Particles and radioactive nuclei in medicine

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Outline

- Sensitive medical diagnosis with
  - Radioactive nuclei
  - Particle detectors

- Selective cancer treatment with
  - Radioactive nuclei
  - Accelerated particles = hadron therapy

Medical diagnosis

- Use sensitivity of particle and radiation detection

- Diagnosis with radioactive nuclei:
  - Radioactive nucleus usually connected chemically to a biological ‘ligand’
  - ‘ligand’ finds areas to be diagnosed: sugars go to cells that need energy, e.g cancer
  - Emitted radiation shows the localisation of the interesting region
  - Efficient particle detectors detect very low unharmful nM or pM concentrations

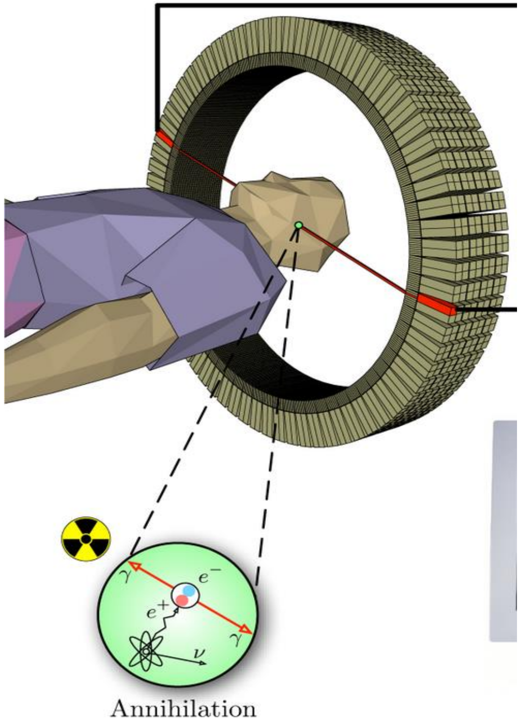
- Suitable isotopes:
  - Isotope of element that can bind to biological ligands
  - Lifetime long enough for delivery and short enough for a body: hours to days
  - Right type of radiation and its energy

- Detection: radiation not particles, because it gets stopped less in the body
  - Gamma rays from decay or annihilation of emitted beta+ particle

- Approaches (nuclear medicine):
  - PET
  - SPECT

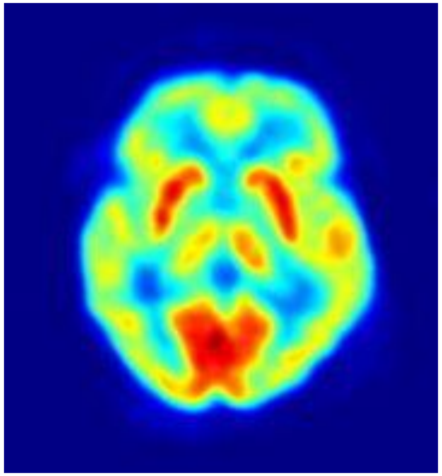
PET: Positron emission tomography

- Signal from beta+ (positron) emitting nuclei
  - Emitted positron stops after travel of some mm in tissue
  - Positron = antimatter, so it annihilates with an electron from a neighbouring molecule (E=mc2)
  - 2 gamma rays of 511keV are emitted at 180 degrees
- Detection:
  - Based on time and position of hits in detectors, place of annihilation is identified



PET

- Some of 1st PET isotopes in the world were produced at ISOLDE and later investigated together with the creators of the PET technique at the Geneva Hospital



