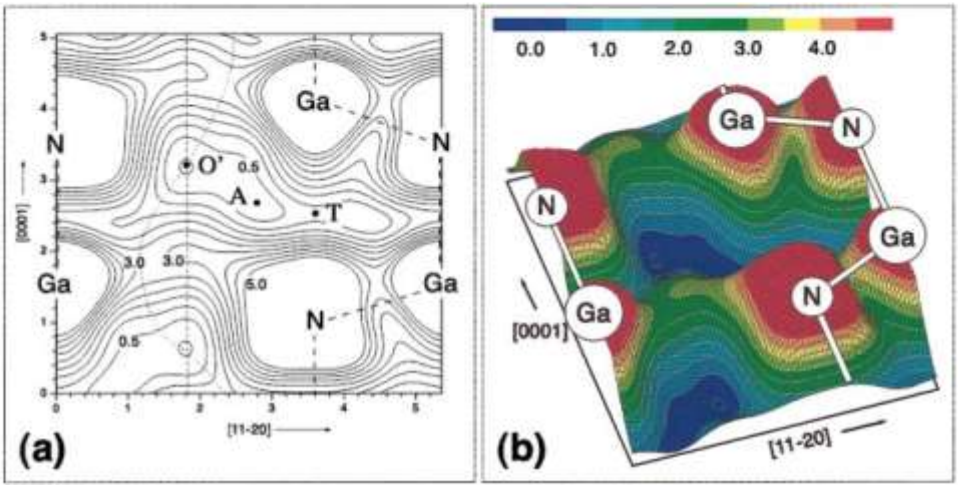
Be doping of GaN

GaN is a wide band gap (3.39 eV) semiconductor with many applications:

- **high-performance blue LEDs**
- **long-lifetime blue/violet laser diodes (Blu-ray Disc)**
- **UV detectors**
- **high-speed field effect transistors**
- **…**

present p-type doping with Mg (208 meV acceptor activation energy) might be replaced by Be (90-250 meV)

Be doping of GaN



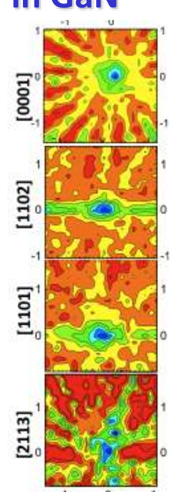
Calculated total energy surfaces for Be interstitials in GaN

C.G. Van De Walle and J. Neugebauer, J. Appl. Phys. 95 (2004) 3851.

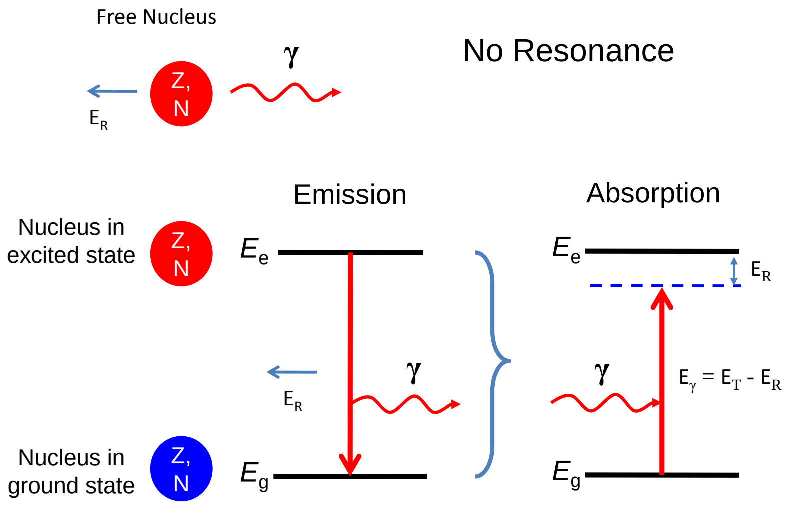
On-line emission channeling

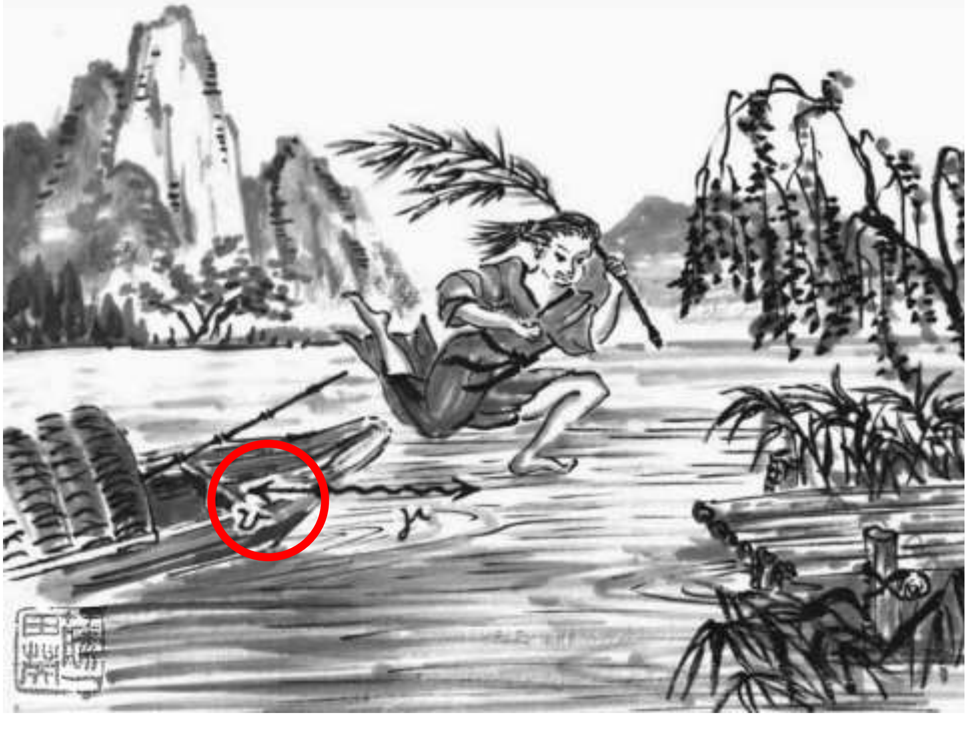
IS453

first β^- EC patterns using ^{11}Be in GaN

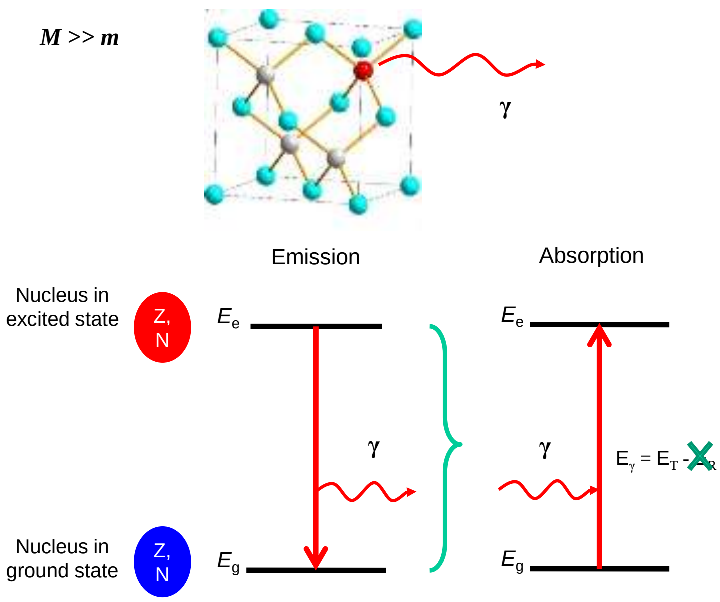


Nuclear resonance fluorescence





Recoilless nuclear resonance fluorescence

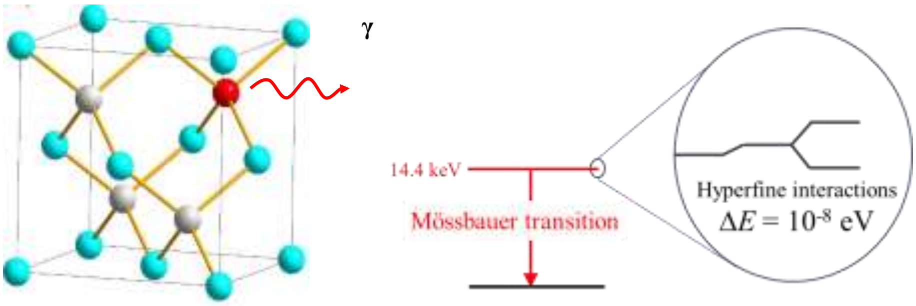


Mössbauer effect

1957 discovery of recoilless nuclear resonance
1961 Nobel Prize in Physics

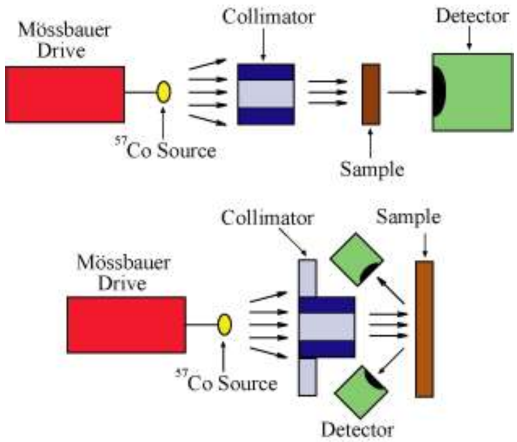
Application of the Mössbauer effect

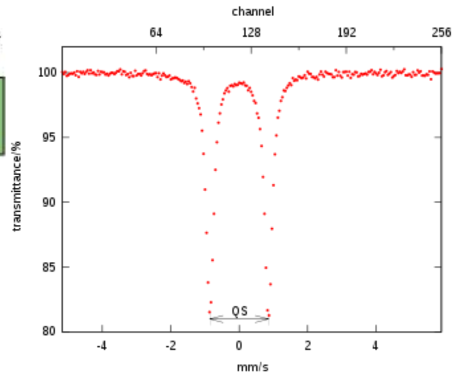
Interactions between the nucleus and its surrounding electrons…



…causing changes in the nuclear (and electronic) energy levels.

