Texas A&M University
US Nuclear Data Program

TAMU NSDD CENTER

Medical Radioisotopes Production Studies:

^{67}Cu Case

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Rationale for Medical Isotopes Production:
The case of ^{67}Cu

- **Medical radionuclides: central in nuclear medicine in the fields of diagnostic imaging and radioimmunotherapy (RIT):**
  - Low-range highly ionizing radiation: β^-, α particles, Auger or conversion electrons
  - New β− emitters of interest: ^{47}Sc ($T_{1/2}$=3.4 d), ^{67}Cu ($T_{1/2}$=2.6 d), ^{105}Rh ($T_{1/2}$=1.5 d), ^{161}Tb ($T_{1/2}$=6.9 d), ^{186}Re ($T_{1/2}$=3.7 d)
  - ^{67}Cu case:
    - Trace element copper takes part in basic biochemical processes
    - Can be linked to biologically important molecules as antibodies, proteins, etc.
    - Theranostic pairs: ^{67}Cu can work in conjunction with same type of radiopharmaceuticals as ^{64}Cu ($T_{1/2}$=12.7 h) or ^{61}Cu ($T_{1/2}$=3.3 h)
    - β^- decay (E_{max}=577 keV); γ radiation of 185 keV (48.7%), 93 keV (16%) and 91 keV (7%).
    - Single-photon emission computed tomography (SPECT) : imaging the radiotracer distribution (with existing technology for the 140 keV γ rays of ^{99m}Tc)
    - ^{67}Cu offers the possibility of SPECT imaging and treatment of smaller size tumors (up to 4 mm)
    - Main factor limiting wider preclinical and clinical use: limited availability

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The case of ^{67}Cu:

Production matters

- Last about 50 years: **nuclear reactors**
- New methods based on: **particle accelerators**
  - ^{68}Zn(p,2p)^{67}Cu, Ep=70–100 MeV; ^{70}Zn(p,α)^{67}Cu; ^{70}Zn(d,αn)^{67}Cu; ^{nat}Zn(d,x)^{67}Cu, ^{64}Ni(α,p)^{67}Cu
  - Accelerator-produced neutrons
  - Photonuclear reactions using bremsstrahlung photons from high-intensity electron linacs
  - New: isotope harvesting in projectile fragmentation (e.g. stopped in aqueous solutions)
  - *All: ^{67}Cu produced inside expensive target materials which should be processed for separating ^{67}Cu and recycling the target materials*
- Innovative approach & advantages: *Inverse-kinematics nuclear reactions*
  - *Reaction products are strongly focused along the beam direction and can relatively easily be collected for immediate use.*
  - *Use low energy beam tuned to maximize ^{67}Cu but reduce impurities.*
  - *Collect almost pure ^{67}Cu in a catcher and use it with radiochemical minimum processing*

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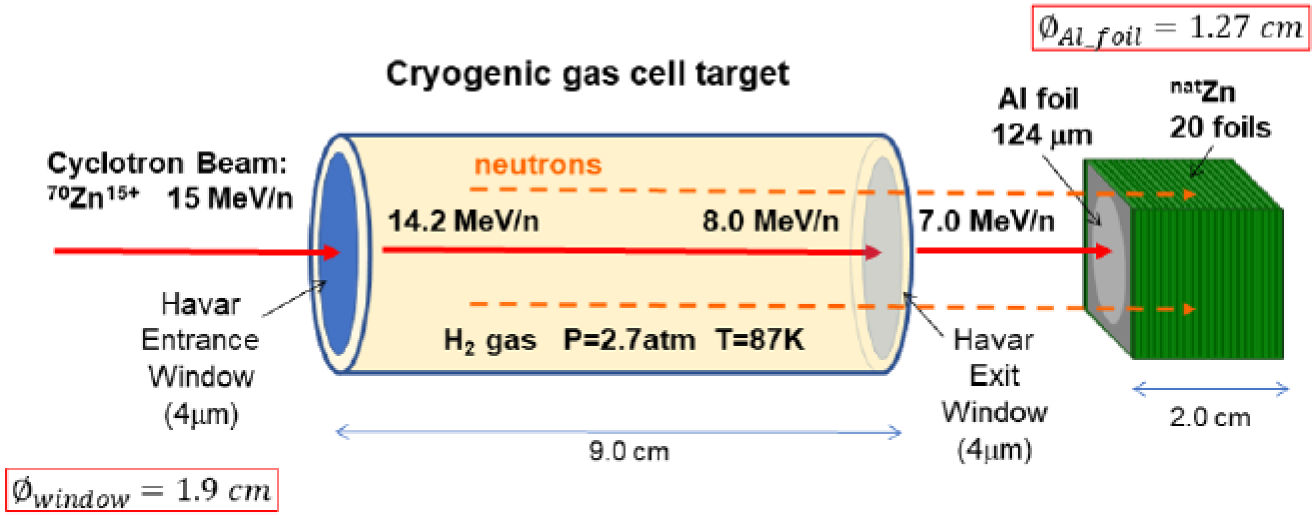
Expanded Involvement in Applied Measurements for Medical Isotopes Production by Inverse Kinematics