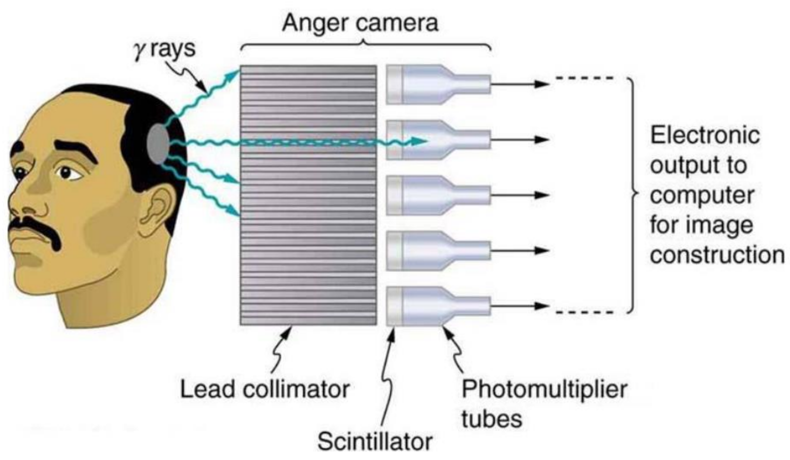
- Strengths:
  - Extremely sensitive

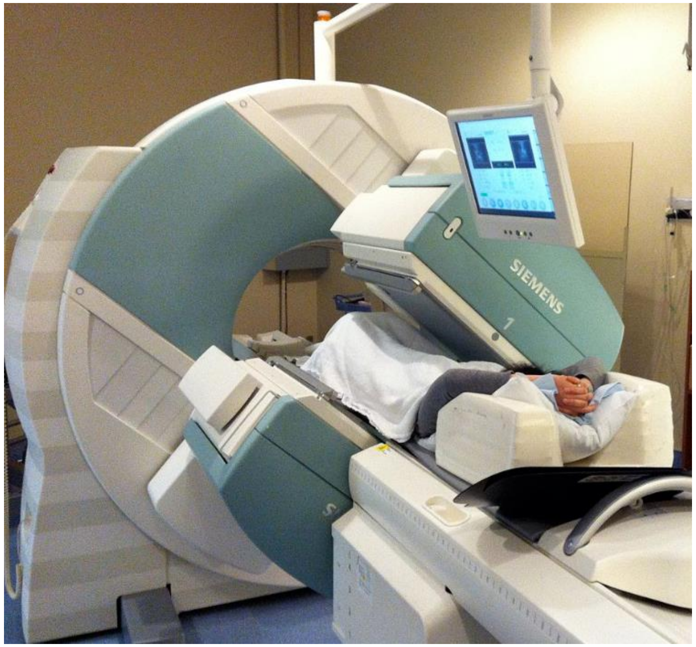
- Relative weaknesses:
  - Time resolution of detectors crucial -> can pinpoint annihilation location better
  - Coincidence between 2 gammas: relatively complex machine and event reconstruction
  - Positron can travel several mm before annihilating: limit in resolution

SPECT: Single photon emission computed tomography

- Signal from gamma-emitting nucleus
  - Direct gamma emission from nuclear isomeric state
  - Gamma emission following beta decay

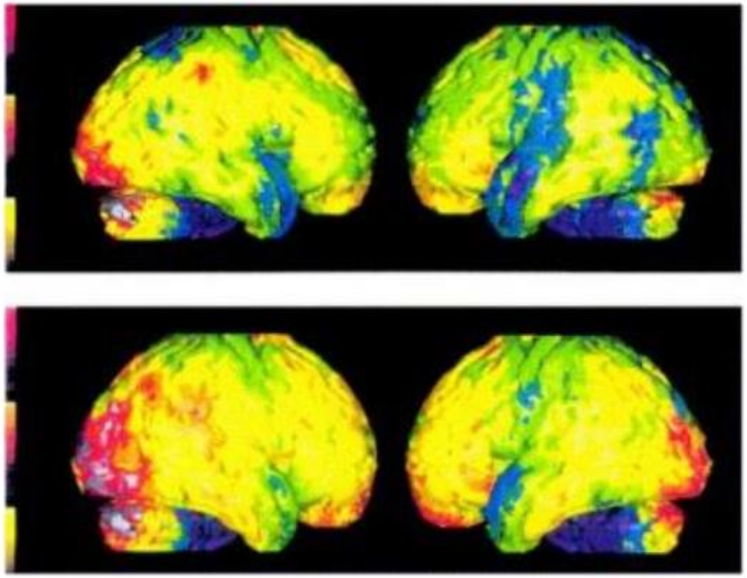
- Detection:
  - Collimated gamma detectors determining direction from which came gammas
  - 3D image reconstructed based on number of counts behind each collimator





SPECT

- Isotopes:
  - Relevant t1/2
  - Emission of easily detectable gamma rays
- Strengths:
  - Less complex than PET
  - Still rather sensitive
- Relative weaknesses:
  - Less sensitive than PET (collimation)



Detectors for medical diagnosis

New 511-keV **PET detectors** from fundamental research:

- Detectors with ns and ps time resolution - better localisation:
    - As in ATLAS tracer: monolytic Si detector – TT-PET project, Uni Geneva
    - Fast scintillating crystals from CMS: CrystalClear at CERN
    - As in nuclear fast timing: U Complutense Madrid

