Argonne NATIONAL LABORATORY

Radionuclides and The Global Fight Against Cancer

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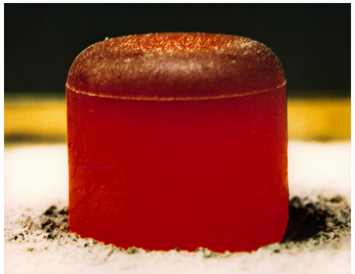
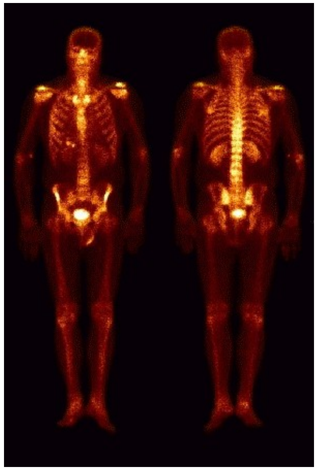
- **Stable and radioactive** isotopes play critical roles in a variety of technological applications important to modern society

  - ✓ Basic scientific research
  - ✓ Nuclear Medicine
  - ✓ Oil Industry
  - ✓ National Security and HMS
  - ✓ Power sources (e.g. nuclear batteries)
  - ✓ Tracers
  - ✓ Many (other) commercial applications





- Production of radioactive isotopes is either using a **nuclear reactor** or an **accelerator**

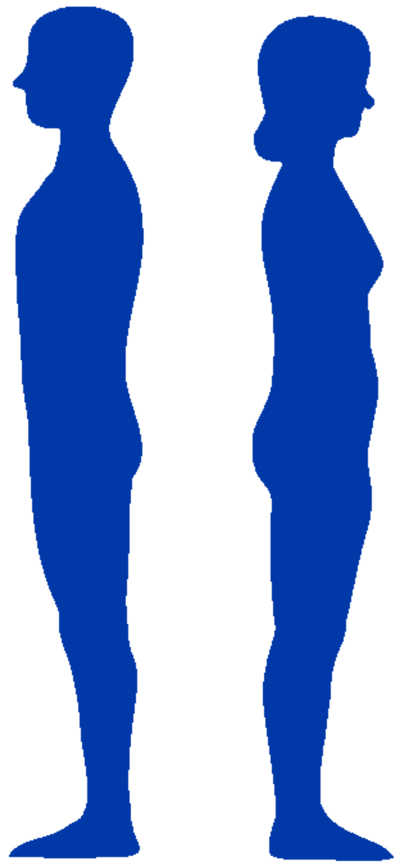
U.S. DEPARTMENT OF ENERGY

Estimated Cancer Deaths in the US in 2013 **~580000**

The second most effective killer, after the heart diseases …

Men
306,920

Lung & bronchus	28%
Prostate	10%
Colon & rectum	9%
Pancreas	6%
Liver & intrahepatic bile duct	5%
Leukemia	4%
Esophagus	4%
Urinary bladder	4%
Non-Hodgkin lymphoma	3%
Kidney & renal pelvis	3%
All other sites	24%



Women
273,430

26%	Lung & bronchus
14%	Breast
9%	Colon & rectum
7%	Pancreas
5%	Ovary
4%	Leukemia
3%	Non-Hodgkin lymphoma
3%	Uterine corpus
2%	Liver & intrahepatic bile duct
2%	Brain/other nervous system
25%	All other sites

Source – American Cancer Society, 2013

Main cancer treatments

- Surgery
- Chemo-, Bio- and Immuno- therapies
- Transplantation
- Cancer vaccines, hyperthermia, etc.
- **Radiation therapy**
  - ✓ using particle accelerators - n, e-,p & HI (hadron)
  - ✓ **using radioisotopes**

Why Radioisotopes are useful?

❑ Diagnostic (imaging):

- ✓ tumors
- ✓ aneurysms (weak spots in blood vessel walls)
- ✓ irregular or inadequate blood flow to various tissues
- ✓ blood cell disorders and inadequate functioning of organs, such as thyroid and pulmonary function deficiencies

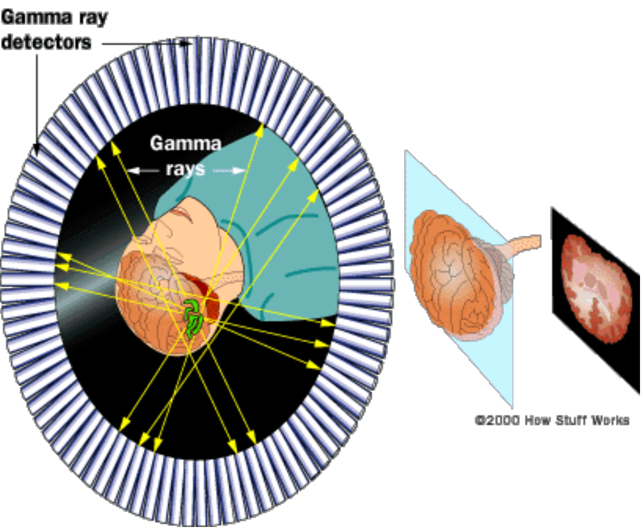
❑ Therapeutic:

- ✓ using radiation (α, β and Auger e-) to kill cancer cells (tumors)

Diagnostic - PET

emission of two 511-keV gamma rays following β+ decay

proton-rich nuclei



short-lived: ^{18}F, ^{11}C, ^{13}N, ^{15}O

generators: ^{68}Ge/**^{68}Ga**, ^{82}Sr/**^{82}Rb**

long-lived: ^{44}Sc, ^{64}Cu, ^{76}Br, ^{86}Y, ^{124}I

^{18}F PET-CT: to identify and localize high-risk coronary plaque

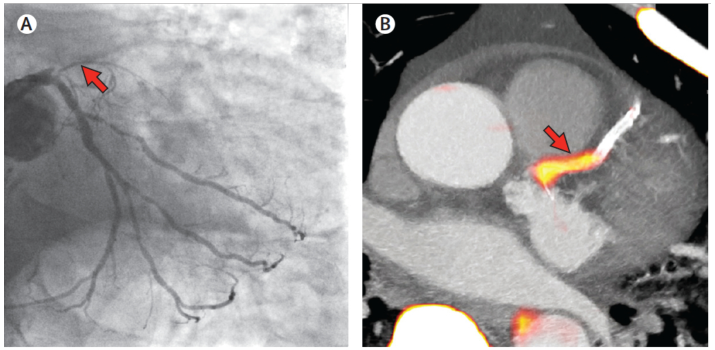
N.V. Joshi et al., The Lancet, http://dx.doi.org/10.1016/S0140-6736(13)61754-7

BBC

10 November 2013 Last updated at 20:14 ET

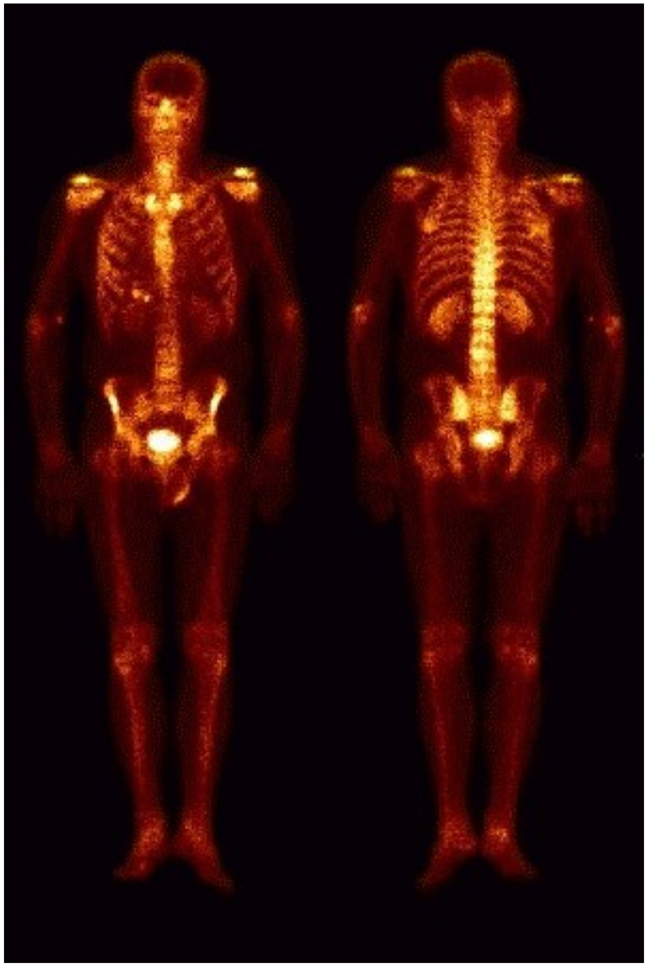
Heart attack risk identified by new scan

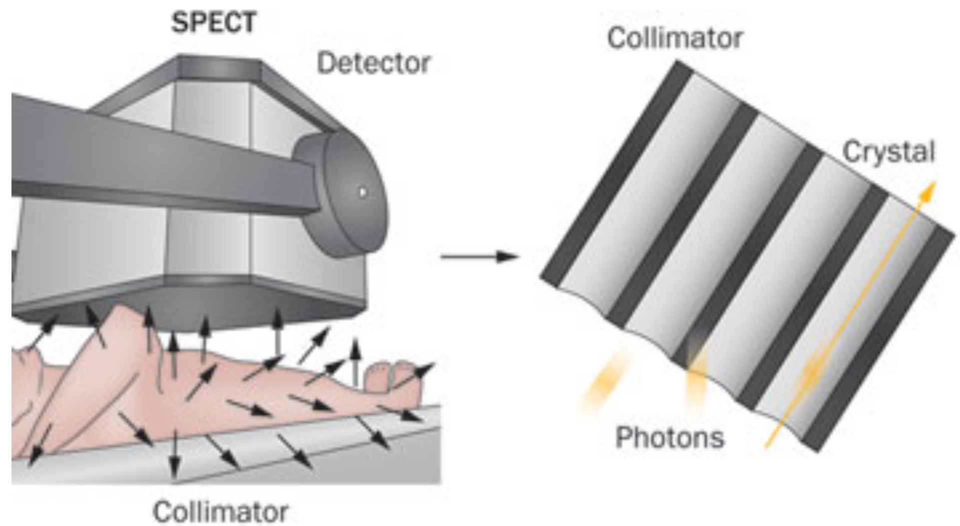
By James Gallagher
Health and science reporter, BBC News