Theme: Research for Medical Isotopes Production by Inverse Kinematics

- **Innovative method for the production of important medical radioisotopes based on the nuclear reaction in inverse kinematics, by:**
  - **Directing a heavy ion beam of appropriate energy on a light target (e.g., H, d, He) and**
  - **Collecting the isotope of interest on an appropriate catcher after the target.**



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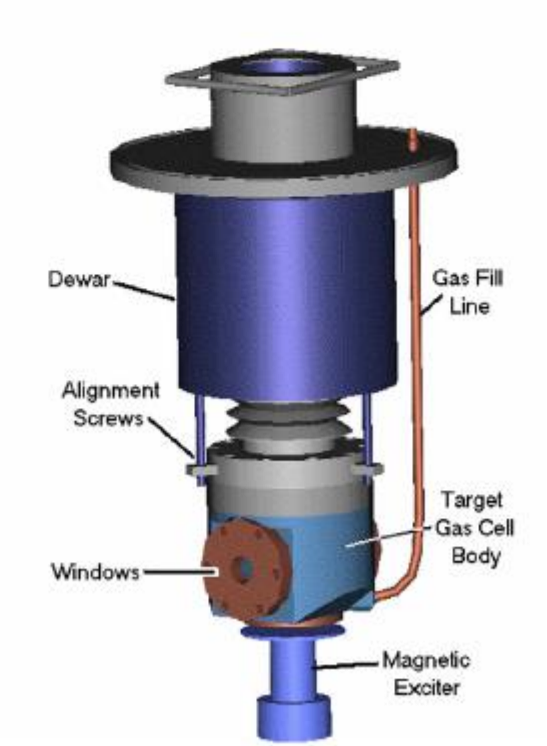
The case of ^{67}Cu:
Cryogenic gas target cell

- Important asset: Cryogenic gas target cell



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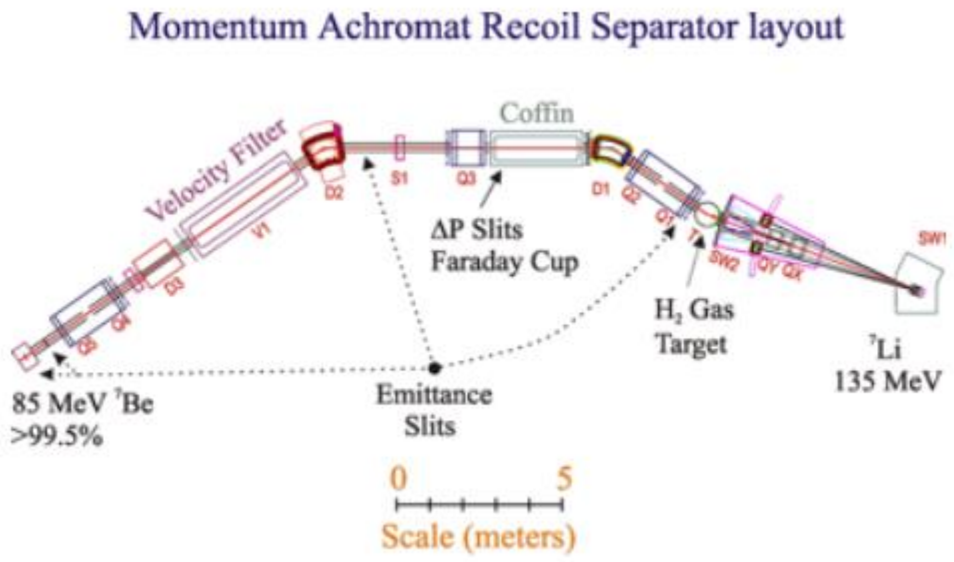
The case of ^{67}Cu:

MARS Spectrometer

- **Important asset: MARS spectrometer to be used for beam and reaction products diagnostics**



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The case of ^{67}Cu:
Irradiation