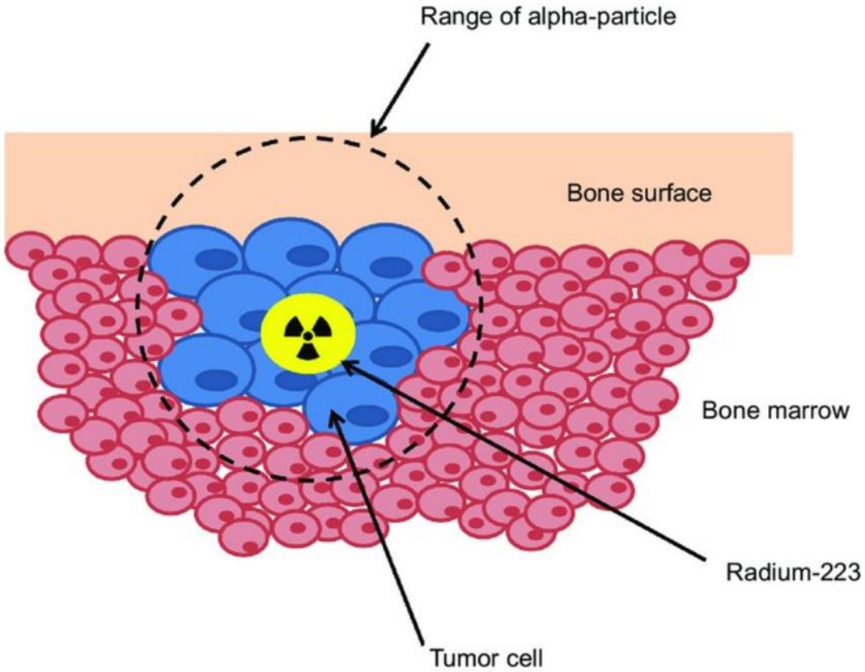
- Cheaper materials:
    - Organic scintillators: J-PET in Krakow

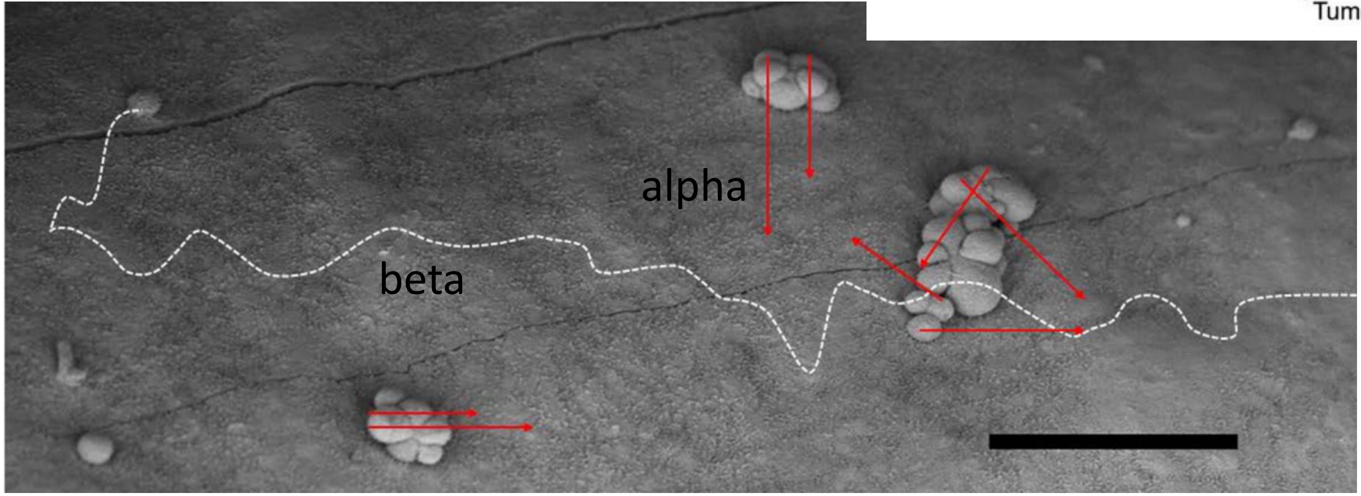
More sensitive **x-ray detectors**:

- MEDIPIX segmented detector from CERN

Cancer treatment with radionuclei

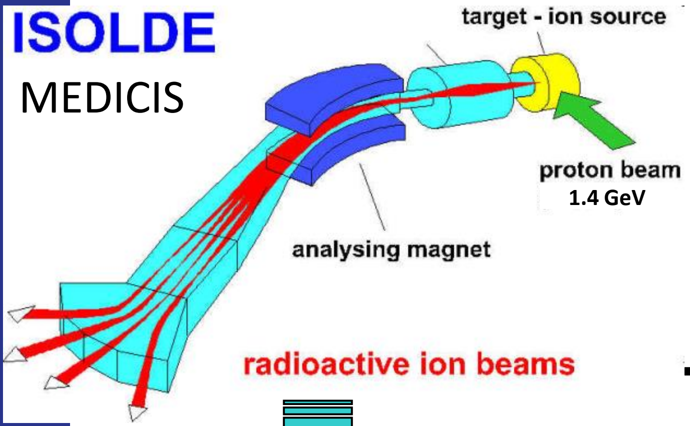
- Treatment via cell (mostly DNA) damage:
  - High dose beta radiation
  - Alpha radiation: heavier, so shorter range but higher lethality
- Isotope delivery to cancer – as in diagnosis: connection to ligand
- Isotope:
  - Suitable half-life
  - Alpha emission