Diagnostic – Gamma Cameras & SPECT

2D (Gamma cameras) & 3D (SPECT): using low energy gamma rays





.. but also novel detector technology for better position resolution

^{99m}Tc (141 keV), ^{67}Ga (185 keV), ^{111}In (171 keV), ^{123}I (159 keV), ^{133}Xe (81 keV), ^{201}Tl (70 keV)

Therapeutic

α emitters:

E=5-9 MeV; R=40-100 μm (5-10 cell diameter);

LET 80-100 keV/μm along the trace path

^{211}At, ^{212}Bi, ^{213}Bi, ^{225}Ac

β– emitters:

E=50 keV-2 MeV; R=50 μm – 12 mm;

LET 0.2 keV/μm

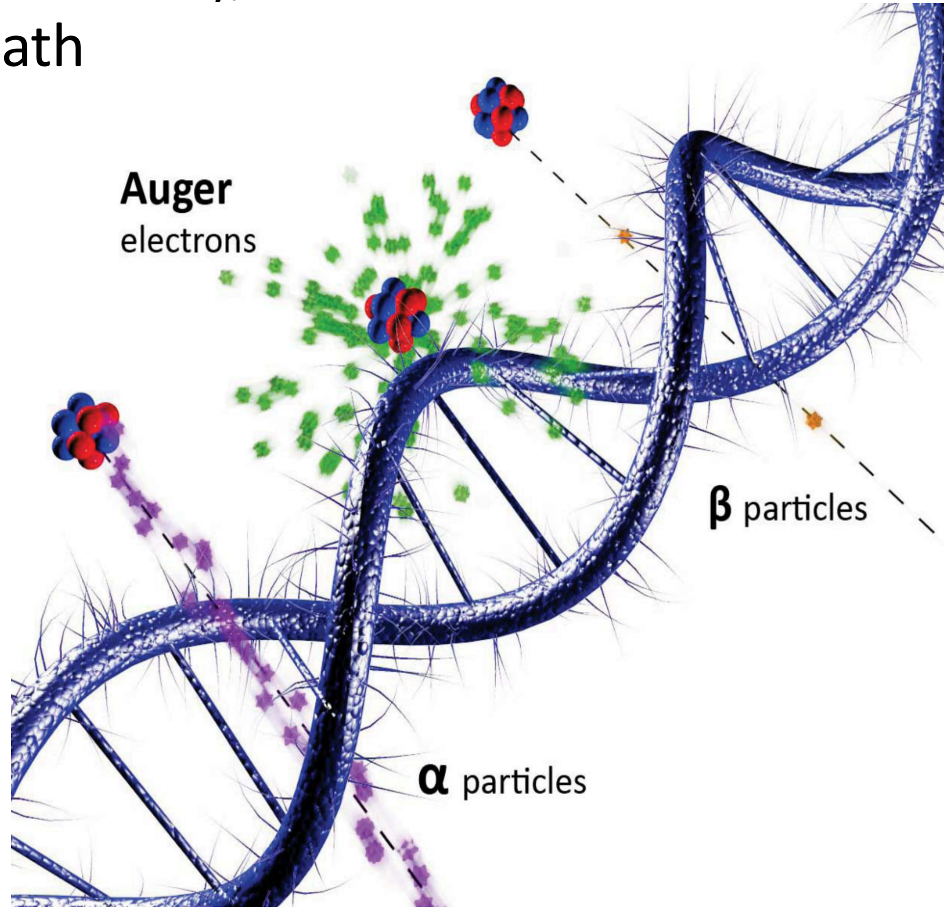
^{32}P, ^{89}Sr, ^{90}Y, ^{131}I, ^{166}Ho, ^{177}Lu, ^{186}Re

Auger emitters:

E=10 eV-10 keV; R=5 – 500 nm;

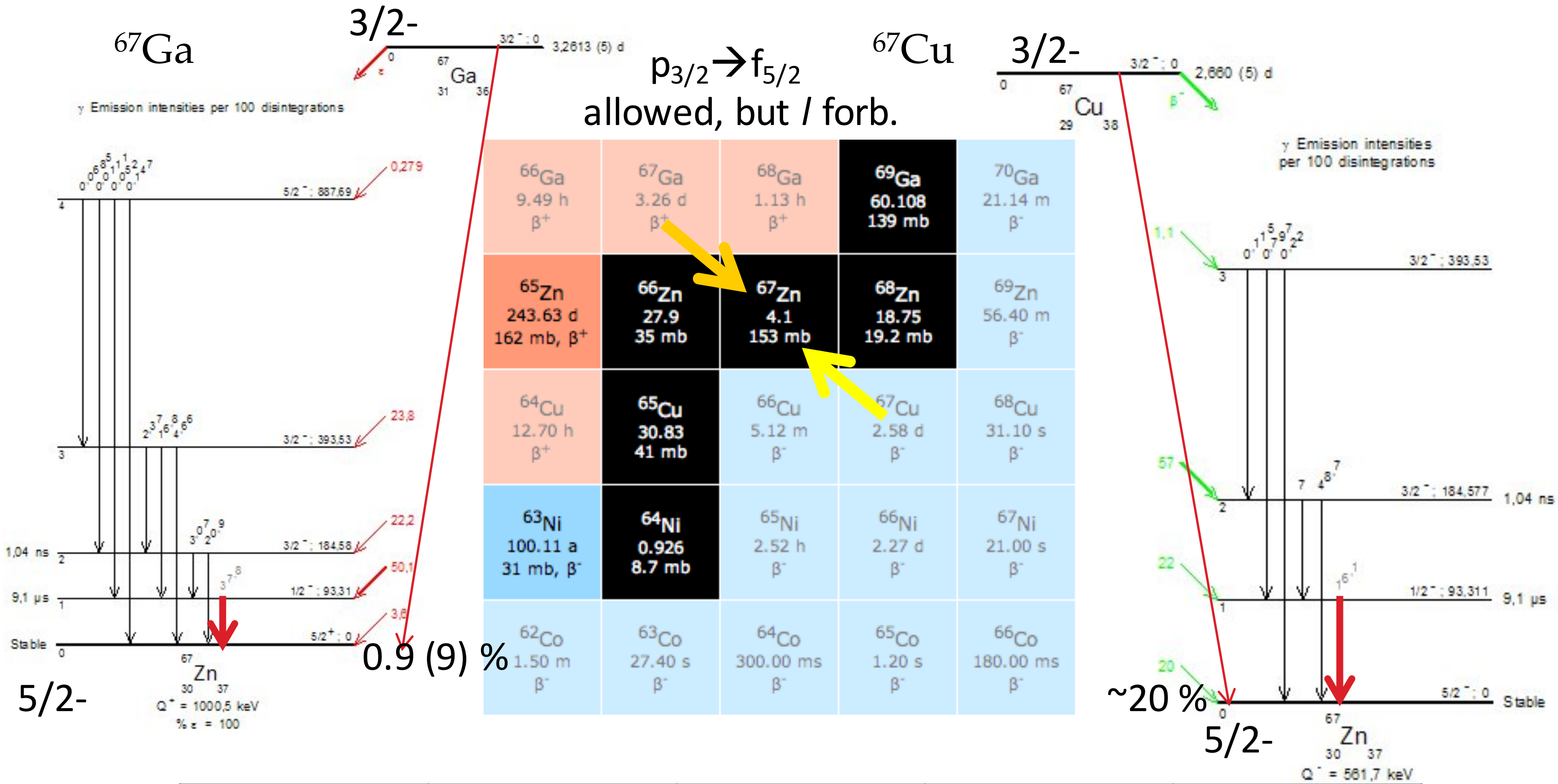
LET 4-26 keV/μm

^{111}In, $^{123,125}I$, ^{67}Ga, ^{193m}Pt



A. Kasis et al., J. Nucl Med. 46 (2005) 3s

^{67}Cu and ^{67}Ga examples



93 keV	ToI	ENSDF	NuDat	DDEP
^{67}Ga	39.2 (10)	38.81 (3) (0.9 (9) %)	38.81 (3)	38.1 (7) (3.6 (20) %)
^{67}Cu	16.1 (2)	16.1 (2) (~20 %)	16.1 (2)	-

Matching Pairs

Diagnostic	Pair	Therapeutic
^{99m}Tc (SPECT)	**^{99m}Tc/^{188}Re**	**^{188}Re ($\beta-$)**
^{123}I (PET)	^{123}I/^{131}I	^{131}I ($\beta-$)
^{124}I (SPECT)	^{124}I/^{131}I	^{131}I ($\beta-$)
^{111}In (SPECT)	^{111}In/^{90}Y	^{90}Y ($\beta-$)
^{86}Y (PET)	^{86}Y/^{90}Y	^{90}Y ($\beta-$)

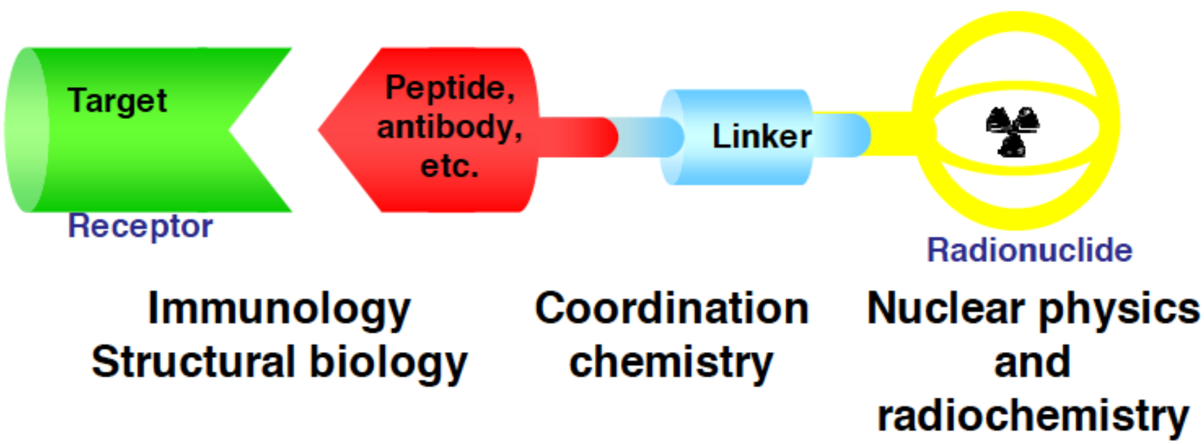
some of the therapeutic radionuclides emit γ rays that can be used for diagnostic (SPECT): ^{177}Lu, ^{186,188}Re & most of the Auger emitters

Which are the best isotopes?