Mössbauer spectroscopy





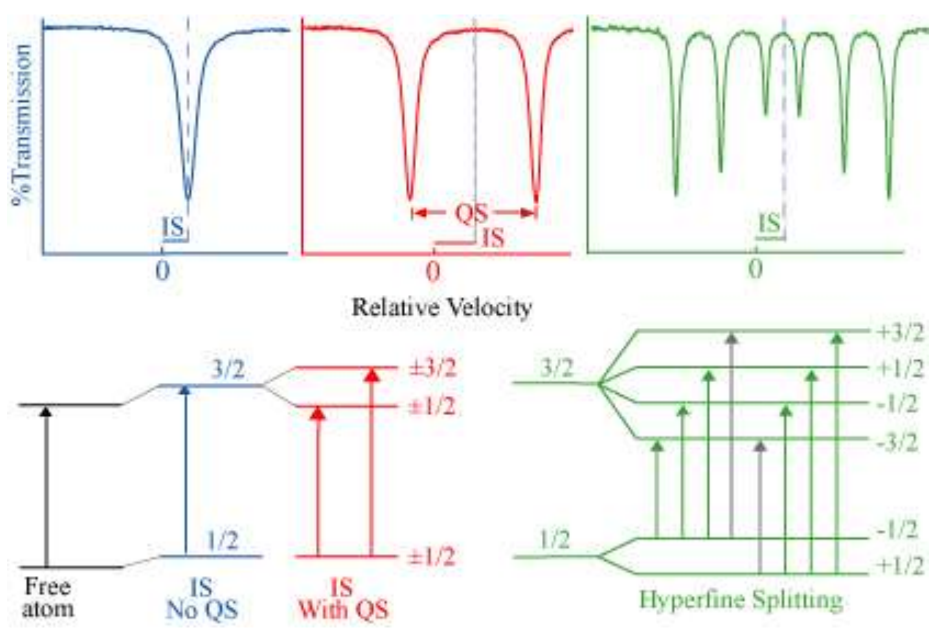
1 mm/s ≈ 4 neV

$\Delta E = \hbar/\tau$

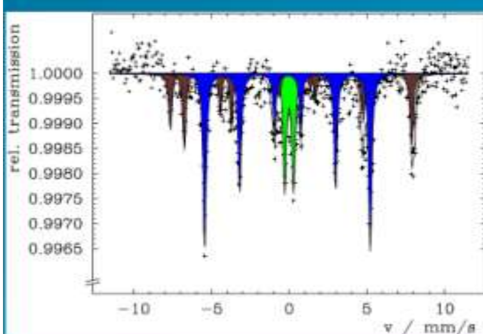
^{57}Fe: τ = 140 ns $\Rightarrow$ ΔE = 5 neV

$\Delta E/E = 3 \cdot 10^{-13}$

Hyperfine interactions



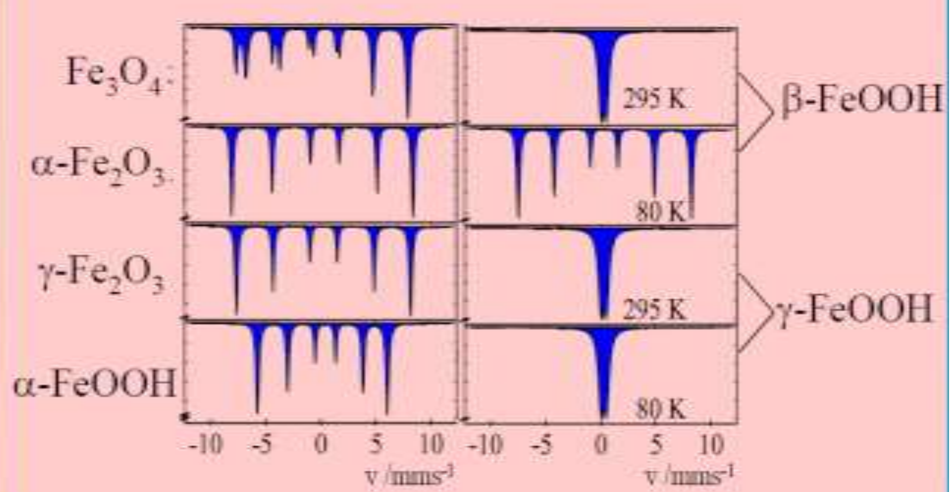
^{57}Fe Mössbauer Spectrum of a 50 Euro Bill



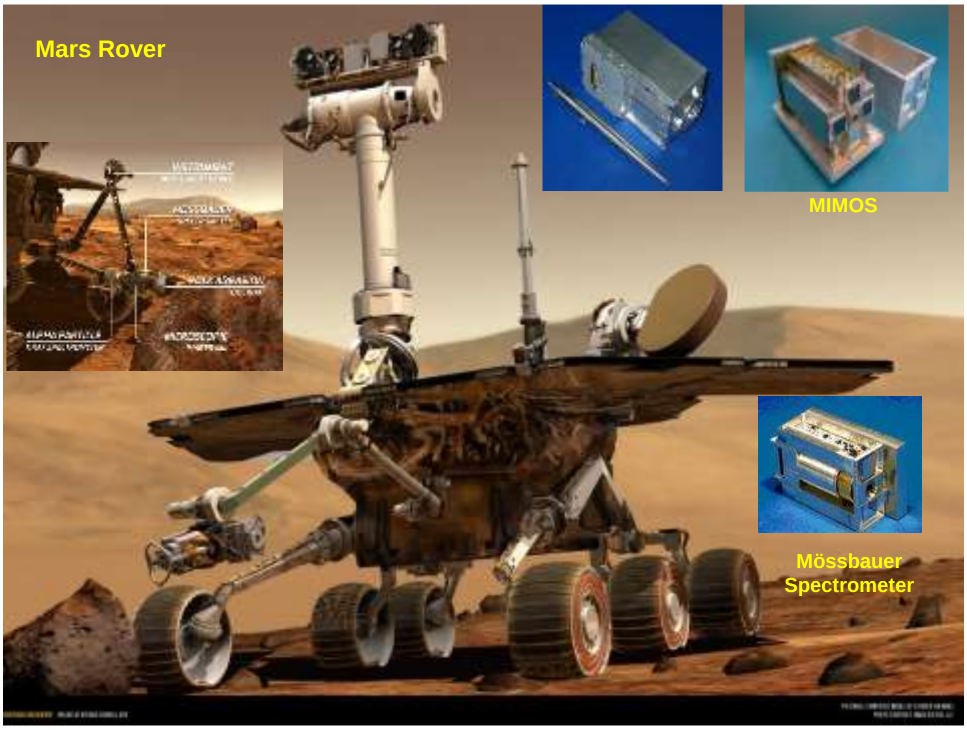
Constituents	area-/%
α Iron	48
Magnetite	36
doublet	16

Philipp Gütlich (Univ. Mainz)

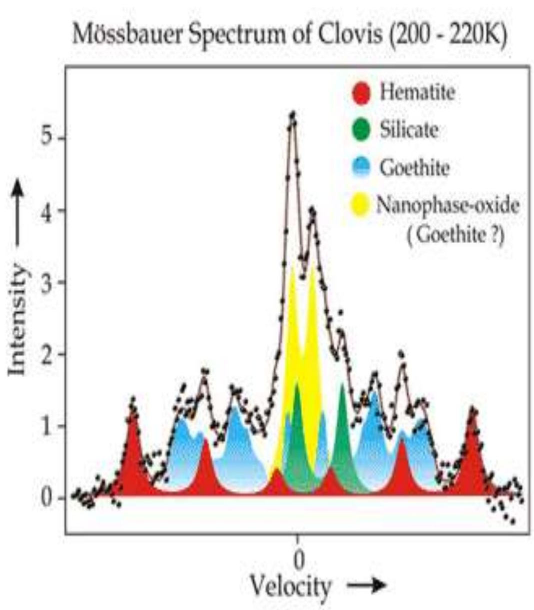
^{57}Fe Mössbauer Spectra of Corrosion Products



Philipp Gütlich (Univ. Mainz)



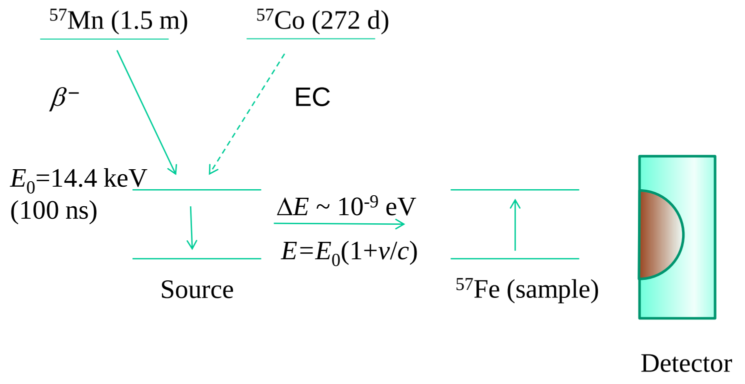
Nuclear method proofs water was on Mars



Goethite contains hydroxyl (OH^-) as a part of its structure.

→ water

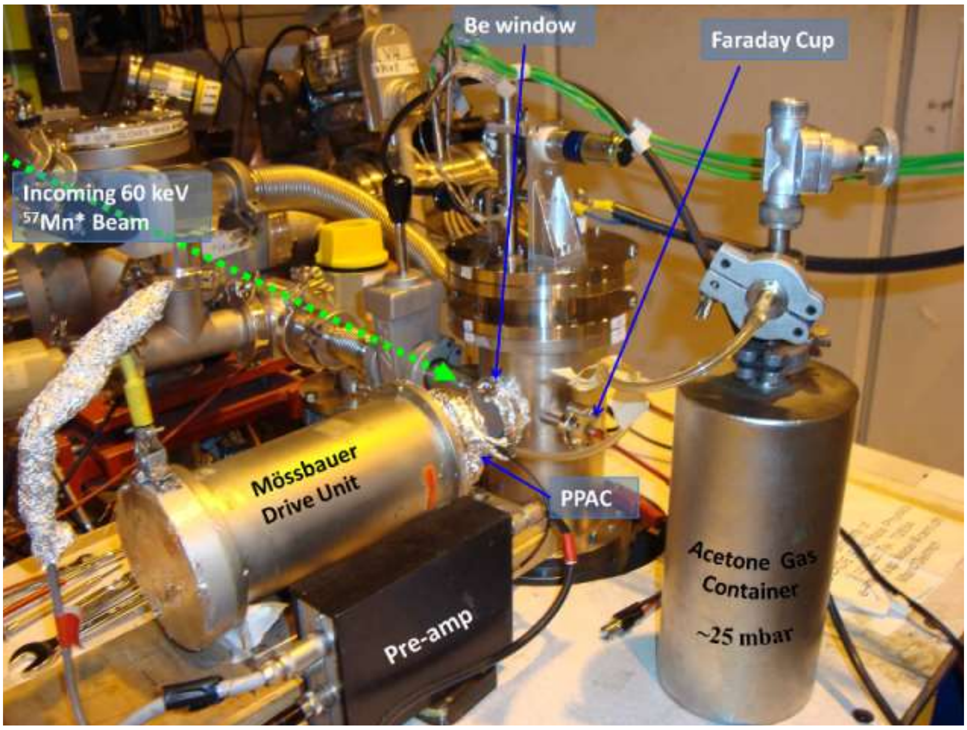
Emission Mössbauer spectroscopy at ISOLDE



^{57}Mn vs. ^{57}Co: 260000 times higher specific activity

Much lower concentration of source atoms

Study of truly dilute impurities at sub ppm-level



Promising semiconductors

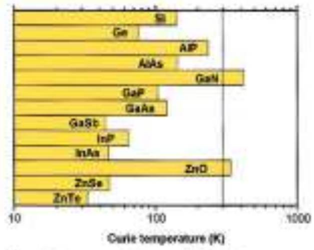
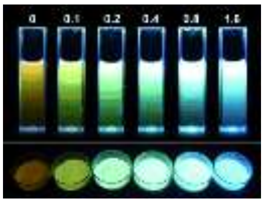


Fig. 3. Computed values of ... ature T_C for various p-ty... containing 5% of Mn and 3... cm^{-3}.

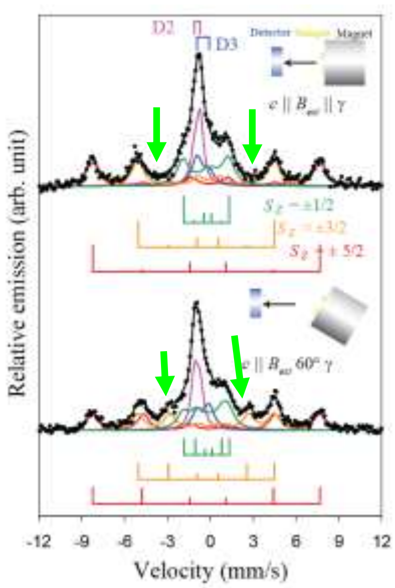
Dietl *et al*, *Science* 287



Wide-band gap semiconductors (ZnO, not cocaine)

Is it possible to create magnetic semiconductors that work at room temperature?
Such devices have been demonstrated at low temperatures but not yet in a range warm enough for spintronics applications.