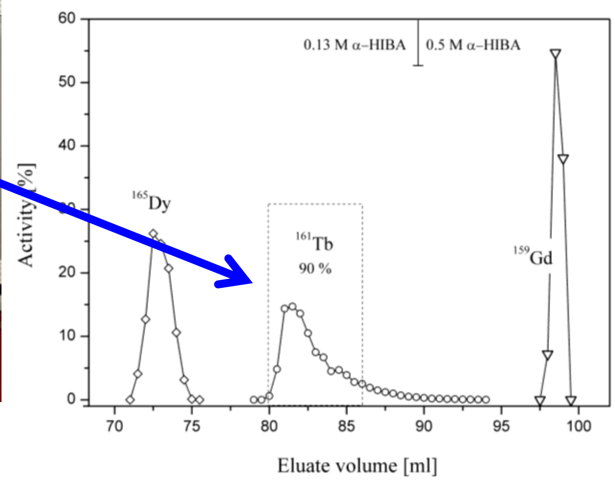
New medical isotopes

i. Collection at ISOLDE



ii. Shipping to PSI

iii. Radiochemical purification and labeling



iv. Injection into mouse

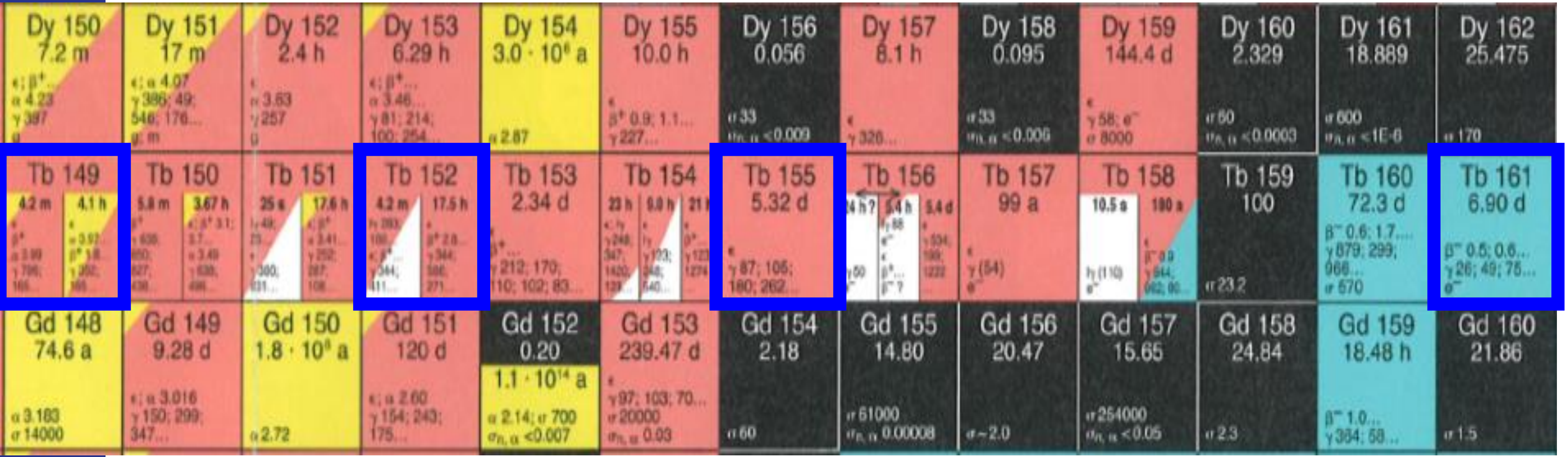
v. PET/SPECT imaging and tumor treatment

After U. Koster

C Müller et al. 2012 J. Nucl. Med. 53 1951

Theranostics

- Theranostics = therapy and diagnostics together
  - One isotope does diagnosis
  - Another isotope of the same element: treatment
- At ISOLDE and Medicis