- Nuclear Physics properties
  - ✓ half-life
  - ✓ decay energies & emission probabilities
  - ✓ production and availability (cost)

- Chemical, Biological and other properties

Targeted radionuclide therapy



Nuclear Data needs

- cross sections for various production reactions – neutrons, charged particles, photons
- decay data
  - ✓ important for cross-sections measurements
  - ✓ important for a specific medical application, e.g. imaging, diagnostic, treatment, etc.
- data associated with atomic radiations produced in radioactive decays - Auger, Coster-Kronig & super-Coster-Kronig and other shake-off electrons

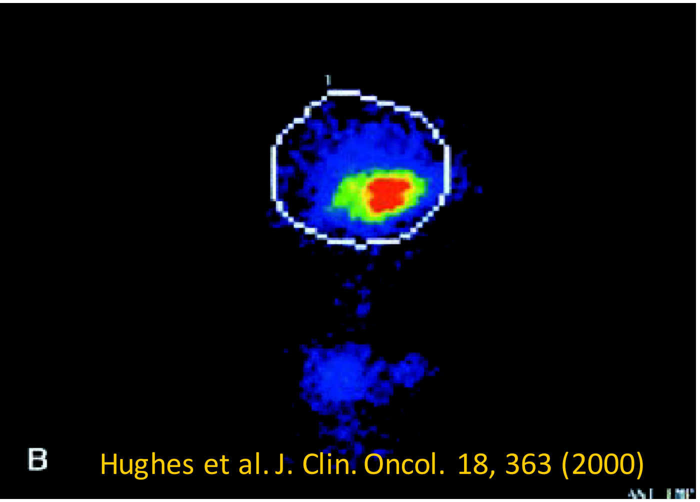
Decay Data needs – cont.

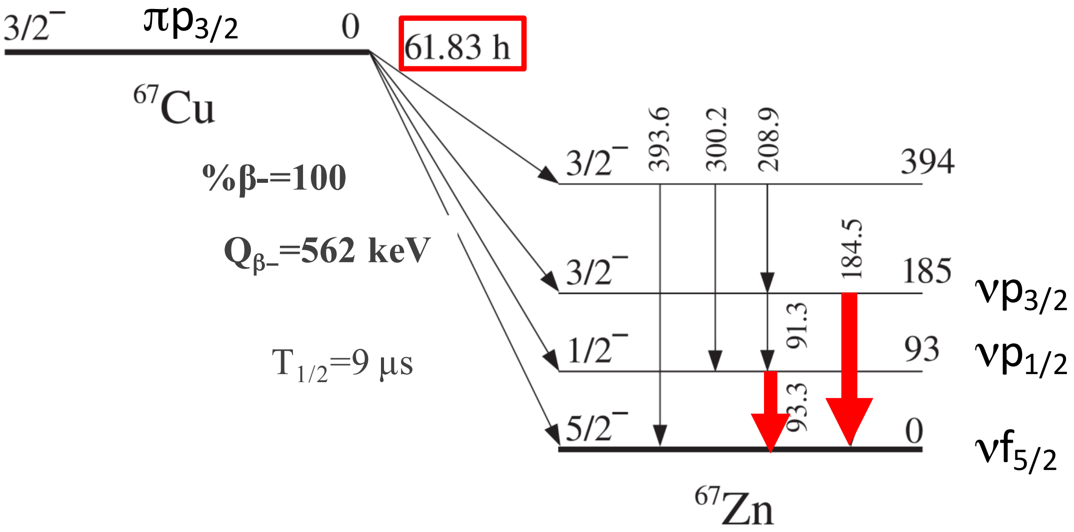
- **Q values –** AME – new tables coming by the end of this year

- **Lifetime (**evaluated) – in most cases under control (except ^{186m}Re for example), but there is no consistency (recipe) between different evaluations

- **Emission energies & probabilities (γ, β–,β+,α, EC, CE, Auger electrons) and relevant spectra**
  - ✓ must know the decay scheme - Ex, J^{π}, mult. (parent-daughter)
  - ✓evaluated data: energies and emission probabilities & δ (for γ's) - usually several measurements, except for **g.s. to g.s β decay** – treatment of discrepant data
  - ✓ CE data – usually from BrIcc, but when mult. are not known or E0?
  - ✓derived data: atomic radiation, EC/B+ ratios, β–decay energies and emission probabilities

Why ^{67}Cu?





- Excellent NP properties: $T_{1/2}$, E_γ & $\langle E_{\beta-} \rangle$
  - ✓ therapeutic: β– emitter
  - ✓ diagnostic (SPECT): 93 keV & 184 keV γ rays
  - ✓ matching pair: ^{64}Cu(PET)/^{67}Cu
- Well suited biological properties & well understood chemistry
- Main issues – production & cost
- ✓ availability is limited
- ✓ $295/mCi DOE-NIDC – 4 doses x 65 mCi = 260 mCi = $77K

^{67}Cu production

Review

Applied Radiation and Isotopes 70 (2012) 2377–2383

The production, separation, and use of ^{67}Cu for radioimmunotherapy: A review

Nicholas A. Smith [a,*], Delbert L. Bowers [a], David A. Ehst [b]

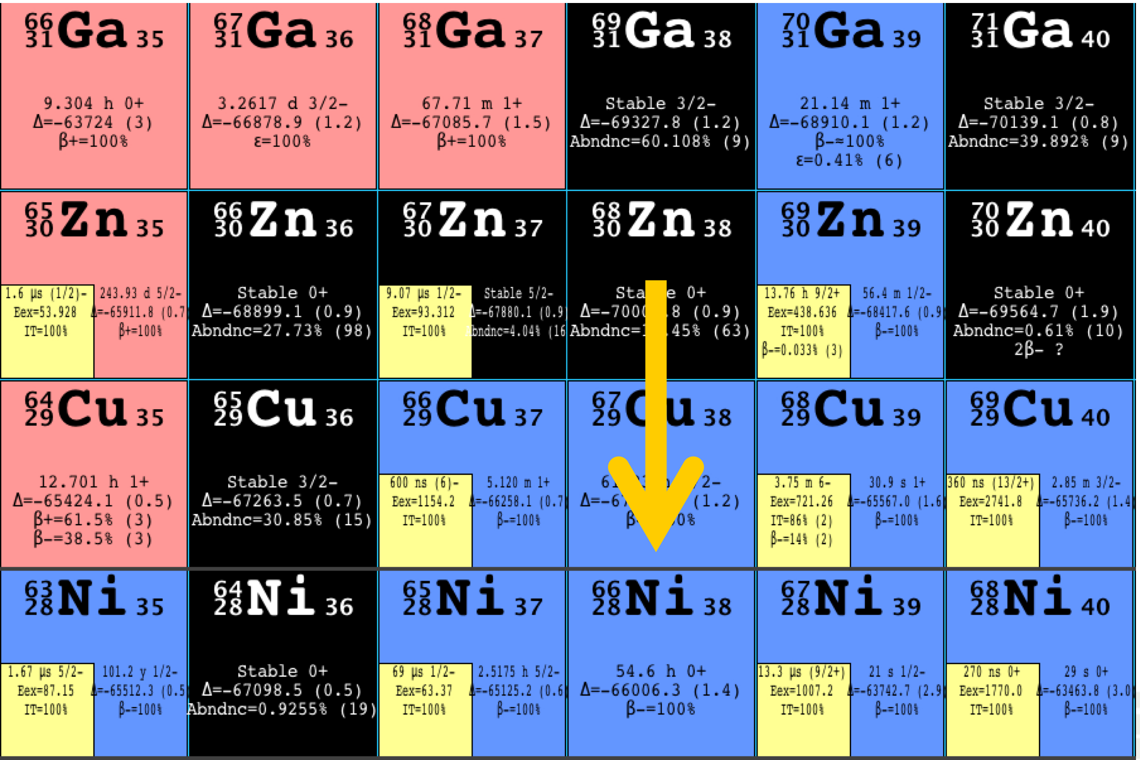
[a] Chemical Sciences and Engineering Division, Argonne National Laboratory, Argonne, IL 60439, USA

[b] Nuclear Engineering Division, Argonne National Laboratory, Argonne, IL 60439, USA

^{67}Zn (4.1%)

^{70}Zn (0.62%)

^{64}Ni (0.93%)



