^{67}Cu radioisotope production with using ^{70}Zn(p,α)^{67}Cu Nuclear Reaction on Cyclone-30 High Current cyclotron

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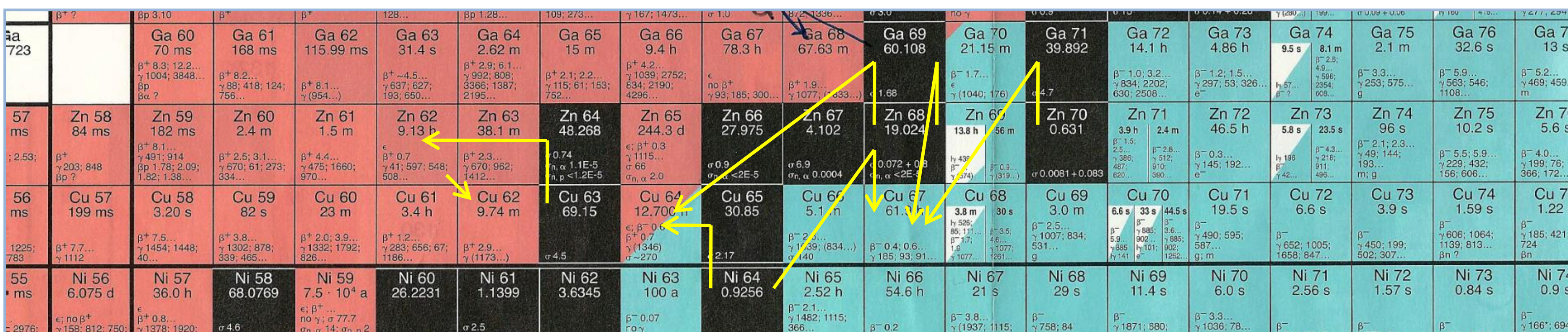
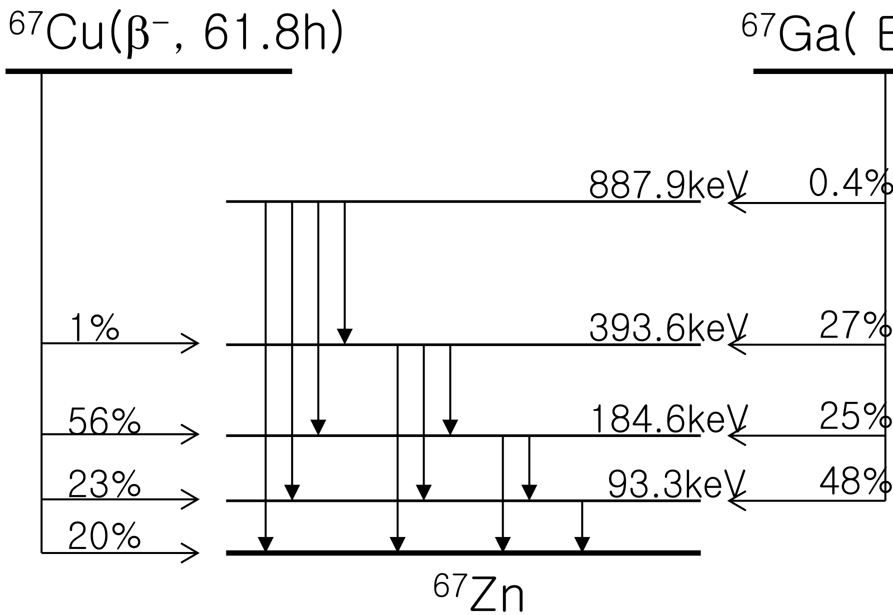
Contents

- **Physical properties of Cu radionuclides**

Radio-nuclide	Half-life	Decay mode(%)	Major γ (keV)	Major β-/ β+ (keV, %)	Application
^{60}Cu	23.7m	β+(93),EC(7)	826(22),1332(88)	872(49)	
^{61}Cu	3.32h	β+(61),EC(39)	282(12),656(10)	523(51)	
^{62}Cu (^{62}Zn/^{62}Cu)	9.74m	β+(97),EC(3)	1173(0.34)	1316(97)	PET
^{64}Cu	**12.7h**	**EC(43.9), β^{-}(38.5) β^{+}(17.6)**	**1345(0.5)**	**β+:278, β-:190**	**Therapy PET**
^{66}Cu	5.4m	β-(100)	1039(9)	1112(91)	Therapy
^{67}Cu	**61.83h**	**β-(100)**	**184(48.7),93(16), 91(7)**	**β-: 121(57)**	**Therapy**