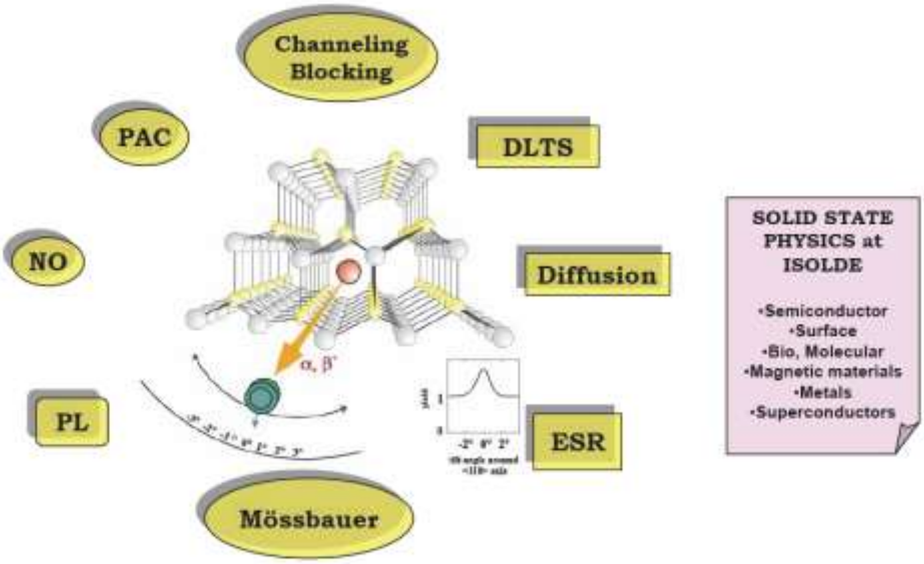
Mn/Fe implanted into ZnO



Only paramagnetism observed (precipitation of metal impurities?).

H.P. Gunnlaugsson et al. Appl Phys Lett 97, 1 (2010)

Solid-state physics with nuclear probes

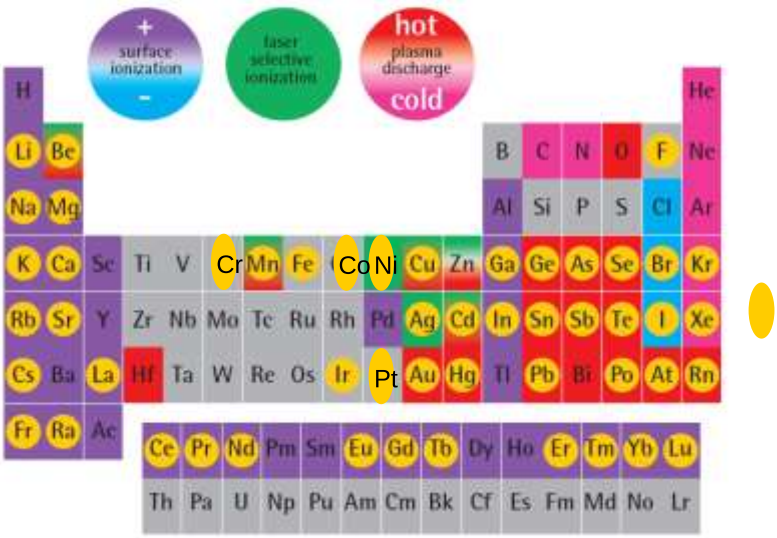


Doris Forkel-Wirth, Rep. Prog. Phys. 62 (1999) 527.

RIBs for nuclear solid state physics

- **(radioactive) ion implantation allows doping of nearly any matrix, irrespective of solubility, chemical compatibility, diffusion coefficient,… ⇒ universal**
- **specific elements/isotopes are required**
  ⇒ often not "easy" elements
- **generally longer-lived isotopes closer to stability**
  ⇒ less challenging for target/ion source
  ⇒ can be populated by decay of "easy" beam
  ⇒ can sometimes be implanted in parallel to other experiment with ISOLDE GPS
- **implantation energy often less important (recoil implantation possible)**
- **emission channeling needs small beam focus**
- **beam purity required to limit implantation damage**

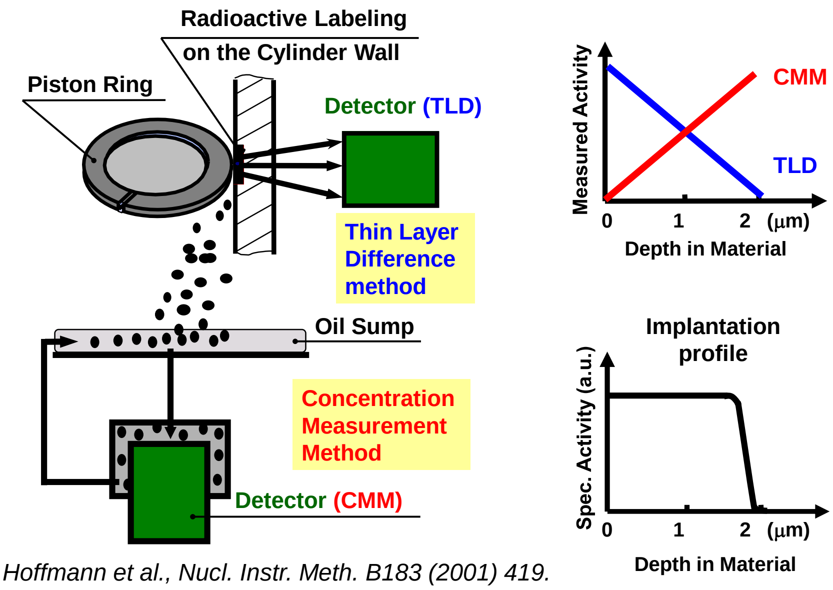
Periodic table of ISOLDE beams



Isotopes of this element used for solid state physics or life science

RIBs for materials science

High sensitivity wear measurements



M. Hoffmann et al., Nucl. Instr. Meth. B183 (2001) 419.

P. Fehsenfeld et al., Nucl. Phys. A701 (2002) 235c.

^{7}Be for wear analysis

Material	Density	Wear rate	Implant. depth in μm at beam energy of:				
	g/cm3	μm/10^6 cyc.	60 keV	260 keV	1.2 MeV	6 MeV	15 MeV
UHMWPE	0.97	50	0.36	1.1	2.9	13	43
Ti	4.52		0.17	0.56	1.5	6.1	18
CoCrMo	8.28		0.11	0.39	1.1	4.1	12
Alumina	3.1	0.15	0.20	0.59	1.6	6.7	21
Zirconia	5.5		0.15	0.48	1.3	5.3	16

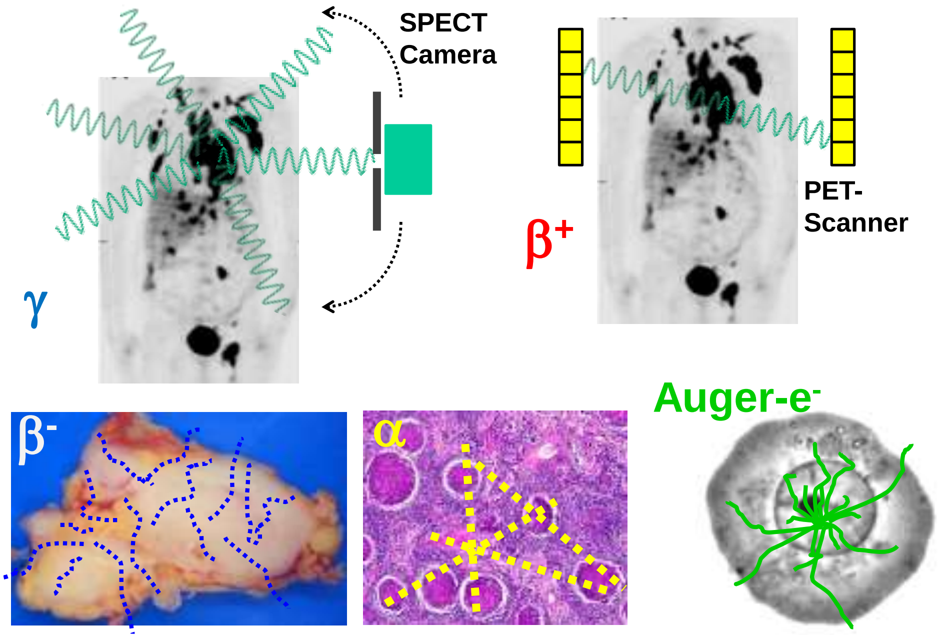
In-vivo use: ≈10^6 cycles/year

Simulator runs: $(2\text{-}10)\cdot10^6$ cycles

Required dose: some pnA per cm^2 (e.g. ball of 22-28 mm diameter)

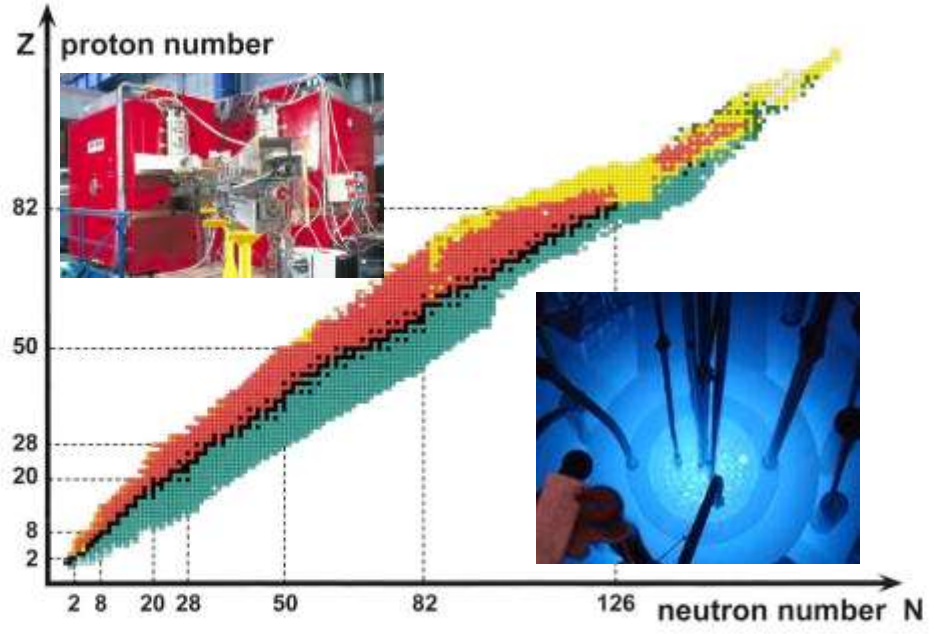
^{7}Be is the optimum radiotracer for tribology!