^{67}Zn(n,p) – ~1.2 mb

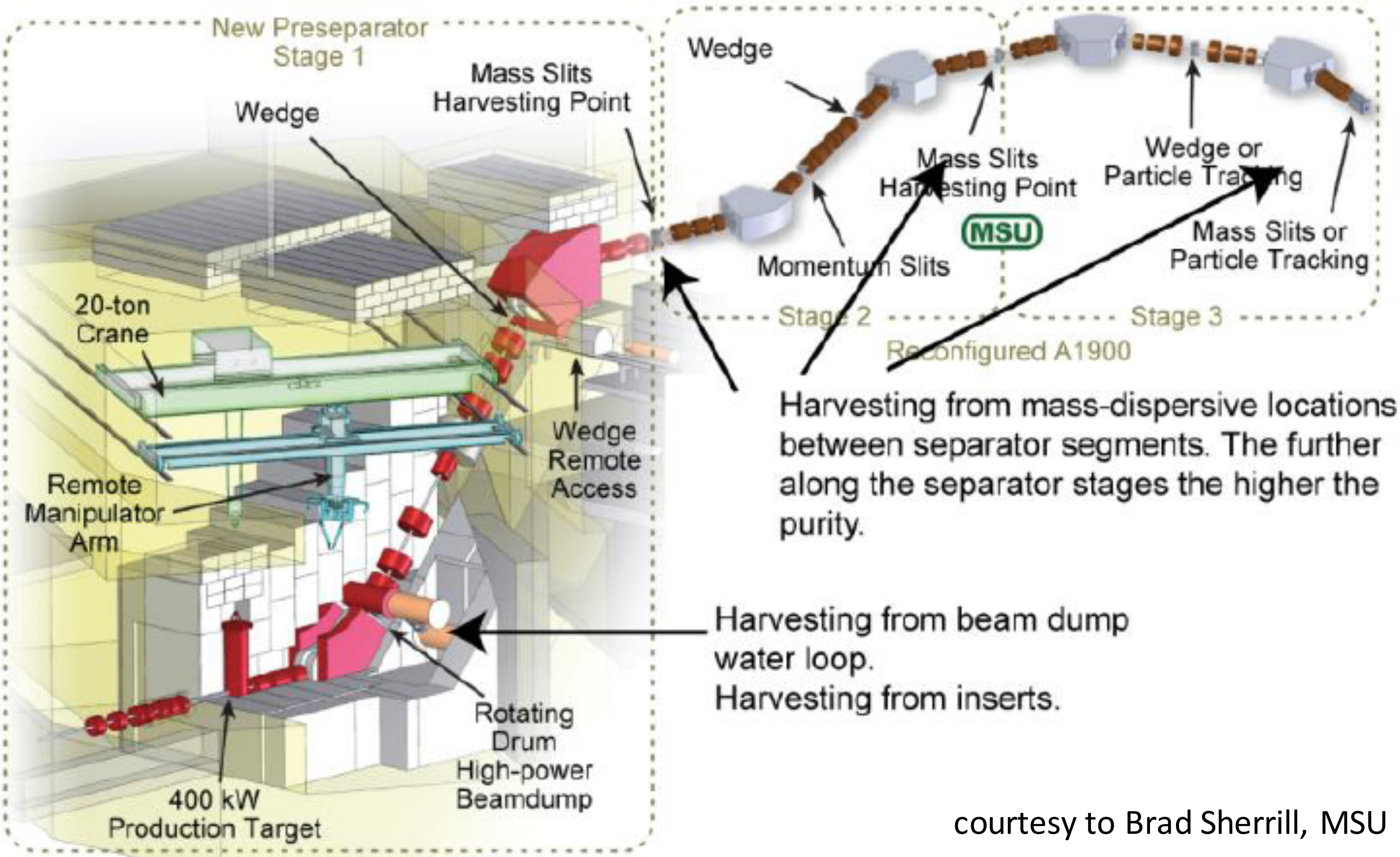
^{70}Zn(p,α) – ~14 mb

^{64}Ni(α,p) – ~25 mb

^{68}Zn(p,2p) – ~25 mb

^{68}Zn(γ,p) – ~10 mb

Isotopes Harvesting at FRIB



courtesy to Brad Sherrill, MSU

Selected Examples …

Nuclide	Primary User	Mass Slits +	Near Dump *	In Dump #
Mg-28	700 mCi/d	Not likely	20 mCi/d	7 mCi/d
Si-32	.063 mCi/d, 23 mCi/y	0.1 mCi/w	0.01 mCi/d	1 mCi/y
Ti-44	10 mCi//y	0.1 mCi/w	0.1 mCi/y	0.1 mCi/y
Cu-67	2000 mCi/d	100 mCi/d	100 mCi/d	100 mCi/d
Mo-99				1500 mCi/d

+ Collection at slits might be available 1 week per year

* The near dump rates are an approximate average of production from favorable beams on the beam list. This production should be available around 40 days/year

This assumes a ^{238}U primary beam and would be available around 150 days/year. Higher yields would come from other primary beams, so the values could be higher.

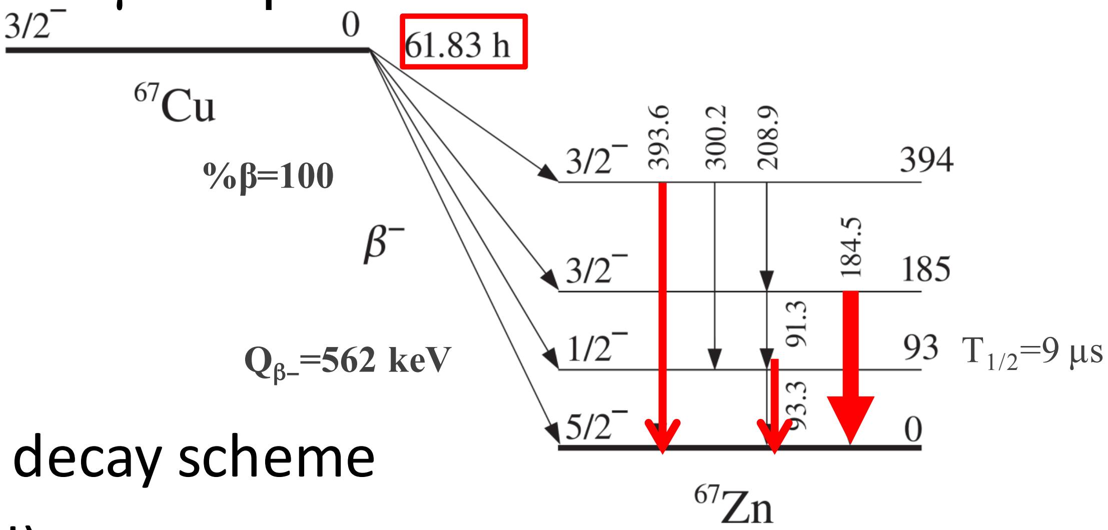
courtesy to Brad Sherrill, MSU

What do we need to know about ^{67}Cu?

for production and dosimetry applications one needs to know absolute (per decay) emission probabilities

- ✓ measure separately absolute γ and $\beta-$

I_{γ} (%) = $(S_{\gamma}/\varepsilon_{\gamma})/(S_{\beta}/\varepsilon_{\beta})$



- ✓ measure $I_{\beta-,0}$ and use the decay scheme

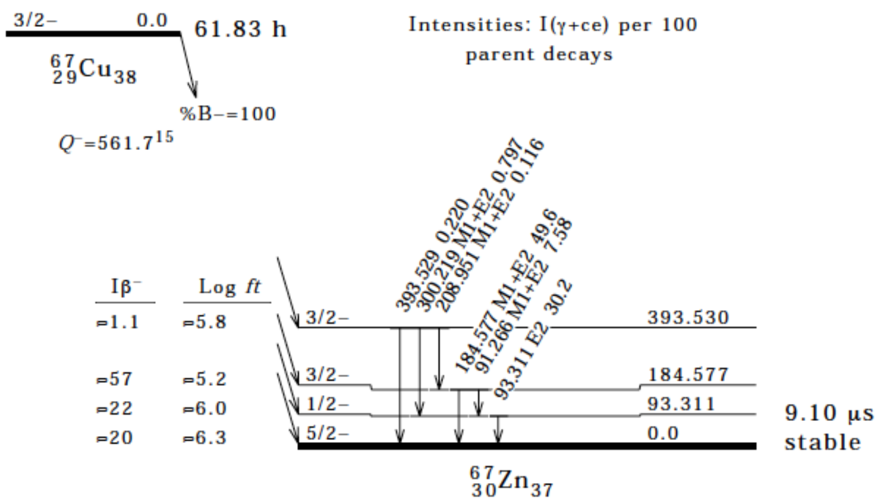
I_{γ} (%) = N x I_{γ}(rel)

$$N = (100 - I_{\beta-,0}) / \sum I_{\gamma i} \times (1 + \alpha_{Ti})$$ (all γ's that feed the gs)

Need to know: I_{γ}(rel), Mult., MR (ICC) & $I_{\beta-,0}$

Huo Junde, Huang Xiaolong, J.K. Tuli Nuclear Data Sheets 106, 159 (2005)

ENSDF & TOI99



^{67}Zn levels

E_{level}[#]	J^{π}[@]	$T_{1/2}$	Comments
0.0	5/2-	stable	
93.311 *5*	1/2-	9.10 μs *7*	$T_{1/2}$: from 1973Le18.
184.577 *6*	3/2-		
393.530 *7*	3/2-		

β⁻ Radiations

E_{β^-}	E_{level}	I_{β^-}[#]	Log *ft*	Comments
(168.2)	393.530	≈1.1	≈5.8	av Eβ=51.0 *25*
(377.1)	184.577	≈57	≈5.2	av Eβ=121 *3*
(468.4)	93.311	≈22	≈6.0	av Eβ=154 *3*
(561.7)	0.0	≈20	≈6.3	av Eβ=189 *3*

I_{β^-}: from 1953Ea11.