• Cu-67 핵적 특성



	^{67}Cu	^{67}Ga
Decay mode	β (100%)	E.C. (100%)
Half-life	61.83 h	78.3 h
γ-rays(keV)	(intensity,%)	(intensity,%)
91.266	7.00	3.11
93.311	16.10	38.81
184.577	48.70	21.41
208.951	0.12	2.46
300.219	0.80	16.64
393.529	0.22	4.56
494.166		0.07
887.688		0.15

- Suitable β- emission are ideal for use with MAbs and other tumor targeting compounds
- half-life : 61.8hr
- decay mode: 100% β- decay to ^{67}Zn
- mean β-ray energy: 141keV
- total β-ray intensity: 100%
- mean β-dose: 0.141MeV/Bq s

- Nuclear Reactions for ^{67}Cu production

Reaction	E-Range (MeV)	$E(\sigma_{max})$ (MeV)	σ_{max} (mb)	Yield(mCi/μAh, @ EOB)
$^{68}Zn(p,2p)^{67}Cu$	30 ~ 430	>430	24.9	2.0(<100MeV)
$^{71}Ga(p,3p2n)^{67}Cu$	19.2 ~ 55.3	>55.3	2	
$^{67}Zn(d,2p)^{67}Cu$	8.1 ~ 15.4	>15.4	5.2	
$^{64}Ni(\alpha,p)^{67}Cu$	12.4 ~ 20.8	15.5	15.9	0.022(<23MeV)
$^{nat.}Zn(p,2p)^{67}Cu$	52.8 ~ 67.7		4.1	
$^{70}Zn(p,\alpha)^{67}Cu$	7.7 ~ 35.1	16.7	14.8	0.21(<40MeV), 0.165(<30MeV)
$^{67}Zn(n,p)^{67}Cu$	Neutron	22	1.07	
$^{68}Zn(\gamma,p)^{67}Cu$	Bremsstrahlung		11	

- **Yield calculation**

$$A(dps) = 6.24 \times 10^{18} \times i \times \frac{N_a \times \rho \times y_i}{M}(1 - e^{-\lambda t})\int_{E_1}^{E_2} \frac{\sigma(E)}{S(E)} dE$$

A : activity(dps)

i : beam current(μA)