The Nuclear Medicine Alphabet

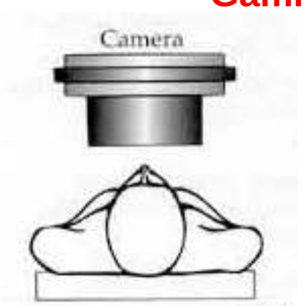


The Tordesillas meridian

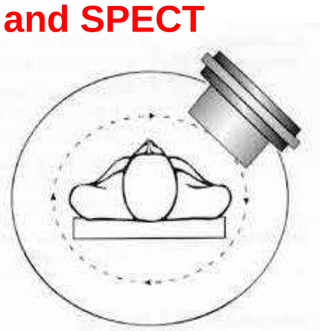
The Tordesillas meridian of radioisotope production



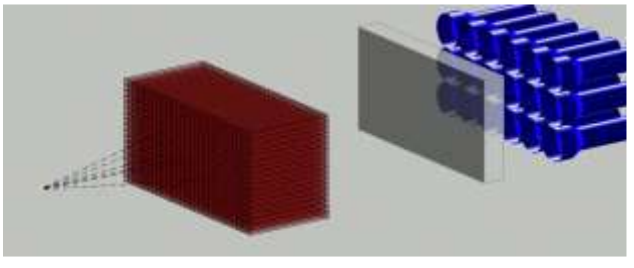
Gamma camera and SPECT



2D: planar scan



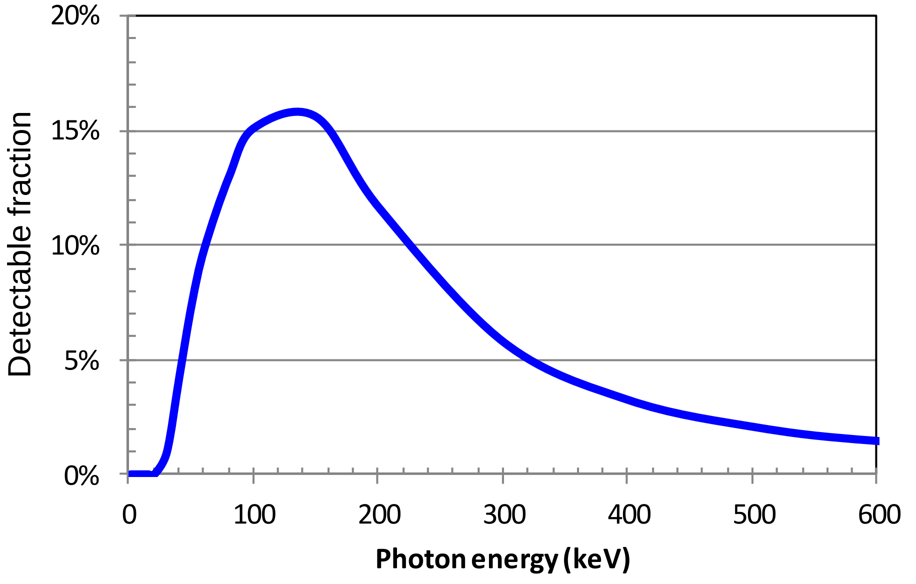
3D: SPECT: Single Photon Emission Computer Tomography



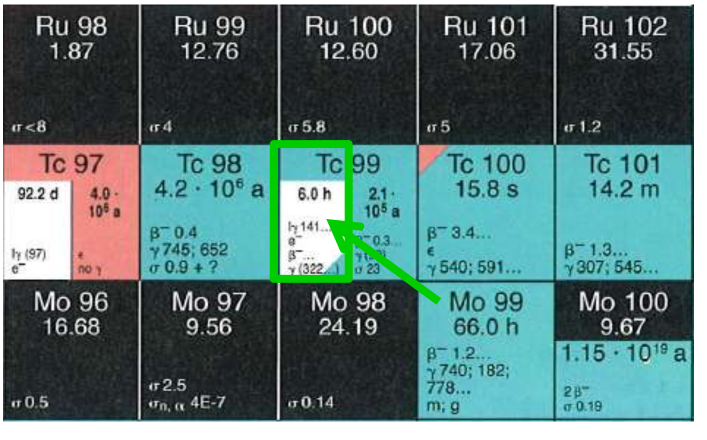
$E_\gamma >$ 60 keV

$E_\gamma <$ 300 keV

Ideal gamma ray energy for SPECT

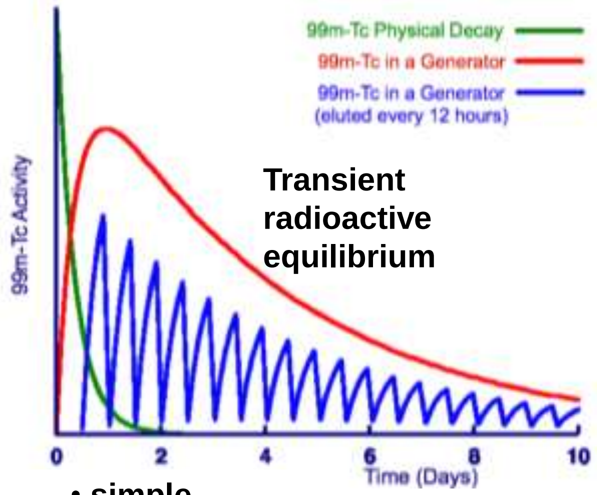


^{99m}Tc: ideal for SPECT and gamma cameras



- 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

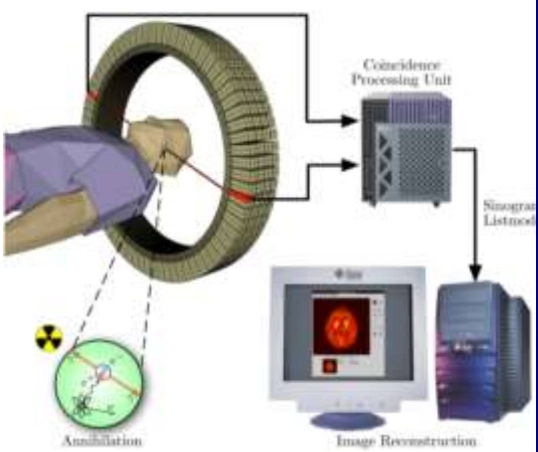
$^{99}Mo/^{99m}Tc$ generator

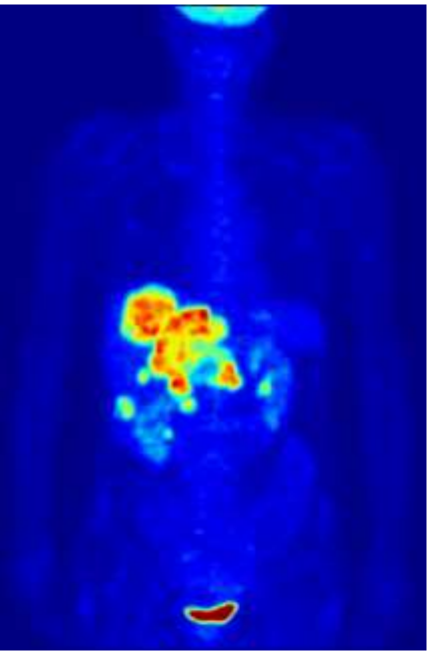


Transient radioactive equilibrium

- simple
- reliable
- portable
- self-shielded

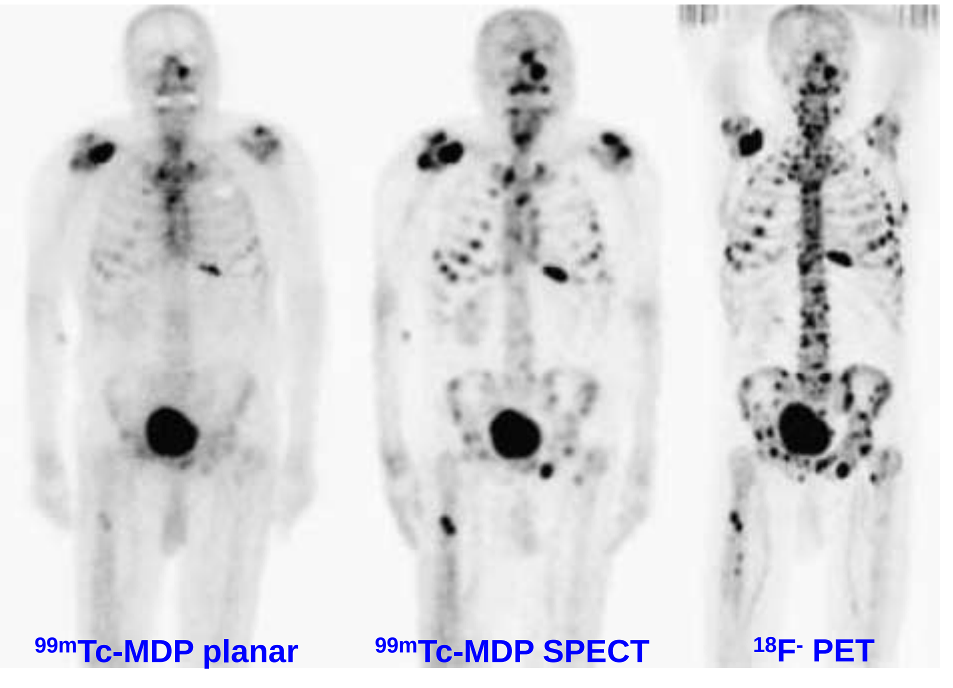
Positron Emission Tomography





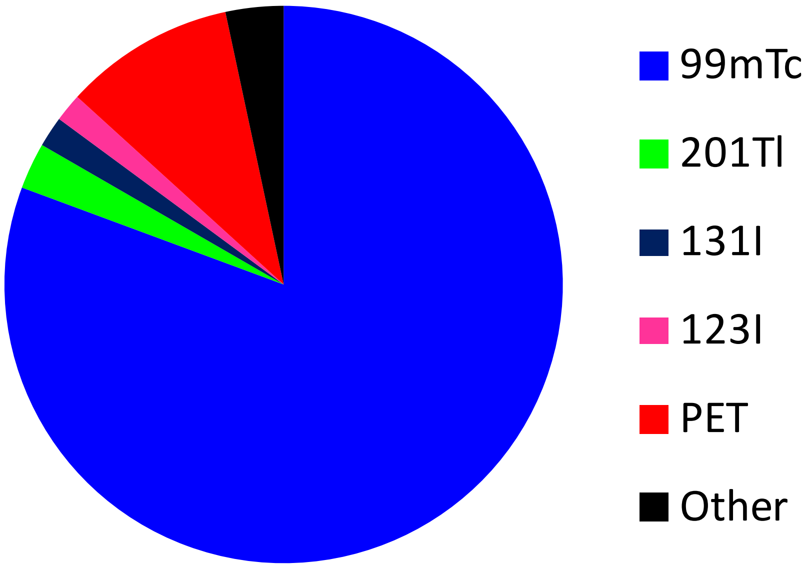
PET isotopes

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

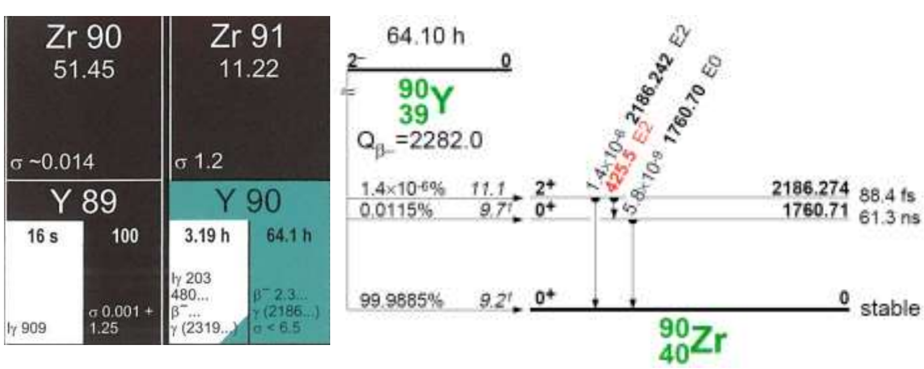


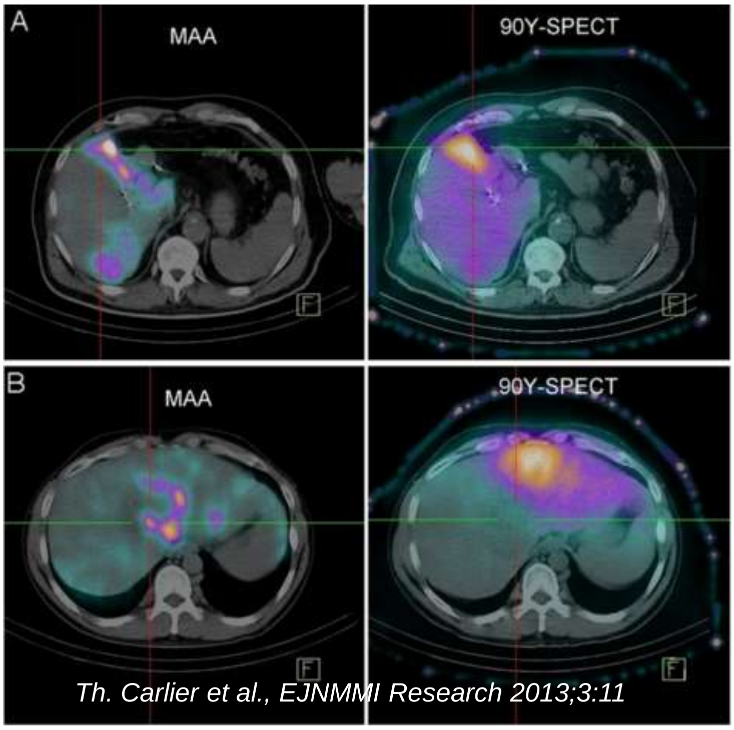
Even-Sapir E *et al., J Nucl Med 2006; 47:287.*