I_γ **Normalization:** Based on a g.s. β⁻ branching of ≈20% (1953Ea11) and 10% E2 for the 184γ corresponding to the δ=0.34 4 derived from the ce data of 1966Fr12.

E_γ[@]	E_{level}	I_γ[#@]	Mult.[&]	δ[&]	α	Comments
91.266 *5*	184.577	7.0 *1*	M1+E2	+0.06 *5*	0.083 *8*	α(K)exp=0.066 10(1969Li04) α(K)=0.073 *7*; α(L)=0.0076 *8*
93.311 *5*	93.311	16.1 *2*	E2		0.873	α(K)exp=0.77 8(1966Fr12) α(K)=0.751; α(L)=0.0920
184.577 *10*	184.577	48.7 *3*	M1+E2	0.34 *4*	0.0180 *13*	α(K)exp=0.0156 10(1966Fr12) α(K)=0.0158 *11*; α(L)=0.00165 *12* **δ:** from α(K)exp+α(L1)exp=1.72×10-2 10(1966Fr12).
208.951 *10*	393.530	0.115 *5*	M1+E2	-0.034 *21*	0.00913 *6*	α(K)=0.00804 *6*; α(L)=0.00082
300.219 *10*	393.530	0.797 *11*	M1+E2	+0.20 *8*		
393.529 *10*	393.530	0.220 *8*				**δ:** -0.17 8 or -2.4 3 for M1+E2.

very precise ... , BUT

[#] For absolute intensity per 100 decays, multiply by 1.00.
[@] From 1978Me10.

PHYSICAL REVIEW VOLUME 91, NUMBER 3 AUGUST 1, 1953

The Radioactivity of Cu^{67}

HARRY T. EASTERDAY
Radiation Laboratory, Department of Physics, University of California, Berkeley, California
(Received March 4, 1953)

The β spectrum of Cu^{67} is found to contain three groups with maximum energies and relative intensities of 577 kev, 20 percent; 484 kev, 35 percent; 395 kev, 45 percent. Conversion electrons from 92- and 182-kev transitions were observed. These results and the absence of the 296-kev γ ray indicate that the β transitions go to the ground and first two excited states of the known Zn^{67} levels.

TABLE I. Beta and gamma rays of Cu^{67}.

	Transition energy (kev)	Relative intensity (percent)	*ft* values
Beta	577	20	6.26 (*l*-forbidden)
	484	35	5.73
	395	45	5.35
Gamma	92		
	182		

no uncertainty – the quoted value is approximate!

Relative γ–ray emission probabilities

PHYSICAL REVIEW C VOLUME 17, NUMBER 5 MAY 1978

Multiparticle configurations in the odd-neutron nuclei ^{61}Ni and ^{67}Zn populated by decay of ^{61}Cu, ^{67}Cu, and ^{67}Ga†

R. A. Meyer, A. L. Prindle, and William A. Myers*
Lawrence Livermore Laboratory, University of California, Livermore, California 94550

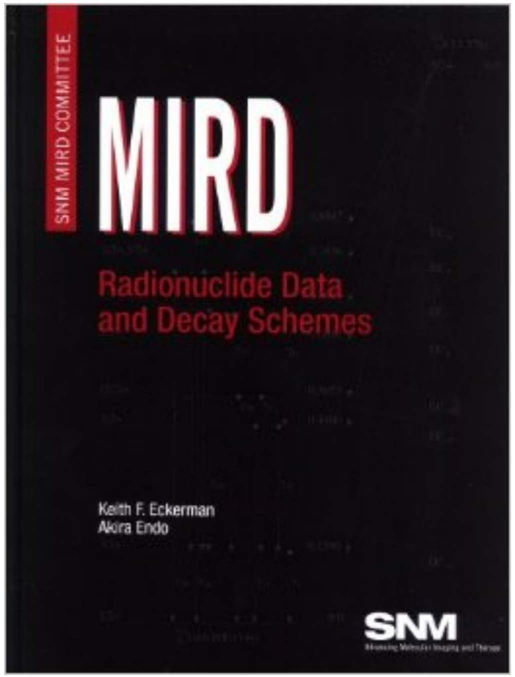
TABLE I. Energies and intensities of γ rays from decay of ^{67}Cu.

E_γ (ΔE_γ) (keV)	I_γ (ΔI_γ) (γ rays per 100 decays)[a]
91.266(5)	7.0(1)
93.311(5)	16.1(2)
184.577(10)	48.7(3)
208.951(10)	0.115(5)
300.219(10)	0.797(11)
393.529(10)	0.220(8)

[a] Based on 20% β^- feeding of the ground state (Ref. 20) and by using 12% $E2$ (Ref. 20) for the 184-keV transition.

Ground-state to Ground-state β– branch

ENSDF	**~20%**
MIRD (NNDC)	20%
MIRD (med)	20%
NUDAT	20 **(2)**%
JEFF3.1	20 **(2)**%
ENDF/B-VII.1	20 **(2)**%



Experimental details – sources

Review

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[a] *Chemical Sciences and Engineering Division, Argonne National Laboratory, Argonne, IL 60439, USA*
[b] *Nuclear Engineering Division, Argonne National Laboratory, Argonne, IL 60439, USA*

- ^{67}Cu production: ^{68}Zn(γ,p)@ 60 MeV bremsstrahlung at Rensselaer Polytechnic Institute (RPI) LINAC; enriched ^{68}Zn target
- chemical purification @ANL-CSE (N. Smith et al. ARI 70 (2012) 2392)
- source preparation @ANL-PHY - several thin (~1μCi) open sources, as well as sealed sources for relative measurements

Experimental details – cont.

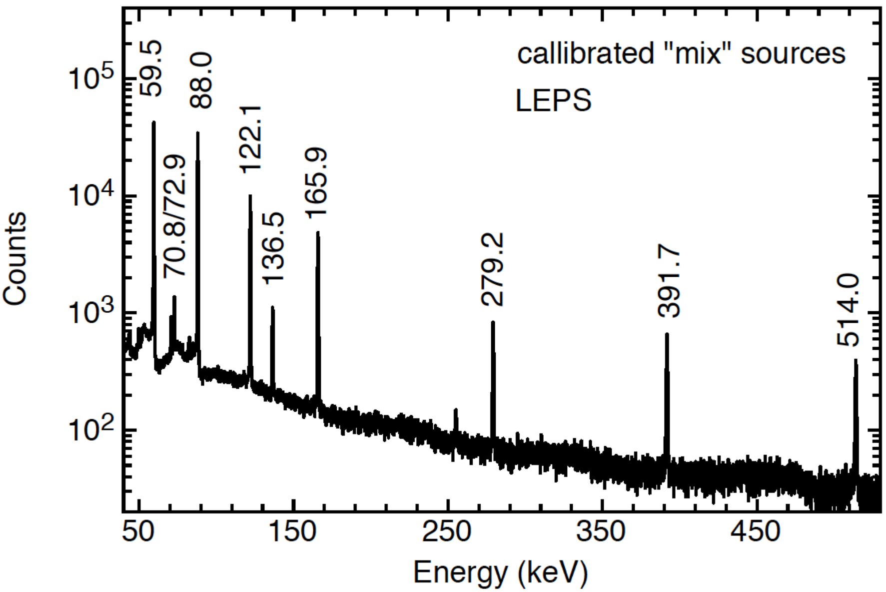
Two independent series of measurements:

- γ- and β-singles measurements using an analog (Canberra) DAQ - measure separately absolute γ and β-decay emission probabilities
- singles & β-γ coincidence measurements using a digital DAQ

- High-resolution germanium detectors
  - ✓ 2-cm^2 x 1 cm LEPS (FWHM=0.5 keV at 122 keV)
  - ✓ 25% coaxial Ge (1.8 keV at 1332 keV)

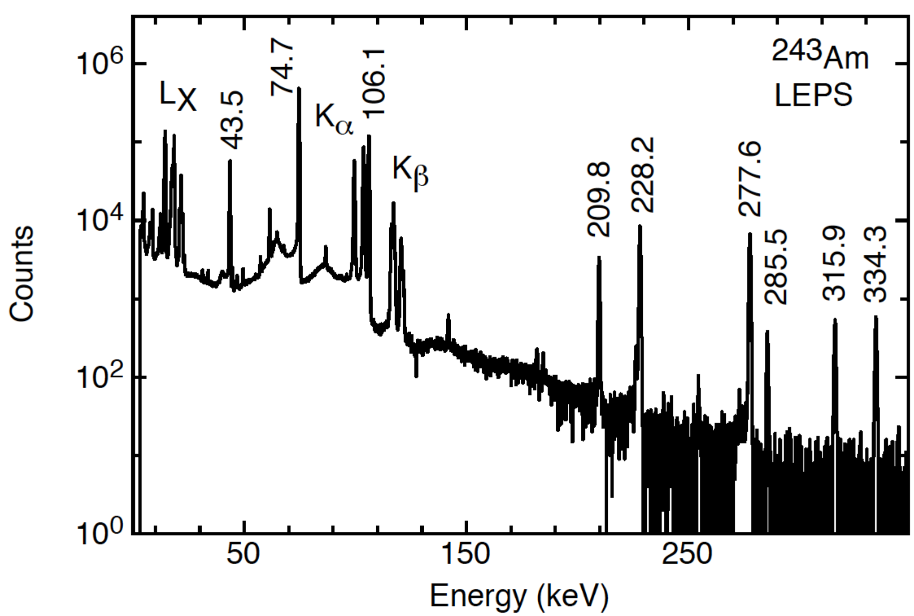
- Passivated Implanted Planar Silicon (PIPS) detector
  - ✓ 500 μm thick (singles)
  - ✓ 1 mm thick (singles & coincidence)