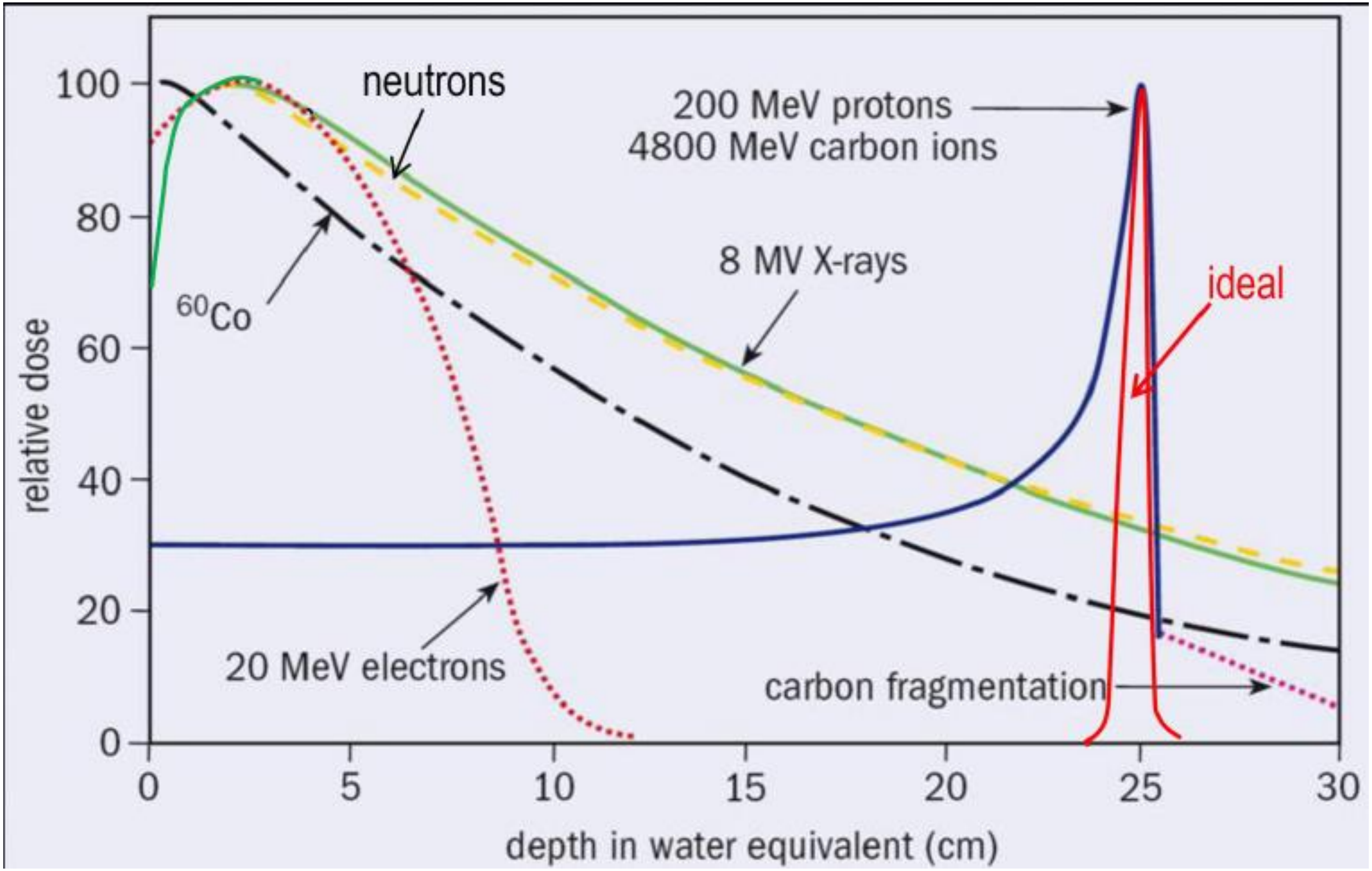


Dy 150 7.2 m	Dy 151 17 m	Dy 152 2.4 h	Dy 153 6.29 h	Dy 154 $3.0 \cdot 10^6$ a	Dy 155 10.0 h	Dy 156 0.056	Dy 157 8.1 h	Dy 158 0.095	Dy 159 144.4 d	Dy 160 2.329	Dy 161 18.889	Dy 162 25.475
Tb 149 4.2 m 4.1 h	Tb 150 5.8 m 3.67 h	Tb 151 25 s 17.6 h	Tb 152 4.2 m 17.5 h	Tb 153 2.34 d	Tb 154 23 h 9.0 h 21 h	Tb 155 5.32 d	Tb 156 24 h? 5.4 h 5.4 d	Tb 157 99 a	Tb 158 10.5 s 180 a	Tb 159 100	Tb 160 72.3 d	Tb 161 6.90 d
Gd 148 74.6 a	Gd 149 9.28 d	Gd 150 $1.8 \cdot 10^6$ a	Gd 151 120 d	Gd 152 0.20 $1.1 \cdot 10^{14}$ a	Gd 153 239.47 d	Gd 154 2.18	Gd 155 14.80	Gd 156 20.47	Gd 157 15.65	Gd 158 24.84	Gd 159 18.48 h	Gd 160 21.86