- **Beam:**
  - 6.5 h with a beam current of 0.19(5) pnA
  - Average equilibrium charge (LISE++): 26+
  - Two Faraday cups: before the gas cell and after same ladder as catcher
  - Suppression test run with ^{21}Ne beam, 28 MeV/nucleon, 40% reduction

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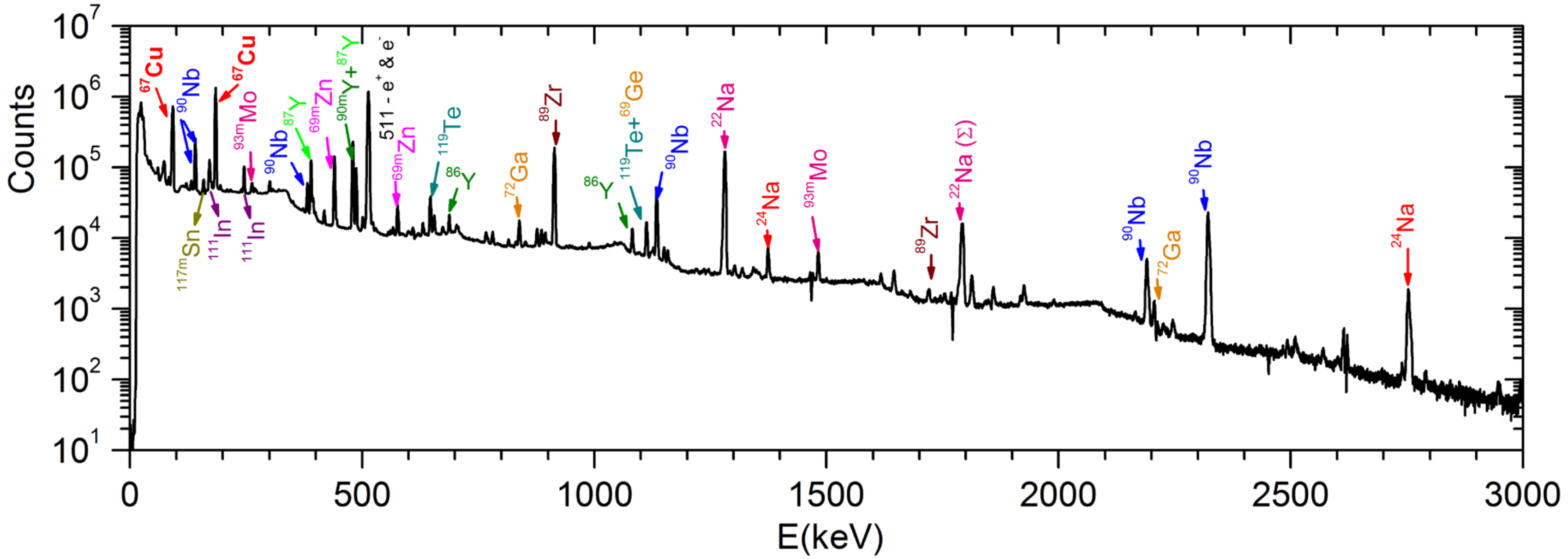
The case of ^{67}Cu:
Off-line γ-spectra measurement

- Cooling time: 36.5 h
- Catcher foil placed at 17.2(10) mm in front of HPGe γ detector, 2-3% dead time
- ^{152}Eu energy calibration
- Absolute efficiency calibration done with GEANT4 and EGSnrc codes: 10% unc
- Spectra acquired for 67.3 h, background-subtracted



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The case of ^{67}Cu:

Activities

Radio-nuclide	Decay mode	Half life	Eγ (keV)	Iγ (%)	Principal Production routes	A_{EOB} (kBq)	H_{EOB} $\left(\frac{kBq}{pnA.h}\right)$
^{67}Cu	β^-	61.83 h 12	91.266(5)	7.0(1)	p(^{70}Zn, ^{67}Cu)α	2.16(12)	1.8(5)
			93.311(5)	16.1(2)			
			184.577(10)	48.7(3)			
^{69m}Zn	IT, β^-	13.76 h 2	438.63(2)	94.77(20)	p(^{70}Zn, ^{69m}Zn)d	2.55(26)	2.2(6)
^{90}Nb	ε^+ β^-	14.60 h 5	1129.224(15)	92.7(4)	^{27}Al(^{70}Zn, ^{90}Nb)x	2.38(23)	2.0(6)
			2318.968(10)	82.03(16)	^{59}Co(^{70}Zn, ^{90}Nb)x		
			2186.242(25)	17.96(16)	^{52}Cr(^{70}Zn, ^{90}Nb)x		
^{87m}Y	IT	13.37 h 3	380.79(7)	78	^{27}Al(^{70}Zn, ^{87m}Y)x	0.87(9)	0.74(22)
^{89}Zr	ε^+ β^+	78.41 h 12	908.96(4)	100	^{27}Al(^{70}Zn, ^{89}Zr)x	0.62(6)	0.52(16)
^{22}Na	ε^+ β^+	2.6019 y 4	1.27453(2)	99.944(14)	^{27}Al(^{70}Zn, ^{22}Na)x	0.46(5)	0.41(12)
					^{27}Al(n,x)^{22}Na		
^{86}Y	ε^+ β^+	14.74 h 2	627.72(10)	32.6(10)	^{27}Al(^{70}Zn, ^{86}Y)x	0.38(4)	0.32(10)
			1153.01(4)	30.5(9)	^{59}Co(^{70}Zn, ^{86}Y) x		
			1920.72(13)	20.8(7)	^{52}Cr(^{70}Zn, ^{86}Y) x		
			1854.38(13)	17.2(5)			
			443.14(9)	16.9(5)			
			703.34(10)	15.4(4)			
^{87}Y	ε^+ β^+	79.8 h 3	484.805(5)	89.7(3)	^{27}Al(^{70}Zn, ^{87}Y)x	0.167(16)	0.15(4)
			388.531(3)	82	^{59}Co(^{70}Zn, ^{87}Y) x		
					^{52}Cr(^{70}Zn, ^{87}Y) x		

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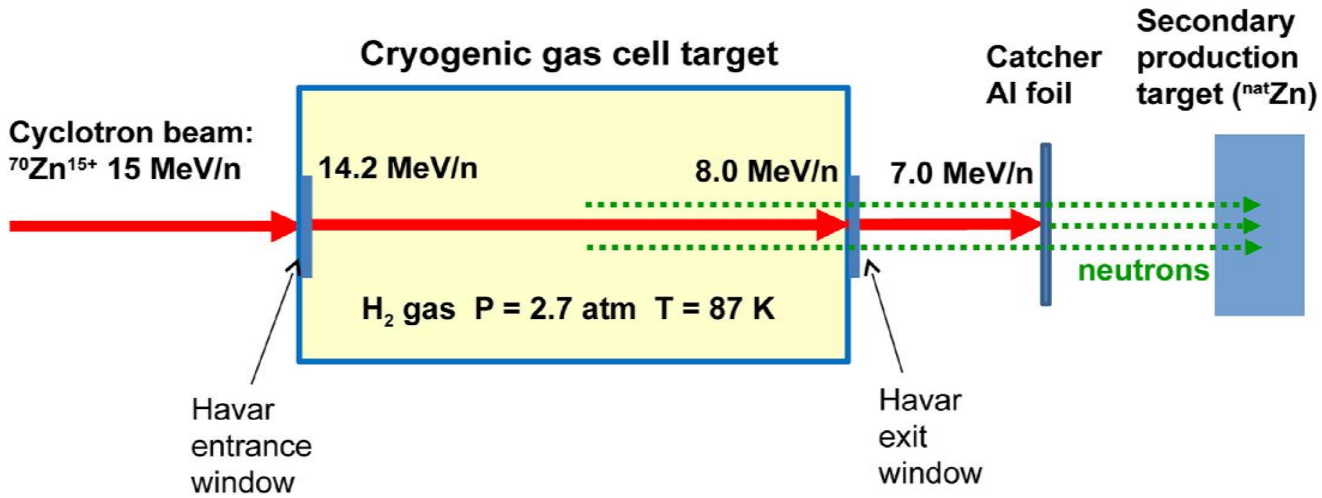
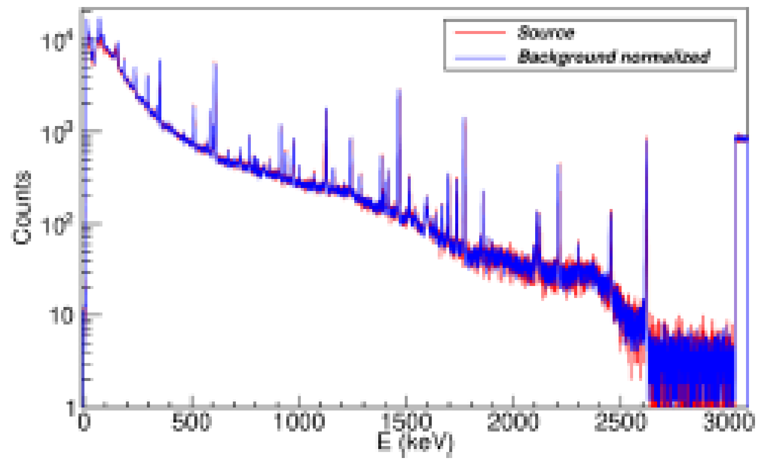
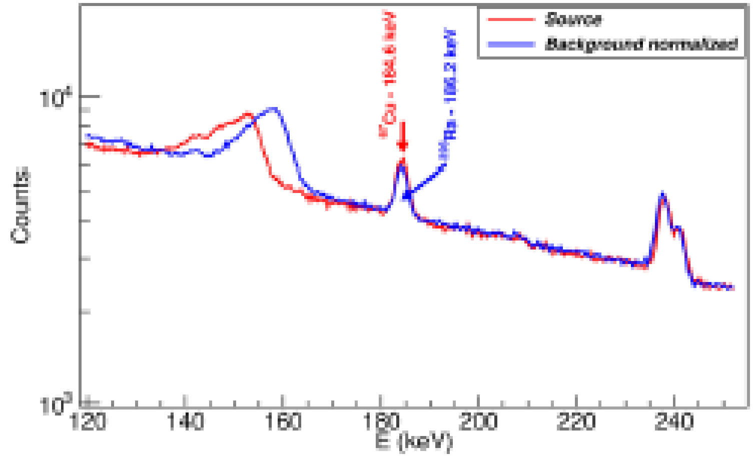
The case of ^{67}Cu:

Use of neutrons







- Block of ^{nat}Zn 25.4×25.4×20 mm^3 activated with neutrons;
- Measured for 40 h starting 7.5 days after the 6.5 h beam irradiation
- TALYS simulation: 1.6 neutron/reaction act on average mainly from ^{67}Zn(n,p)^{67}Cu reaction
- Exerimental result: 5.3(8) Bq of ^{67}Cu (end of irradiation)
- Still to correct for neutron ang. distribution (2% n flux collected), γ attenuation in the source (about 50%) and ^{67}Zn natural abundance (4.04%)

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The case of ^{67}Cu:

Conclusions

Advantages of inverse kinematics and setup

- Enhanced isotope collection at forward angles and easier harvesting and use of ^{67}Cu.
- Advantage of minimizing expensive ^{70}Zn isotope (0.6% natural abundance) at mg/day rate as projectile instead of g/day as source (plus radiochemistry & recycling).
- Minimize the production of radioimpurities arising from the main reaction by choosing the appropriate reaction channel and the subsequent cooling time of the products.
- Entrance Havar Window (Co, Cr, Ni, W, etc.) :
  - Peripheral or semiperipheral (deep-inelastic) collisions have rather wide angular distributions and are expected to mostly miss the catcher foil
  - Products of complete or nearly complete fusion are forward-focused but are heavier and slower than the beam and may mostly stop in the gas.
- Exit Havar Window & Catcher:
  - Adjust gas cell parameters (pressure, temperature, length) in order that primary beam reaches this Window & Catcher near or below the Coulomb barrier of the relevant reactions (e.g., 3.5-4.0 MeV/nucleon).
  - For Catcher one can use water or other material (salt, sugar, etc.) in order to collect the radioisotopes in a convenient chemical form for further processing.

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The case of ^{67}Cu:

Conclusions

Advantages of inverse kinematics and setup

- 1 particle µA beam can produce mCi's of ^{67}Cu per 24 h of irradiation.
  - stable isotopes (^{70}Zn, ^{69}Ga, etc) implanted in the catcher should be produced at biochemically insignificant quantities
- Use cooled windows, lower pressure (1.0-1.5 atm), increase length, lower temperature (with cryo-coolers)
- Can use liquid H_2 targets (1-2 mm for 8-10 mg/cm^2) at 20 K (with Gifford-McMahon refrigerator)
- Cyclotron Institute at TAMU, the facility houses two cyclotrons:
  - K150 cyclotron which can produce high-intensity heavy-ion beams (up to around Kr) with energies up to around 12–15 MeV/nucleon, suitable for the production of relatively large activities of radioisotopes
  - K500 cyclotron, employed in the present experiment, which can produce lower currents of heavy-ion beams (up to U) and in a broader energy range (up to 20–40 MeV/nucleon depending on the isotope).
- Both the K150 and the K500 cyclotrons may be successfully used for the development and production of a variety of non-standard radioisotopes at activities appropriate for medical studies on small animals.