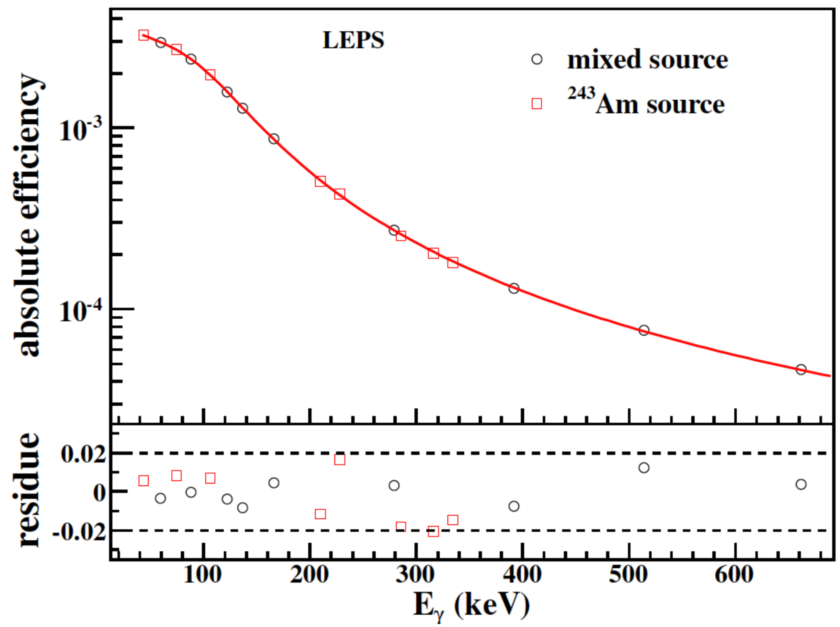
Calibration – gammas



^{57,60}Co,^{85}Sr,^{88}Y,^{109}Cd,^{113}Sn,^{137}Cs,^{139}Ce,^{203}Hg, ^{241}Am calibrated by Eckert & Ziegler

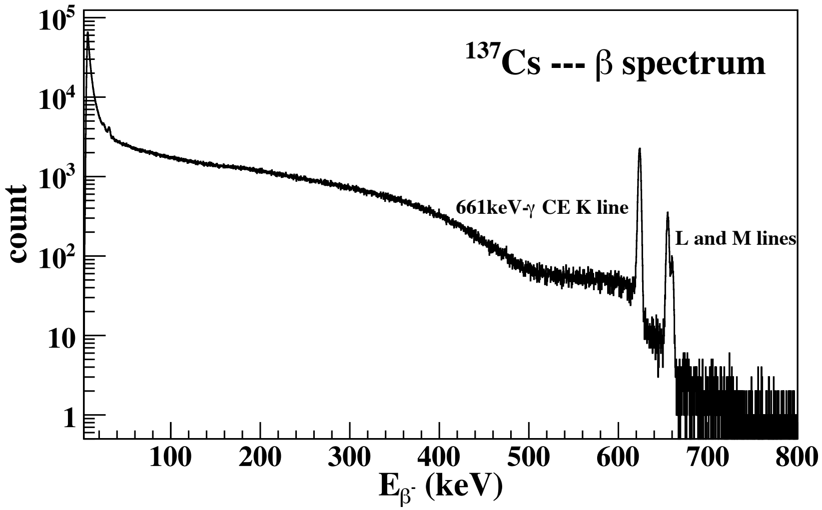
^{243}Am, ^{243}Cm, ^{249}Cf, ^{182}Ta for relative efficiency

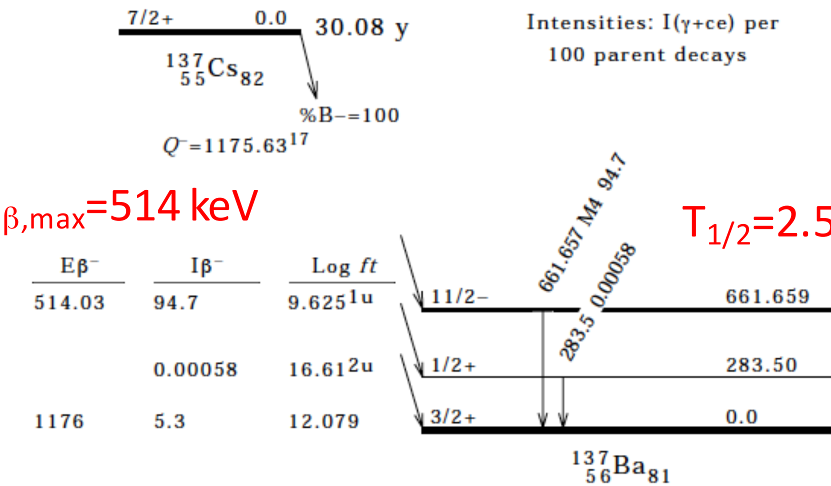




gamma-ray efficiency within 2%

Calibration – betas

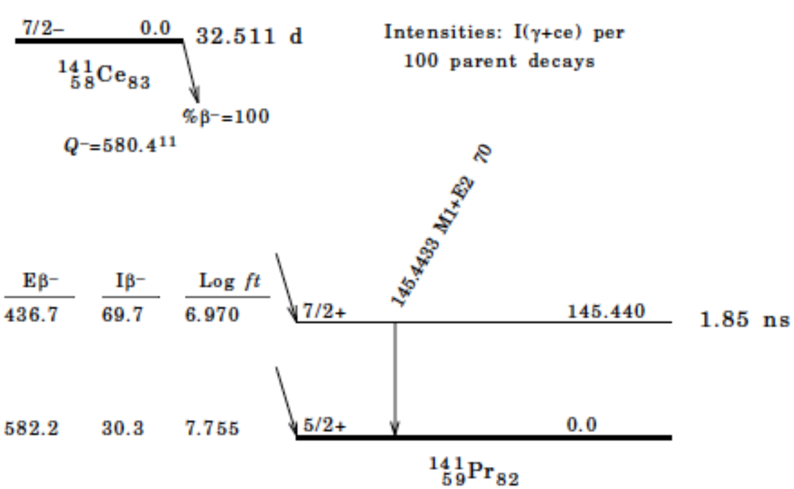


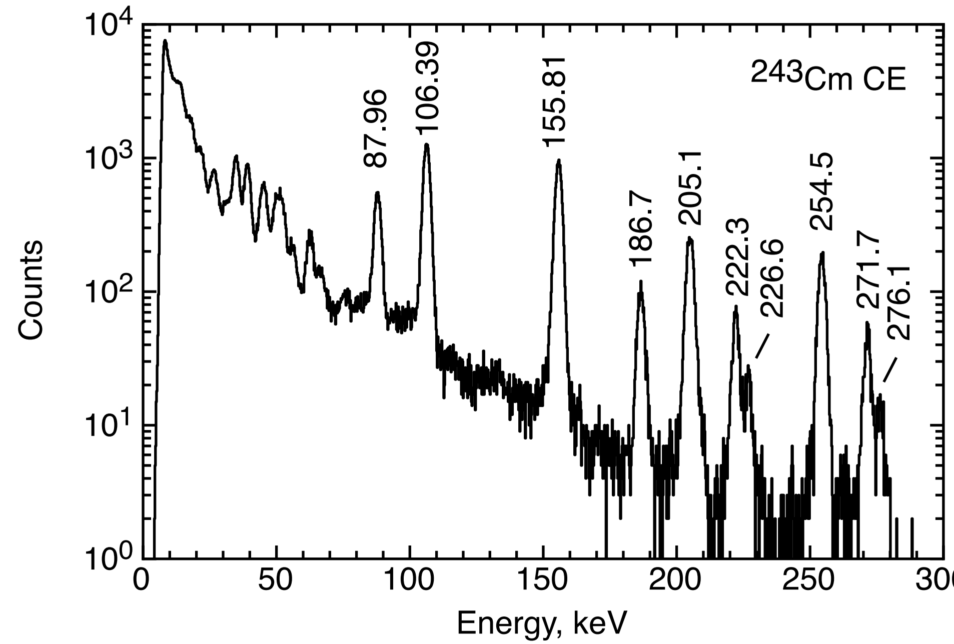


$E_{\beta,max}$=514 keV

$T_{1/2}$=2.552 m

$E_{\beta,max}$=435 keV

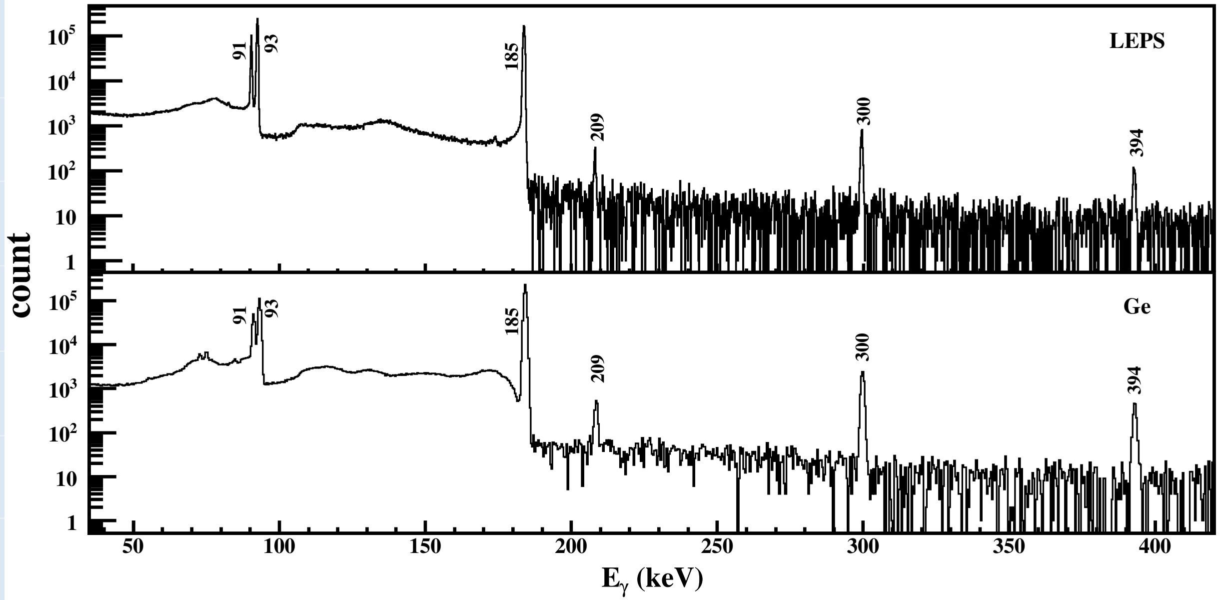




^{67}Cu results - singles

relative γ–ray intensities

E_γ (keV)	present	Meyer et al.
93	**33.5 (3)**	**33.1 (5)**
91	**14.23 (14)**	**14.37 (22)**
185	**100**	**100**
209	**0.243 (5)**	**0.236 (10)**
300	**1.68 (3)**	**1.64 (3)**
394	**0.448 (11)**	**0.452 (17)**