Cumulative use of diagnostic isotopes in Europe



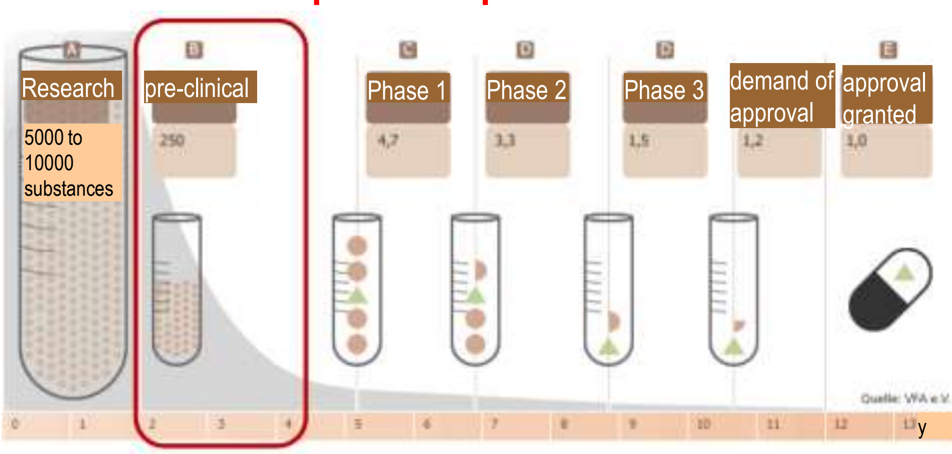
http://www.nupecc.org/npmed/npmed2014.pdf





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

Development of pharmaceuticals



Screening

in vitro tests
animal exp.

tests with humans

toxicity
side effects

wanted effect

comparison
with standard

20-80 healthy volunteers

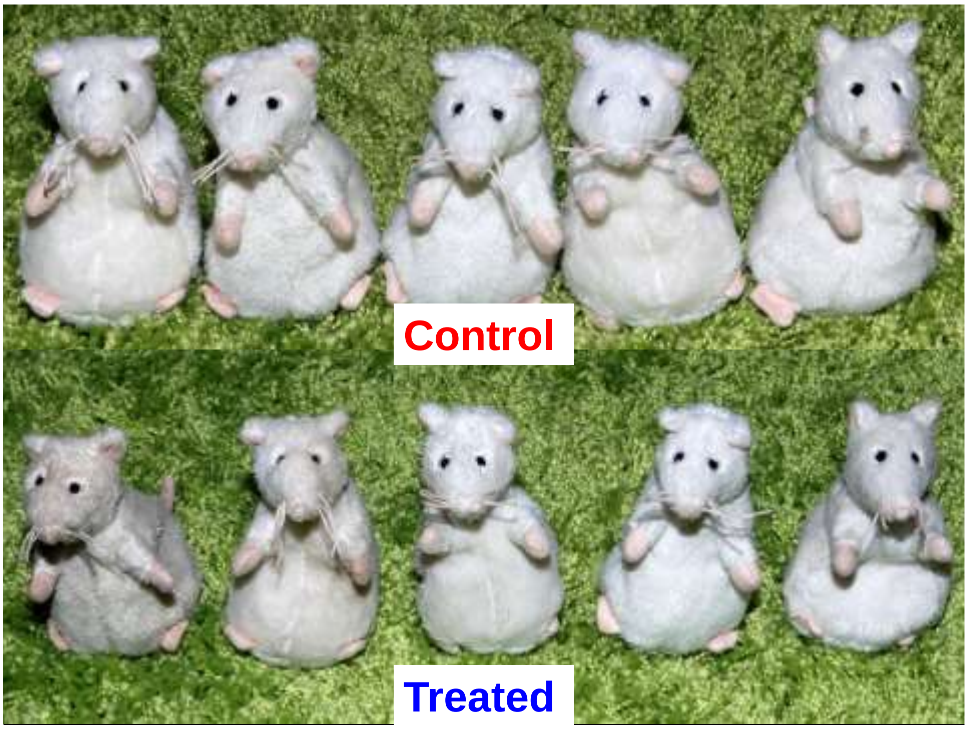
100-300 patients

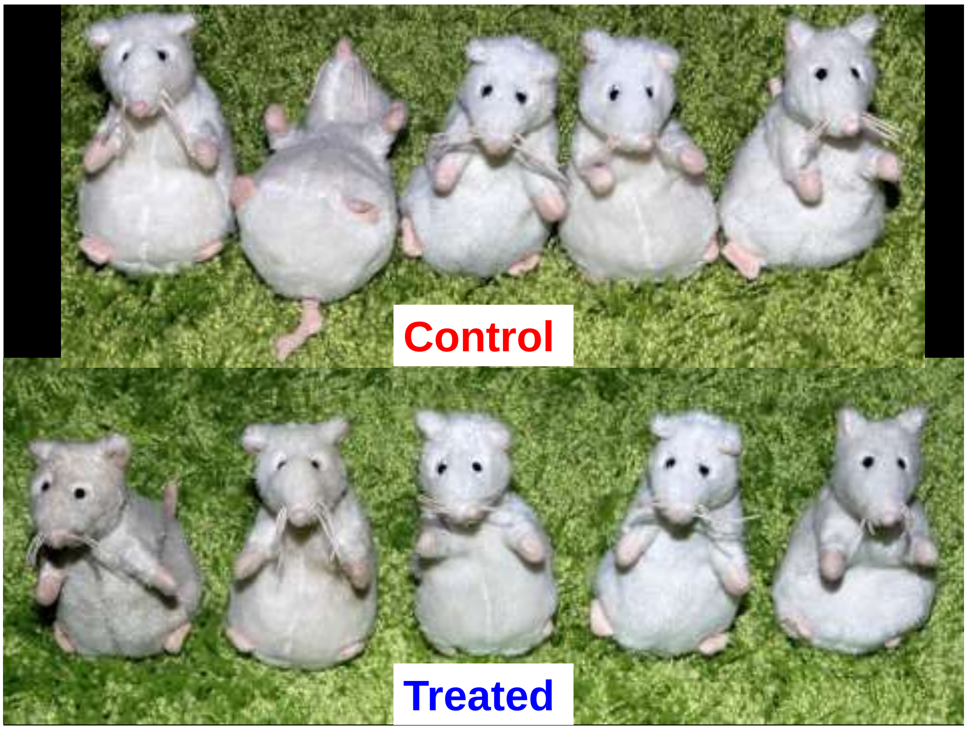
x00-x000 patients

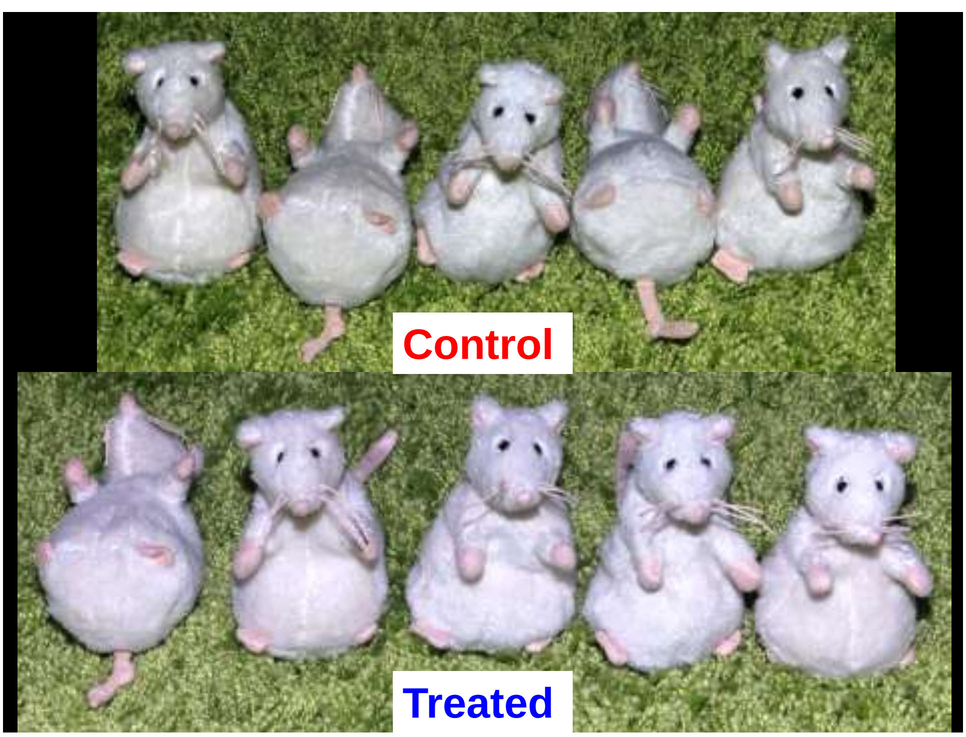
Pre-clinical studies (1)

Pre-clinical studies (2)

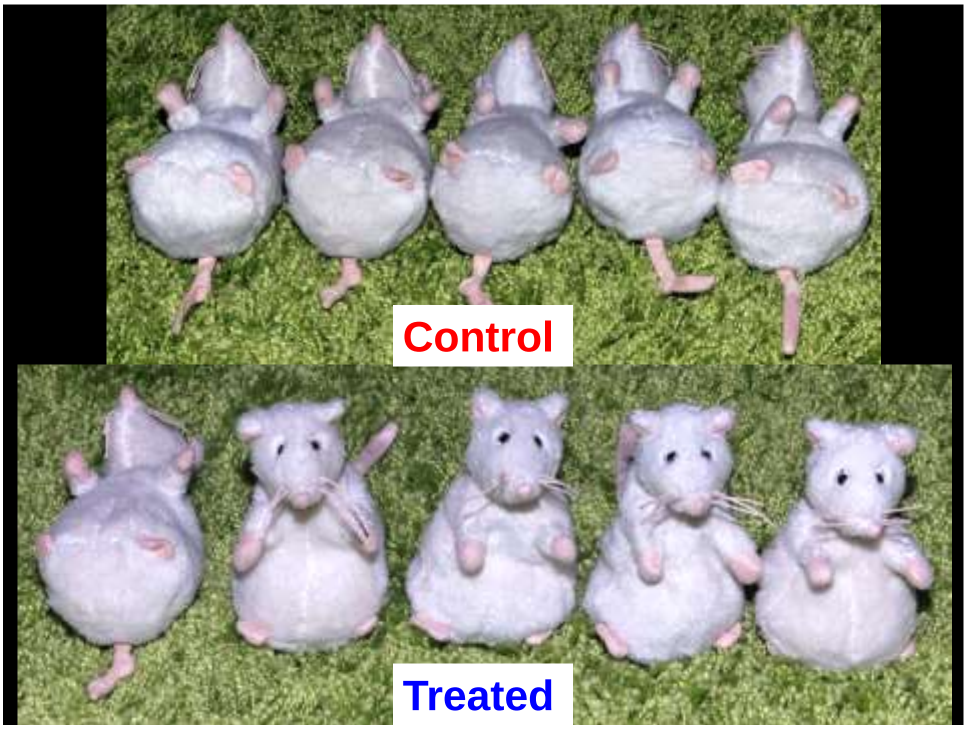
Pre-clinical studies (3)