N_a: Avogadro's number

ρ: target material density

Y_i : isotopic abundance

M: target material MW

λ : decay constant

t : irradiation time

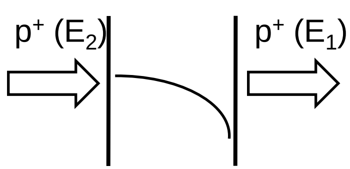
σ(E) : cross section

$S(E)$: stopping power

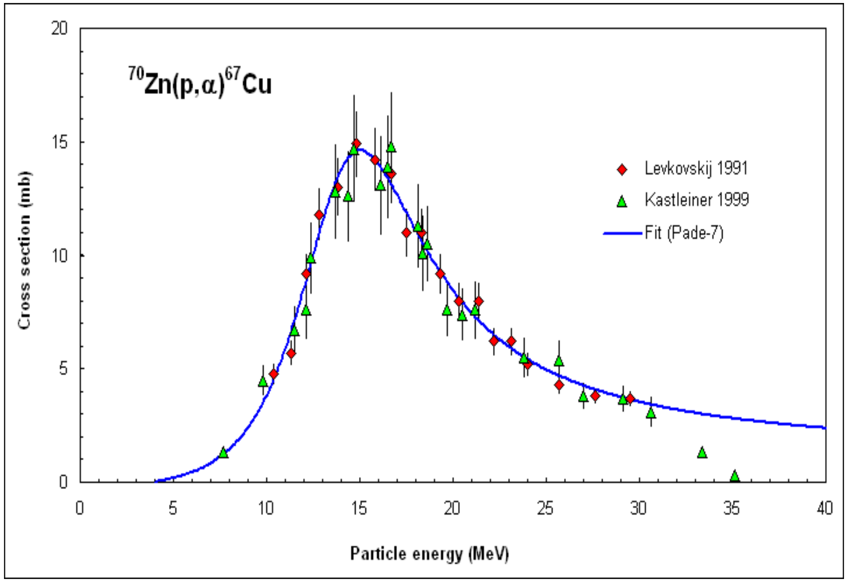
E_2 : initial energy

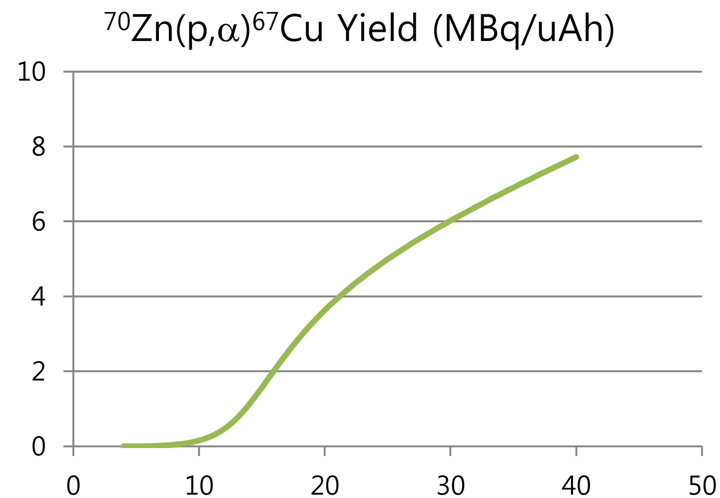
E_1 : final energy

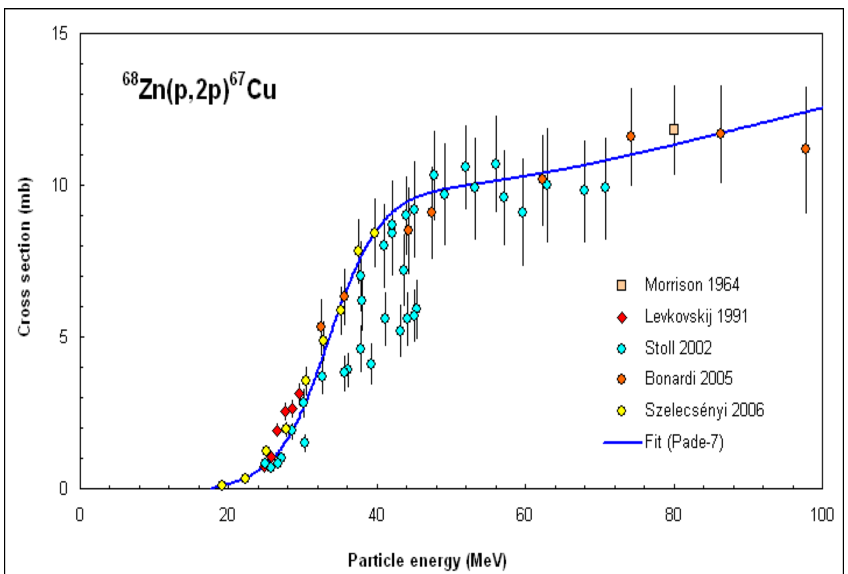
$1-e^{-\lambda t}$: saturation factor

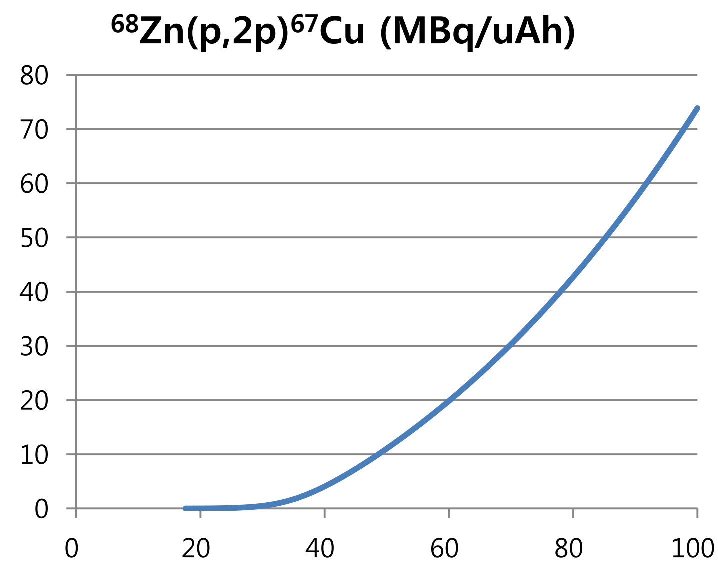


• $^{70}Zn(p,\alpha)^{67}Cu$, $^{68}Zn(p,2p)^{67}Cu$ 여기함수와 누적 수율 평가 :