- ✓ consistent results between LEPS and HPGe
- ✓ very good agreement with R. Meyer et al. (LLNL)

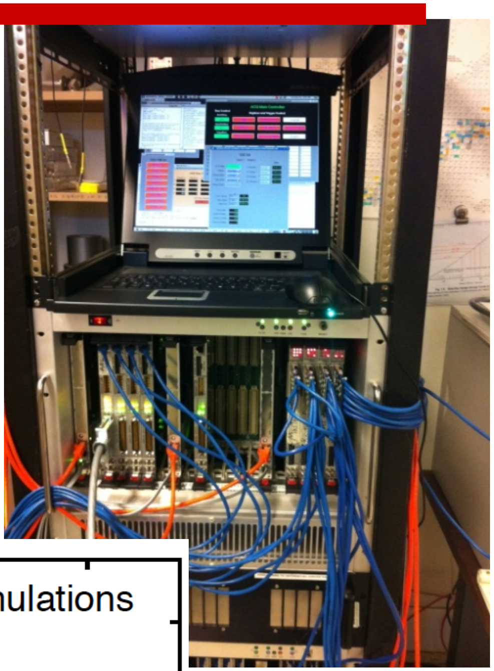
R. A. Meyer et al., Phys. Rev. C 17, 1822 (1978)

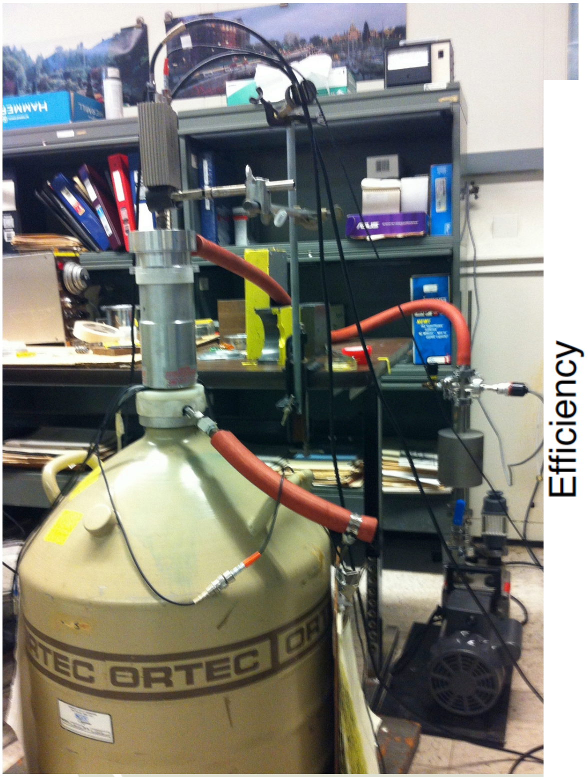
Experimental details - coincidences

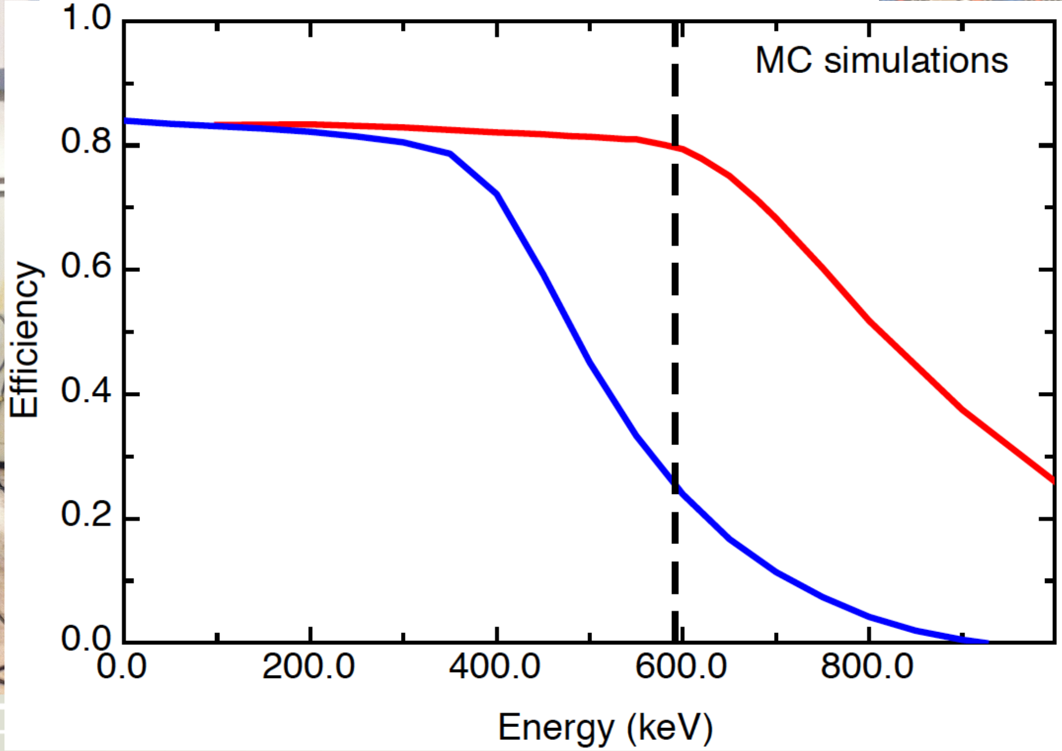
- ✓ β-γ coincidence measurements using a digital DAQ
- ✓ γ– and β– singles in parallel using analog (Canberra) DAQ

same LEPS and HpGe
13.8-mm diam. x 1 mm thick PIPS

GRETINA digitizer
100 MHz clock



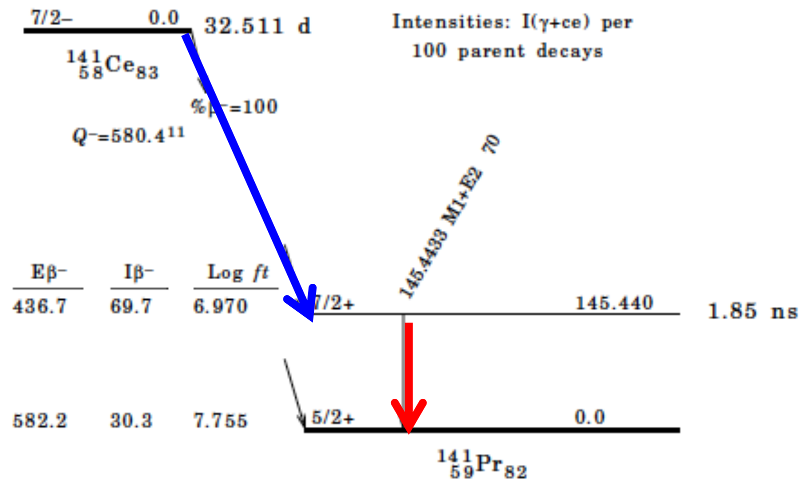


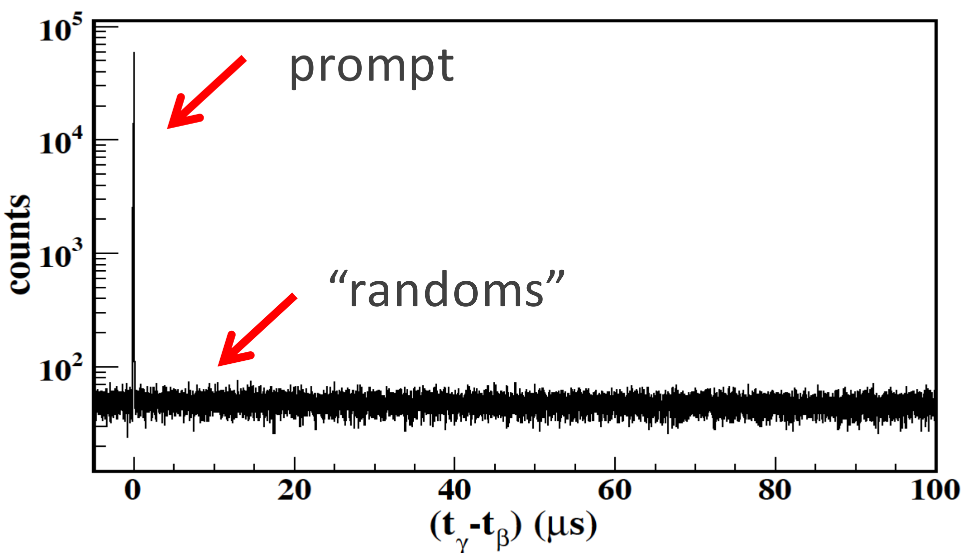


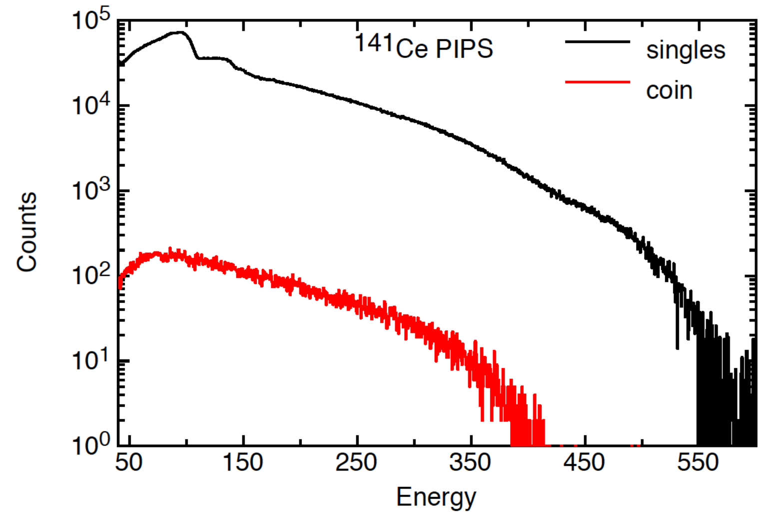
^{141}Ce – βγ coincidences

$I_{145\gamma}$ (%) = cor x $(S_{\beta\gamma coin}/\varepsilon_{145\gamma})$ / $S_{\beta sin}$