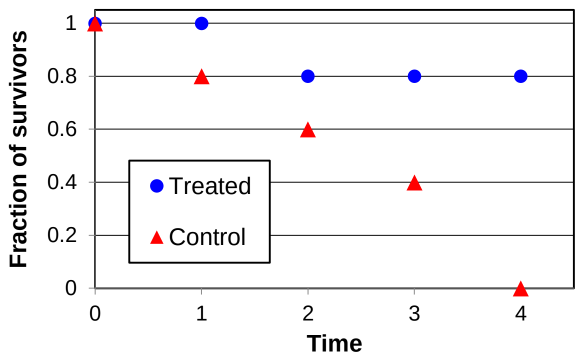

Control
Treated


Control
Treated


Control
Treated


Control
Treated

Survival curve

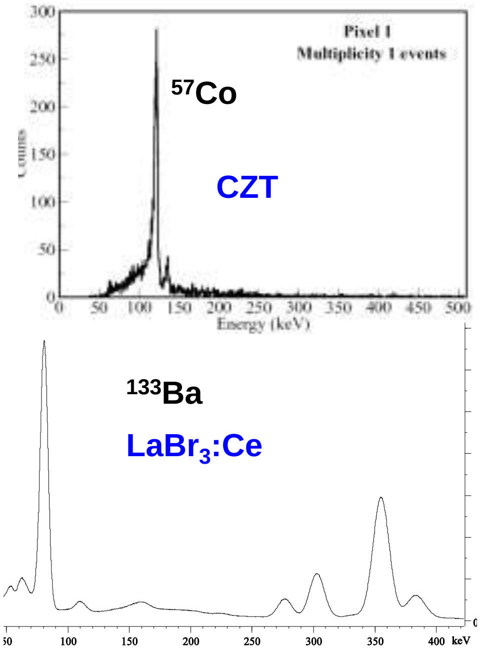


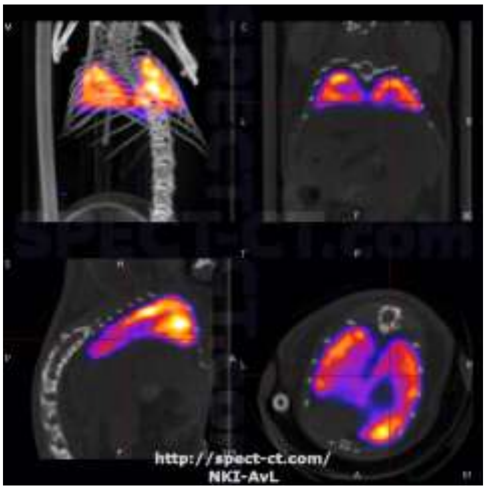
- medium survival time, median survival time, survival benefit
- shows final benefit but not detailed mechanism

- more information from bio-distribution studies
- preferentially on-line with suitable radiotracers
  and small animal SPECT or PET

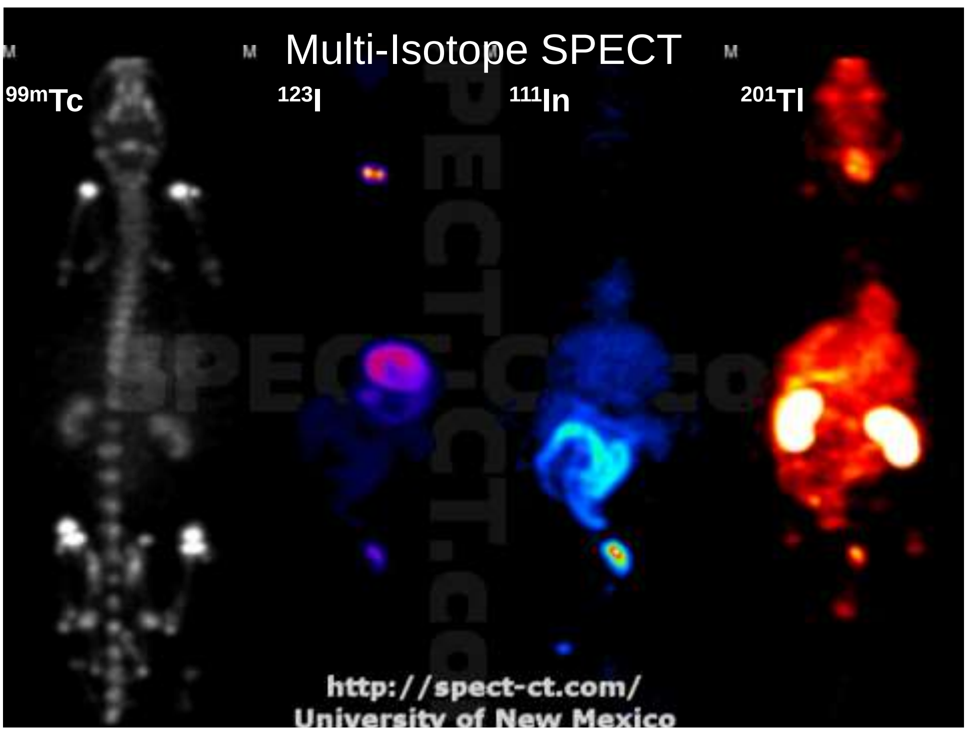
Small animal imaging

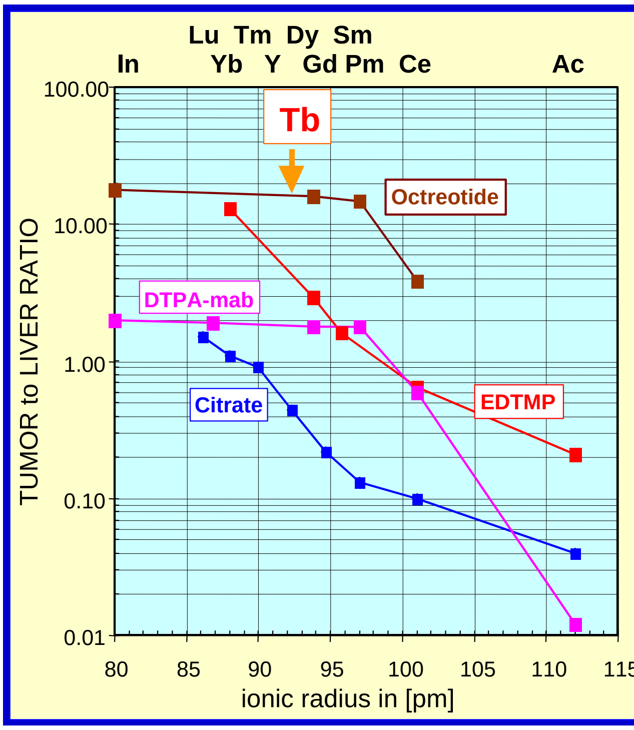
New generation of small animal SPECT





systematic biodistribution studies with different radiotracers become possible with dedicated small animal SPECT





Comparison
of the
bio-distribution
of different
tumor seeking tracers
labeled with
radio-lanthanides, ^{225}Ac and ^{111}In

free chelates:
Citrate
EDTMP
specific tracers:
Octreotide
and
Mab
Linker: Aminobenzyl-DTPA

*G.J.Beyer, Hyperfine Interactions **129** (2000) 529.*

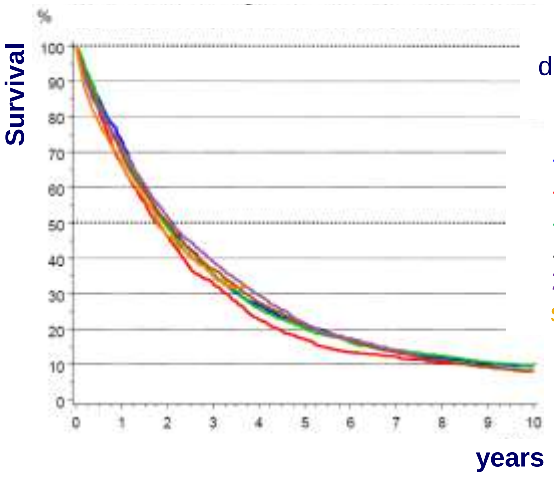
Cancer and efficiency of treatments

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**

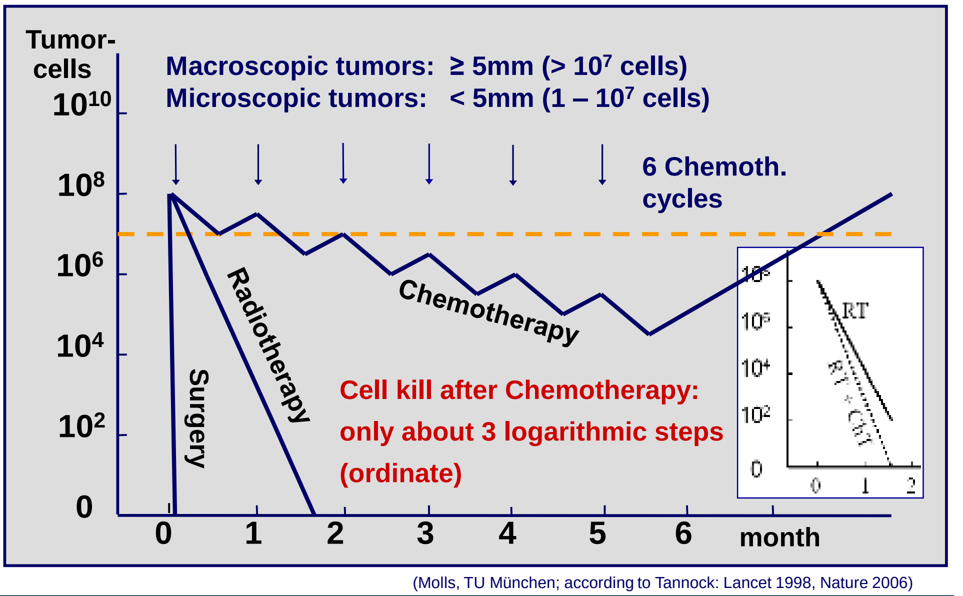
Mammary Carcinoma
Survival time since diagnosis of metastases



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

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

Comparison of Therapies

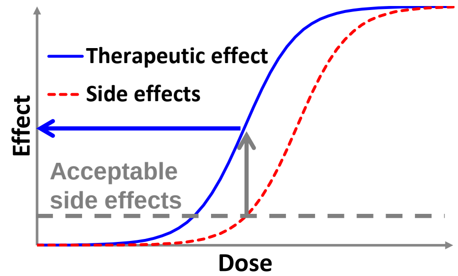


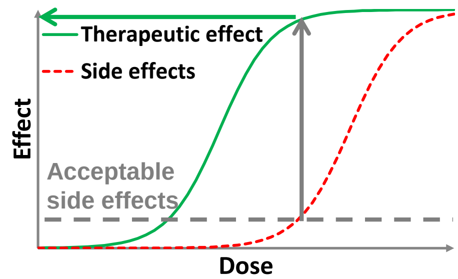
(Molls, TU München; according to Tannock: Lancet 1998, Nature 2006)

Targeted therapies

Paracelsus (1493-1541)

"All things are poison, and nothing is without poison; only the dose permits something not to be poisonous."



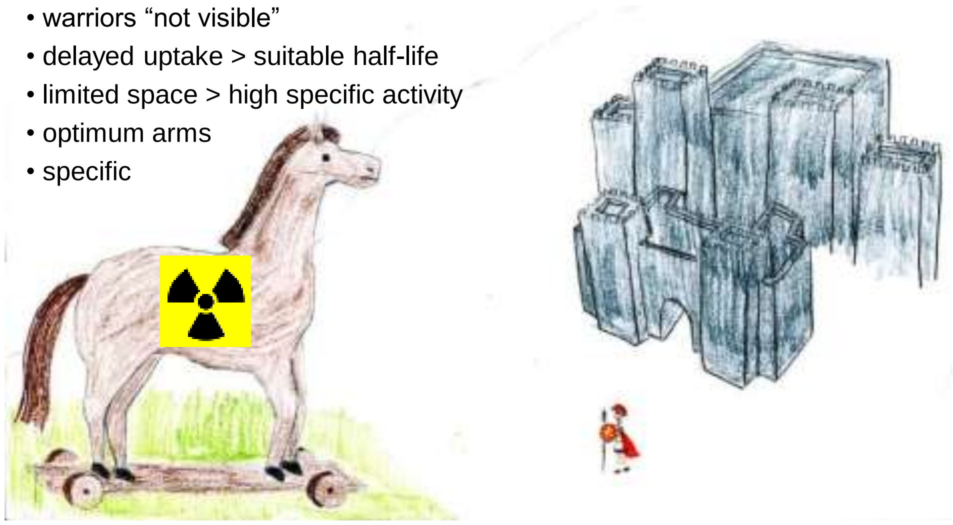


Selectivite targeting is essential to widen the therapeutic window!