After U. Koster, C Müller et al. 2012 J. Nucl. Med. 53, 1951

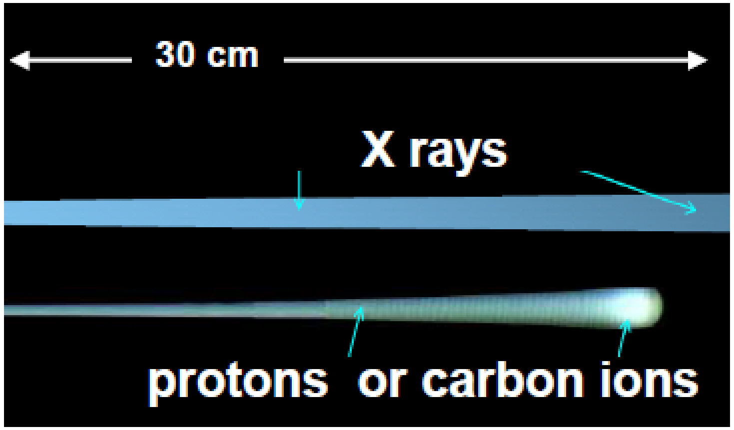
Cancer therapy with beams

- Different particles cause different damage



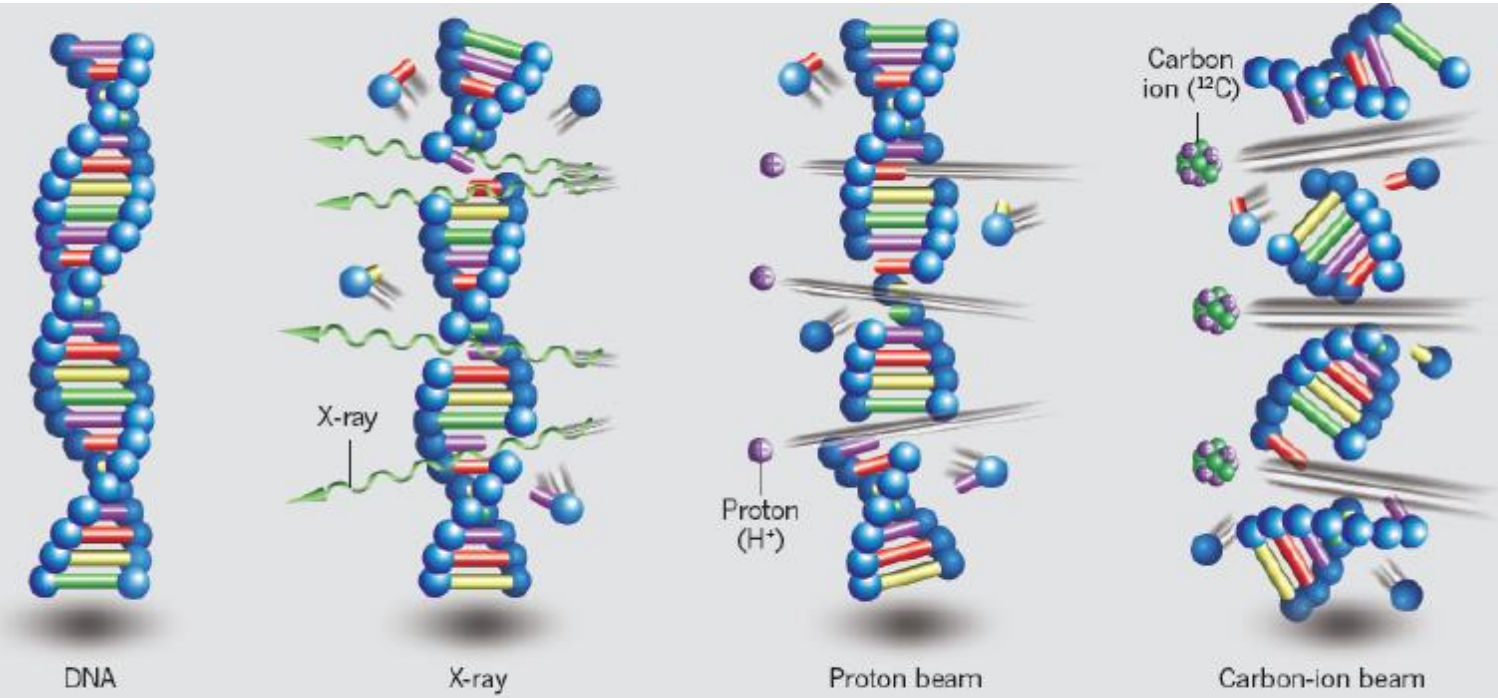
Cancer therapy with beams

- Protos and ‘heavy’ ions (> proton) are best:
  - Most energy deposited in limited space
  - More damage than other radiation