(β–γ coincidences)

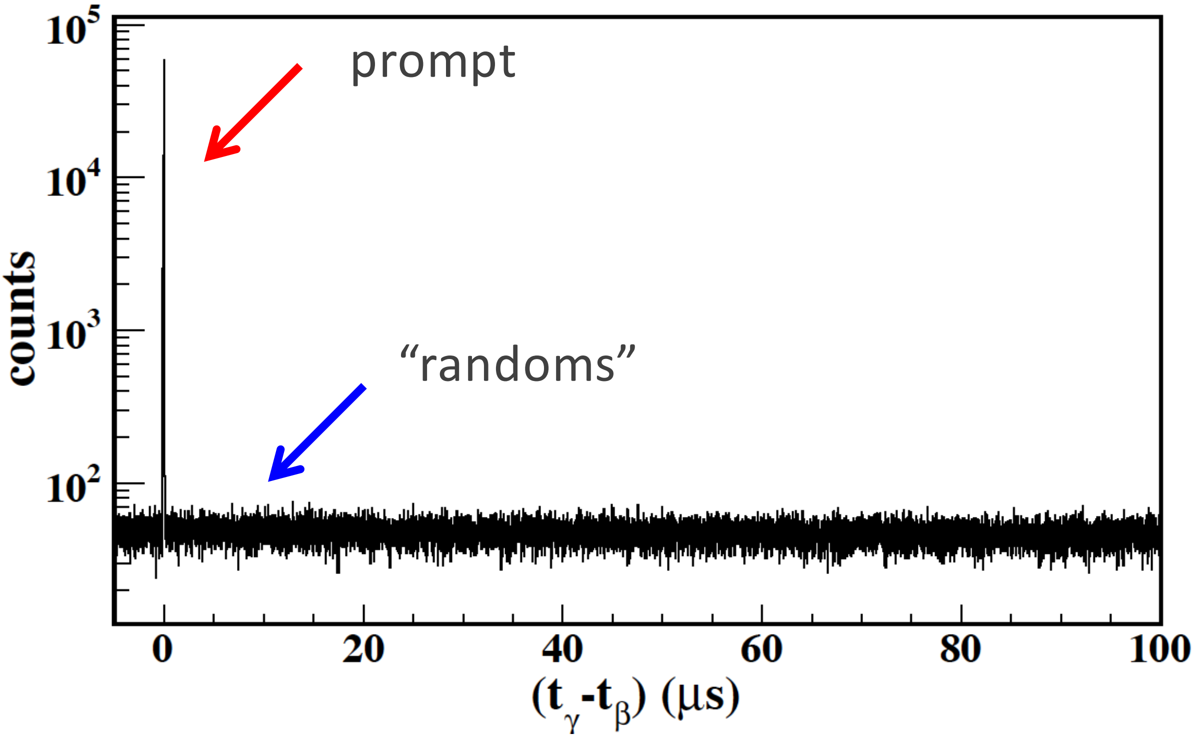


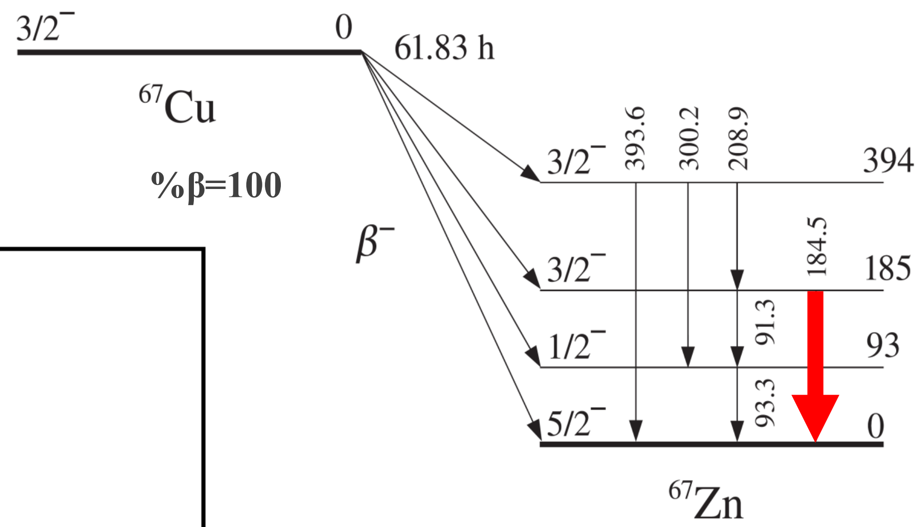




cor (e.g.)$(\varepsilon_{\beta i}/\varepsilon_{\beta})$ = **1.030 (25)%** using $I_{145\gamma}$ (%) = **48.29 (19)%**

^{67}Cu results - coincidences





$I_{184\gamma}$ (%) = $(S_{\beta\gamma coin}/\varepsilon_{184\gamma}) / S_{\beta sin}$

I_γ (184 keV) = **44.2 (6)%**

(β–γ coincidences)

^{67}Cu: measurements – cont.

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Precise absolute γ-ray and β^--decay branching intensities in the decay of $^{67}_{29}$Cu

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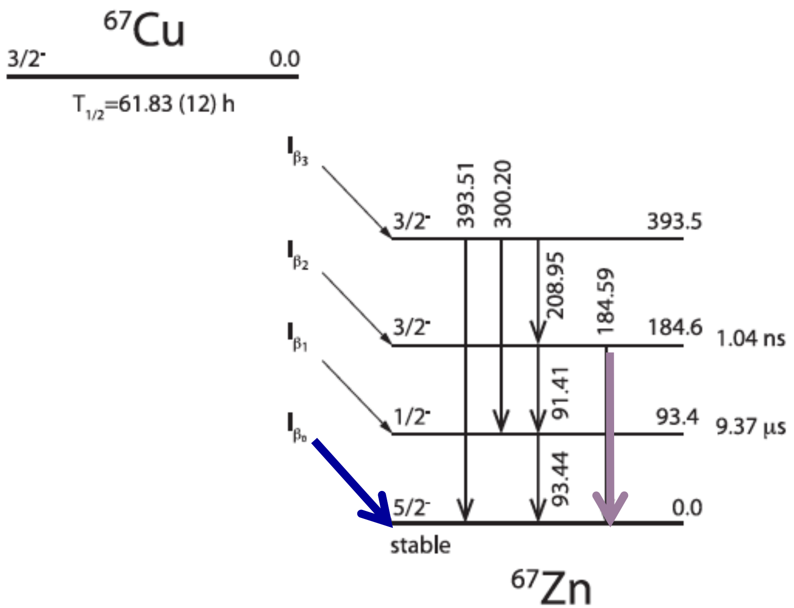
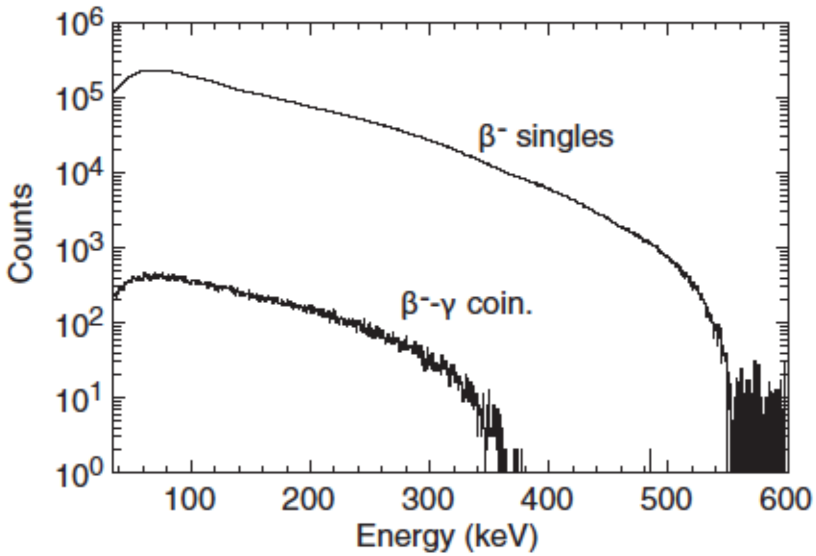
$I_{184\gamma}$ (%) = $(S_{\beta\gamma coin}/\varepsilon_{184\gamma})\ /S_{\beta sin}$=**44.2(6)%** -> **48.7(3)**: **9.2%** difference





$I_{\beta-0}$= **27.4 (5)%** - > **~20%**: **37%** difference