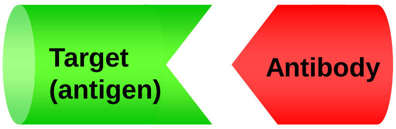
Learning from history

The principle of targeted therapies

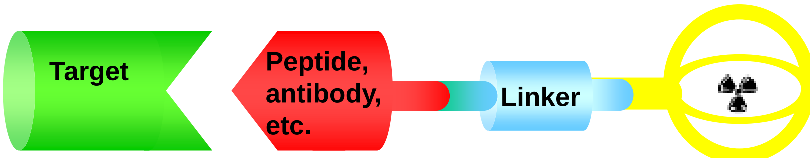
- “attractive” vector > high uptake by the target
- transportable
- good in-vivo stability
- warriors “not visible”
- delayed uptake > suitable half-life
- limited space > high specific activity
- optimum arms
- specific



Immunology approach



Multidisciplinary collaboration to fight cancer



Receptor | **Radionuclide**

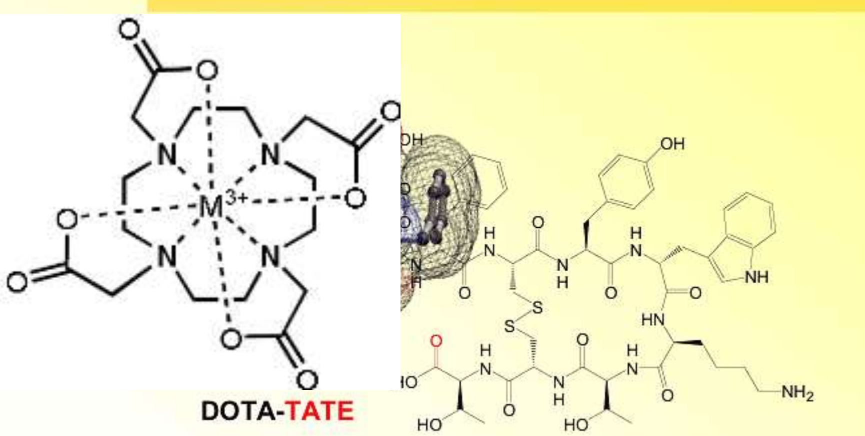
Immunology
Structural biology

Coordination
chemistry

Nuclear physics
and
radiochemistry

Nuclear medicine and medical physics

Structural Formula of DOTA-TOC/TATE



DOTA-TATE

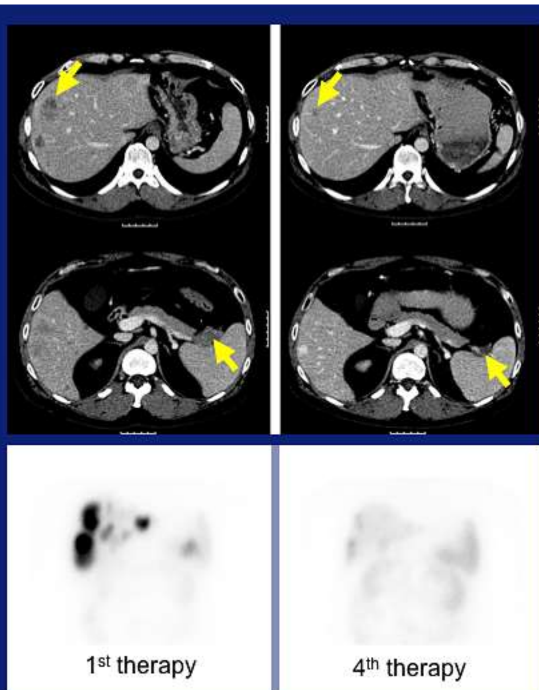
1,4,7,10-tetraazacyclododecantetraacetate

^{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)

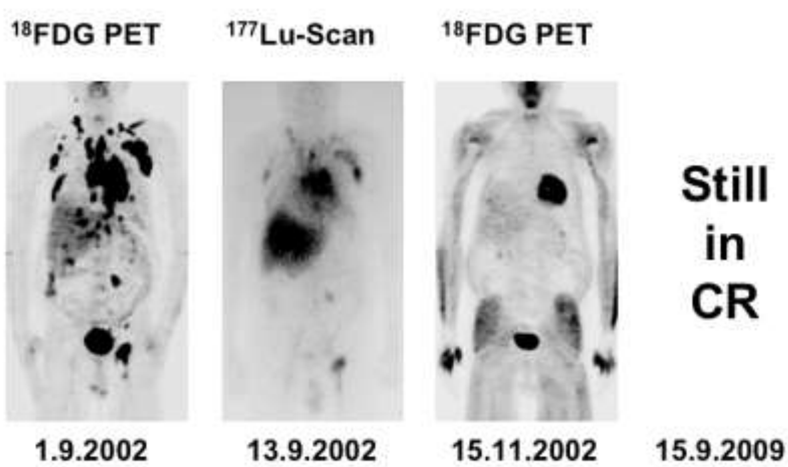
4 cycles with ^{177}Lu-octreotate and capecitabine

Partial remission

Roelf Valkema, EANM-2008.

Lymphoma therapy: RITUXIMAB+^{177}Lu

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



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

University Hospital Basel, CH

The rising star for therapy

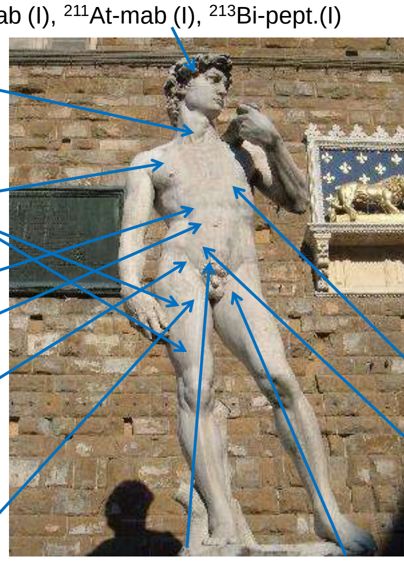
Radiopharmaceuticals for targeted therapy: clinical use

Brain:
^{90}Y-mab ,^{131}I-mab (I), ^{211}At-mab (I), ^{213}Bi-pept.(I)

Lymphoma:
Zevalin® (^{90}Y-mab),
Bexxar® (^{131}I-mab),
Betalutin® (^{177}Lu-mab, I/II)

Thyroid: ^{131}I-

Bone metastases:
Metastron® (^{90}SrCl$_2$),
Quadramet® (^{153}Sm-EDTMP)
Xofigo® (^{223}RaCl$_2$)



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

Melamoma:
^{213}Bi-mab(I)

Neuroblastoma:
^{131}I-MIBG

Pancreas:
^{90}Y-mab (II)

Breast:
^{90}Y-mab, ^{90}Y-pept.

Lung (SCLC):
^{177}Lu-mab (II)

Neuroendocrine (GEP-NET):
Lutathera® (^{177}Lu-pept., III)
^{90}Y-peptide

Liver (HCC):
Theraspheres and SIRspheres (^{90}Y),
^{166}Ho-microspheres
^{188}Re-Lipiodol

Ovary:
^{90}Y/^{177}Lu-mab

Colon et rectum:
^{131}I-mab (II)

Prostate:
^{177}Lu-mab (II)

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

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!

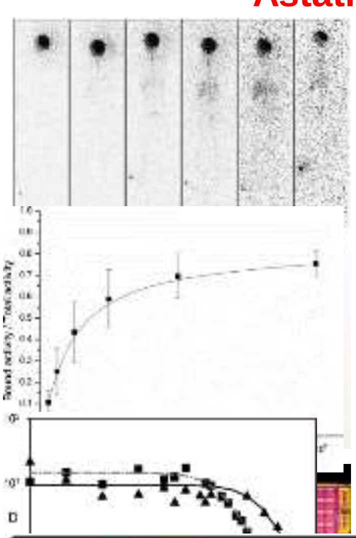
localized

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

Isotopes for targeted alpha therapy

Astatine: a chemical hybrid – halogen/metalloid

Astatine (bio-)chemistry ?



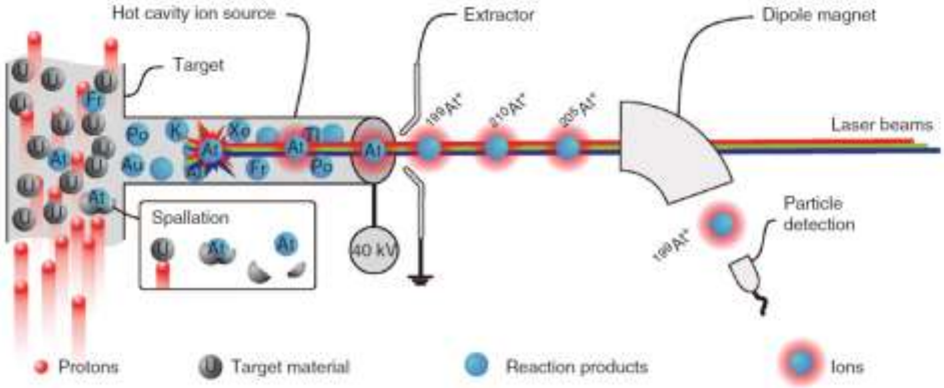
in vivo
73 MBq ^{211}At-ch81C6
γ camera images with 77-92 keV X-rays
M. Zalutsky et al., J. Nucl. Med. 49 (2008) 30.

in vitro
S.H. Cunningham et al., Br. J. Cancer 77 (1998) 2061.
S.H.L. Frost et al., Cancer 116 (2010) 1101.
J. Champion et al., J. Chem. Phys. A114 (2010) 576.

in silico
J. Champion et al., PCCP 13 (2011) 14984.

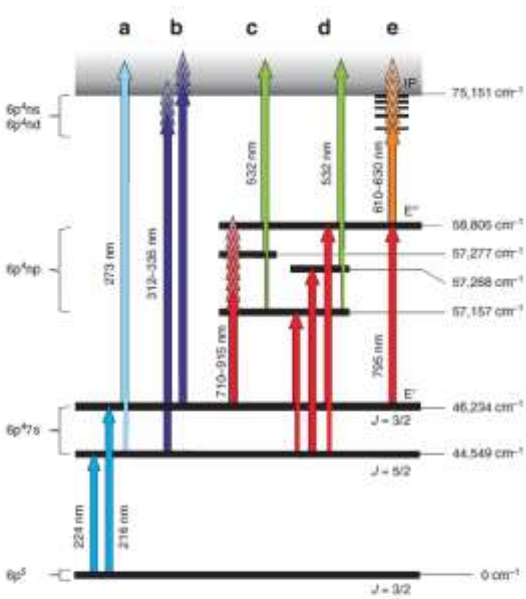
Atomic spectroscopy of astatine

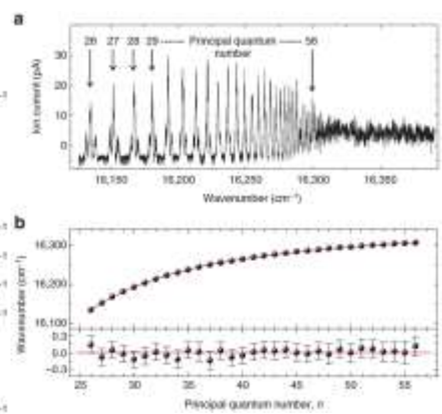
Author	Year	Method	IP (eV)
Finkelnburg *et al.*[10]	1950	Extrapolation	9.5(2)
Varshni *et al.*[11]	1953	Extrapolation	10.4
Finkelnburg *et al.*[12]	1955	Extrapolation	9.2(4)
Kiser *et al.*[13]	1960	Extrapolation	9.5
Mitin *et al.*[14]	2006	HF	9.24
Chang *et al.*[15]	2010	MCDF, up-shift	9.35(1)