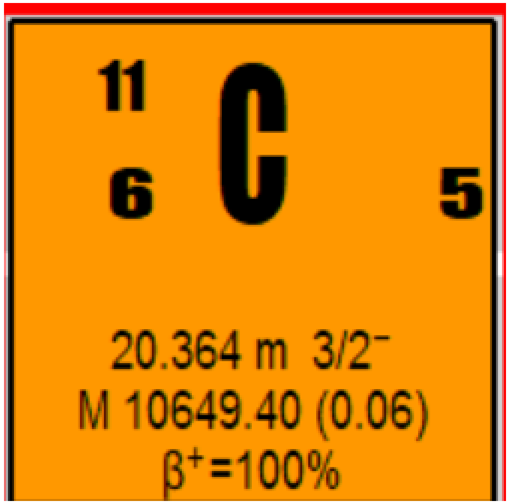
GREATEST HITS

Radiation can kill cancer cells by damaging their DNA. X-rays can hit or miss. Protons are slightly more lethal to cancer cells than X-rays. Carbon ions are around 2–3 times as damaging as X-rays.



Therapy and control at once

- New idea: implant PET isotope together with treatment beam:
  - 12C and PET nucleus together
  - Even newer: 11C for simultaneous PET and therapy at once



11 C

6 5

20.364 m $3/2^-$

M 10649.40 (0.06)

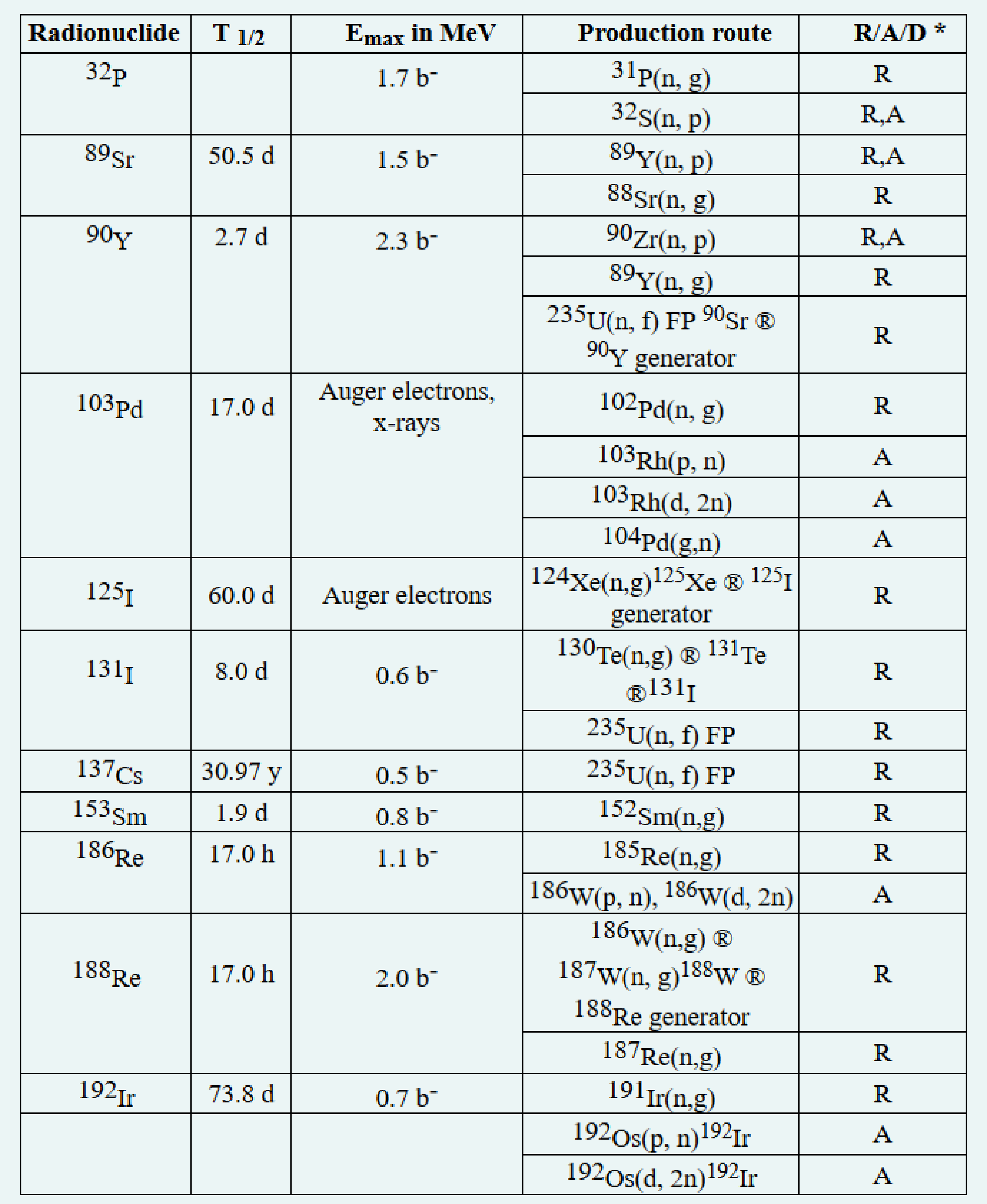
β^+=100%

Summary

- Radioactive nuclei and particle detectors can be used in very sensitive:
  - Medical diagnosis
  - Treatment of cancer