S. Rothe et al., Nature Comm. 4 (2013) 1835.

Atomic spectroscopy of astatine

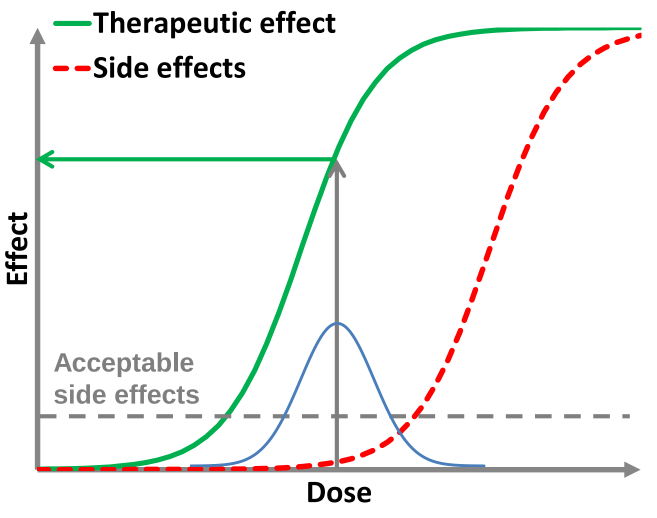




IP(At) = 9.317510(8) eV

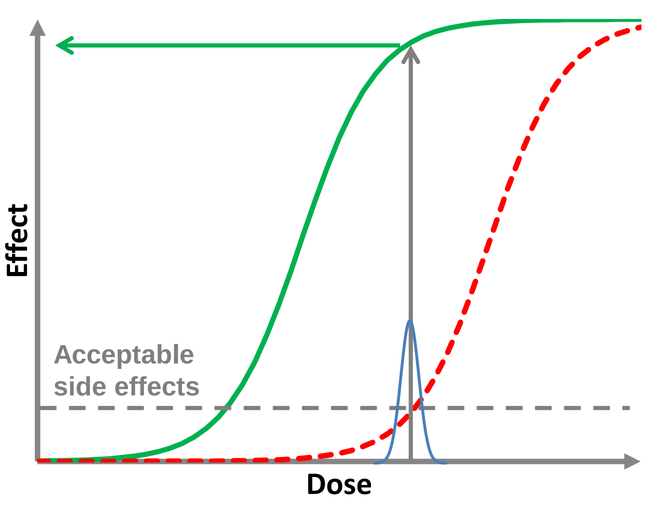
S. Rothe et al., Nature Comm. 4 (2013) 1835.

Theranostics



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

Theranostics



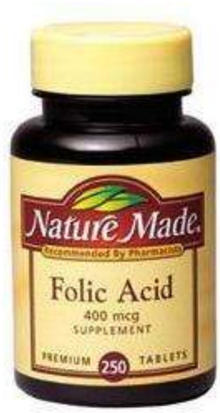
Accurate dosimetry is essential for optimum use of the therapeutic window.

Terbium: a unique element for nuclear medicine

Folate-receptor positive cancers

Frequent overexpression of folate receptor in cancer of:

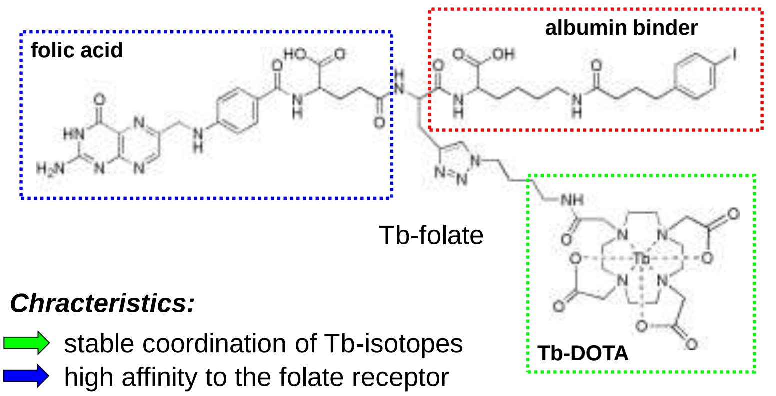
- ovaries
- cervix uteri
- lung
- kidney
- brain
- colon
- breast
- leukemia



folic acid = vitamine B9

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

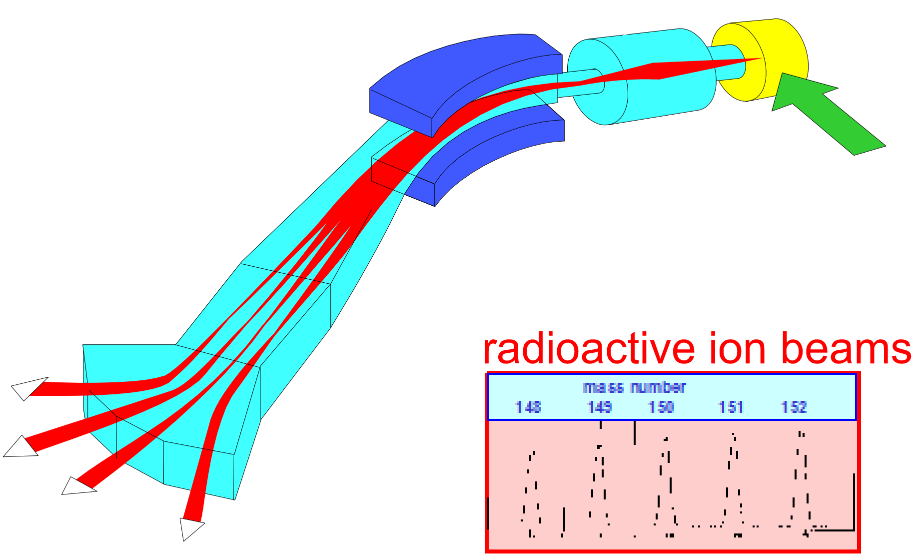
Tumor Targeting Agent for Tb-Coordination
Chemical Structure with 3 Functionalities



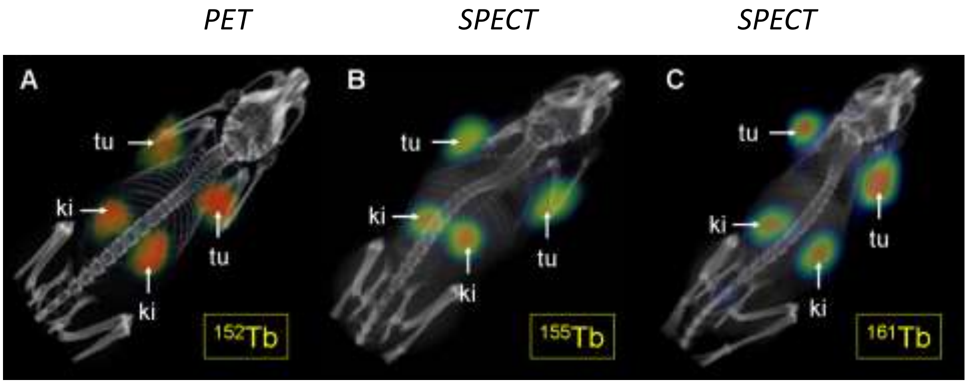
Chracteristics:

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

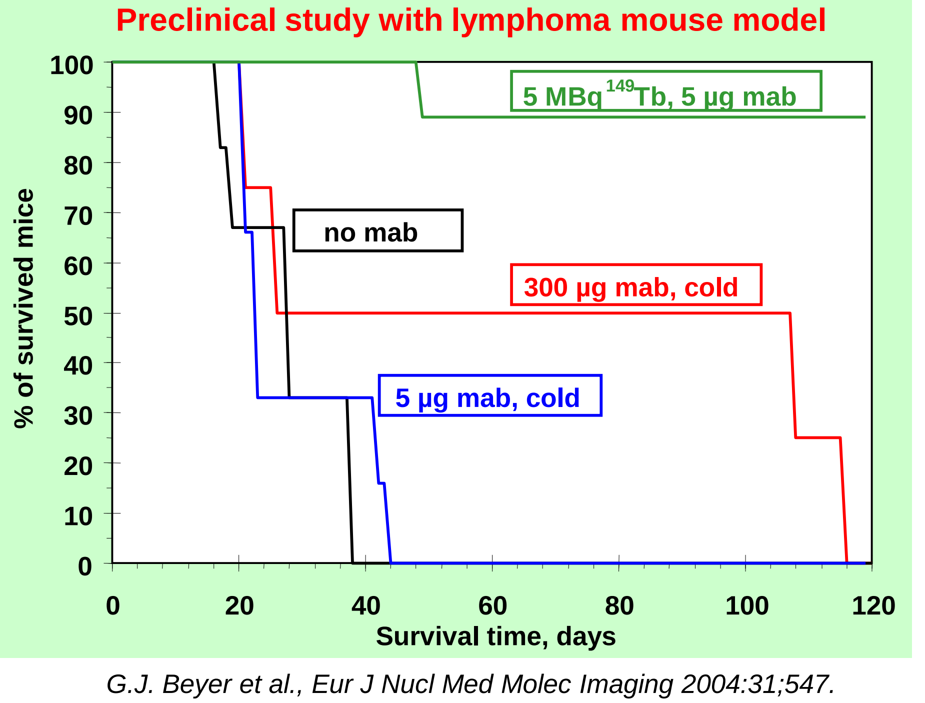
Production of ^{149}Tb, ^{152}Tb and ^{155}Tb at ISOLDE



Theranostics with terbium isotopes



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.

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www.cern.ch/medicis-promed

Kostya Novozelov

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ESR2 @CERN(CH) Facility development and safety
ESR3 @CERN(CH) Fast injection & charge breeding of isotope beams
ESR4 @Graphene Nat'l Inst(UK) Graphene coating on foil isotope prod target
ESR5 @Mainz univ(DE) Laser Ion Source for isotope beam purification
ESR6 @Advanced Accelerator Application(FR) Mass separation for isotopes produced at cyclotron

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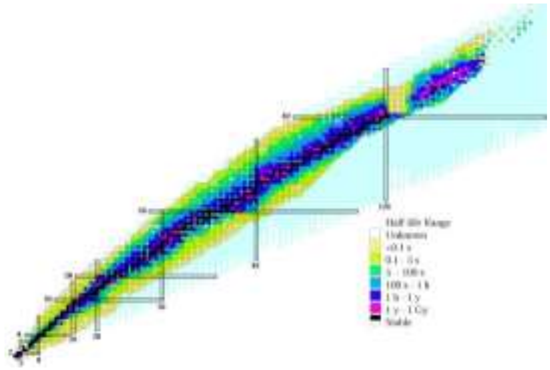
Medicis Promed

ESR7 @Instituto Sup Tecnico(PT) Uranium nanofiber isotope prod targets
ESR8 @Instituto Sup Tecnico(PT) Radiopharmaceutical for DNA targeting
ESR9 @CNAO(IT) 11C PET Aided hadron therapy
ESR10 @Lemer Pax(FR) Container technology for isotope dispatching
ESR11 @Kat Univ Leuven(BE) Mass separated molecular beams

ESR12 (CH1)@Geneva University Hospital(CH) Ovarian cancer bimodal imaging
ESR13 (CH2)@Lausanne University Hospital(CH) Radioimmunotherapy and imaging of ovarian cancer
ESR14 (CH3)@Geneva University Hospital(CH) Robotic surgery for internal radiotherapy
ESR15 (CH4)@Swiss Fed Inst Tech Lausanne EPFL (CH) Bimodal Radiopharmaceutical synthesis for ovarian cancer



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 **isotopes (plus Ca, Ni, No, etc.).** For me such is not the **only** aim, but **also** to consider what virtue and power may lie in **it for** medicine."

Acknowledgements

Useful slides and input from:
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