- Particle beams can be used also in treatment of cancer

common



Radionuclide	T 1/2	E_{max} in MeV	Production route	R/A/D *
^{32}P		1.7 b^-	^{31}P(n, g)	R
			^{32}S(n, p)	R,A
^{89}Sr	50.5 d	1.5 b^-	^{89}Y(n, p)	R,A
			^{88}Sr(n, g)	R
^{90}Y	2.7 d	2.3 b^-	^{90}Zr(n, p)	R,A
			^{89}Y(n, g)	R
			^{235}U(n, f) FP ^{90}Sr ® ^{90}Y generator	R
^{103}Pd	17.0 d	Auger electrons, x-rays	^{102}Pd(n, g)	R
			^{103}Rh(p, n)	A
			^{103}Rh(d, 2n)	A
			^{104}Pd(g,n)	A
^{125}I	60.0 d	Auger electrons	^{124}Xe(n,g)^{125}Xe ® ^{125}I generator	R
^{131}I	8.0 d	0.6 b^-	^{130}Te(n,g) ® ^{131}Te ®^{131}I	R
			^{235}U(n, f) FP	R
^{137}Cs	30.97 y	0.5 b^-	^{235}U(n, f) FP	R
^{153}Sm	1.9 d	0.8 b^-	^{152}Sm(n,g)	R
^{186}Re	17.0 h	1.1 b^-	^{185}Re(n,g)	R
			^{186}W(p, n), ^{186}W(d, 2n)	A
^{188}Re	17.0 h	2.0 b^-	^{186}W(n,g) ® ^{187}W(n, g)^{188}W ® ^{188}Re generator	R
			^{187}Re(n,g)	R
^{192}Ir	73.8 d	0.7 b^-	^{191}Ir(n,g)	R
			^{192}Os(p, n)^{192}Ir	A
			^{192}Os(d, 2n)^{192}Ir	A

Less common

Radionuclide	T ½	E_{max} in MeV	Production route	R/A/Decay *
^{64}Cu	12.7 h	0.6 b^- 0.7 b^+	^{63}Cu(n, g)	R
			^{64}Ni(p, n)	A
			^{64}Ni(d, 2n)	A
			^{64}Zn(n, p)	R
			^{64}Zn(d, x)	A
^{67}Cu	2.6 d	0.6 b^-	^{67}Zn(n, p)	R
			^{68}Zn(p, 2p)	A
			^{70}Zn(p, a)	A
^{67}Ga	3.2 d	Auger electrons	^{68}Zn(p,2n)	A
			^{67}Zn(p,n)	A
^{86}Y	14.74 h	b^+	^{86}Sr(p, n)	A
^{105}Rh	35.4 h	b^-	^{104}Ru(n,g)^{105}Ru ® ^{105}Rh	R
^{111}In	2.8 d	Auger electrons	^{111}Cd (p, n)	A
			^{111}Cd(p, 2n)	A
^{114m}In	2.8 d	Auger electrons	^{114}Cd (p, n)	A
			^{114}Cd(d, 2n)	A
			^{116}Cd(p, 3n)	A
^{124}I	4.2 d	2.1 b^+	^{124}Te(p, n)	A
			^{124}Te(d, 2n)	A
			^{125}Te(p, 2n)	A
^{149}Pm	2.12 d	b^-	^{148}Nd(n, g)^{149}Nd ® ^{149}Pm	R
^{166}Ho	26.8 h	1.9 b^-	^{165}Ho(n, g)	R
			^{164}Dy(n, g) ® ^{165}Dy(n, g) ® ^{166}Dy ® ^{166}Ho	R
^{169}Yb	32.0 d	Auger electrons	^{168}Yb(n, g)	R
			^{169}Tm(p, n)	A
^{177}Lu	6.7 d	0.5 b^-	^{176}Lu(n, g)	R
			^{176}Yb(n, g)^{177}Yb ® ^{177}Lu	R
^{211}At	7.2 h	5.9 a	^{209}Bi(a, 2n)	A
^{213}Bi	45.6 m	8.4 a	Decay of ^{225}Ac	D
^{225}Ac	10.0 d	5.8 a	^{226}Ra(p, 2n)	A
			decay of ^{233}U ® ^{229}Th	R,D