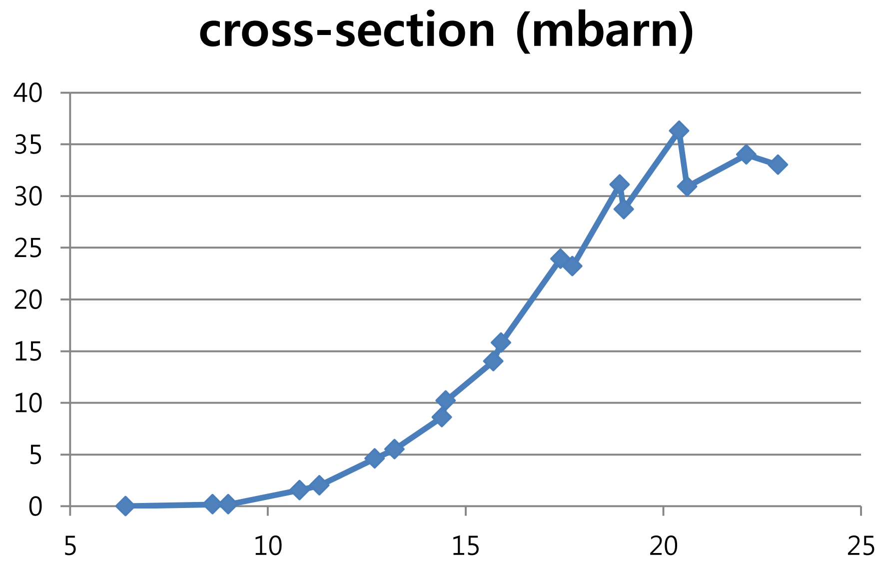








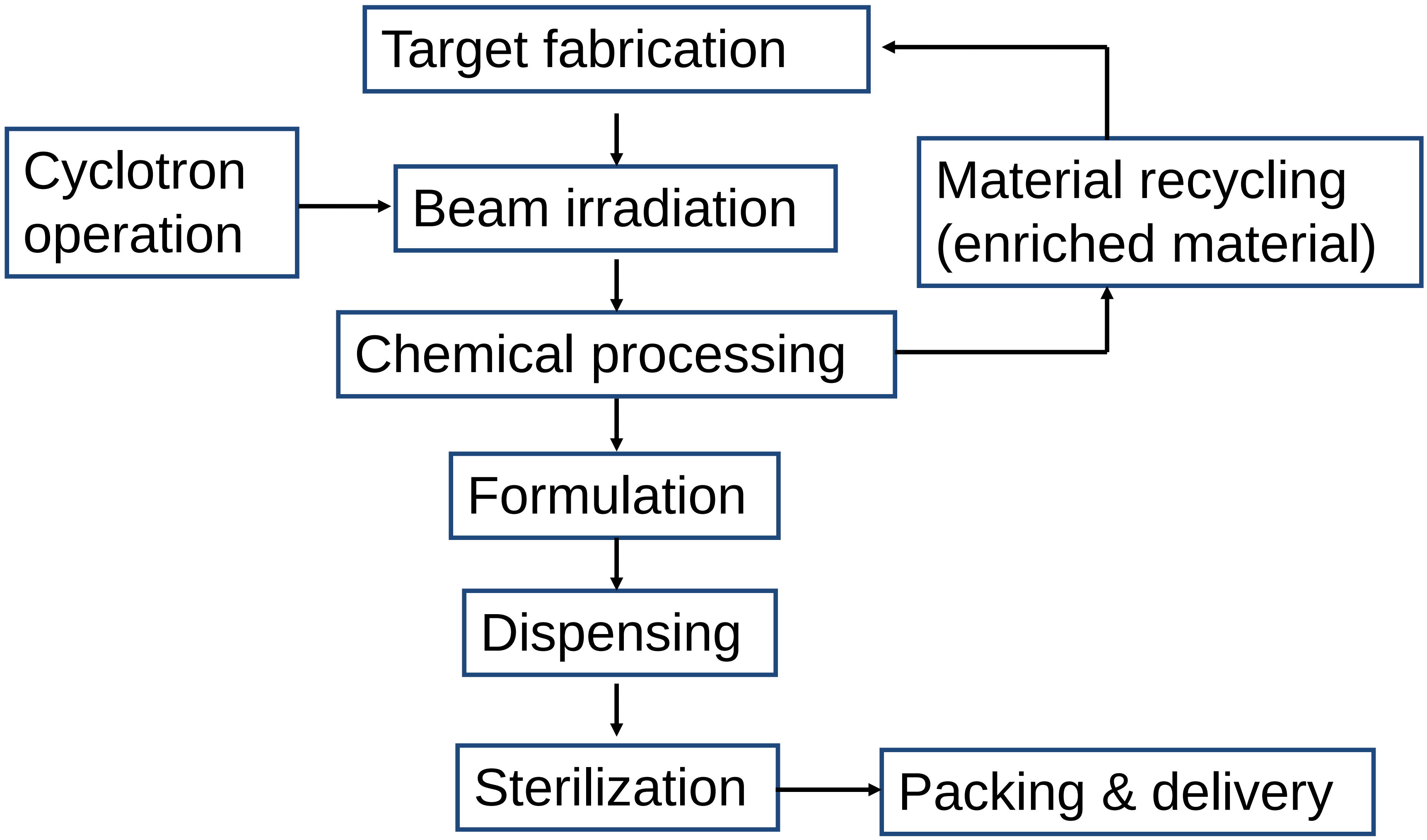
- $^{64}Ni(\alpha,p)^{67}Cu$ reaction의 cross–section



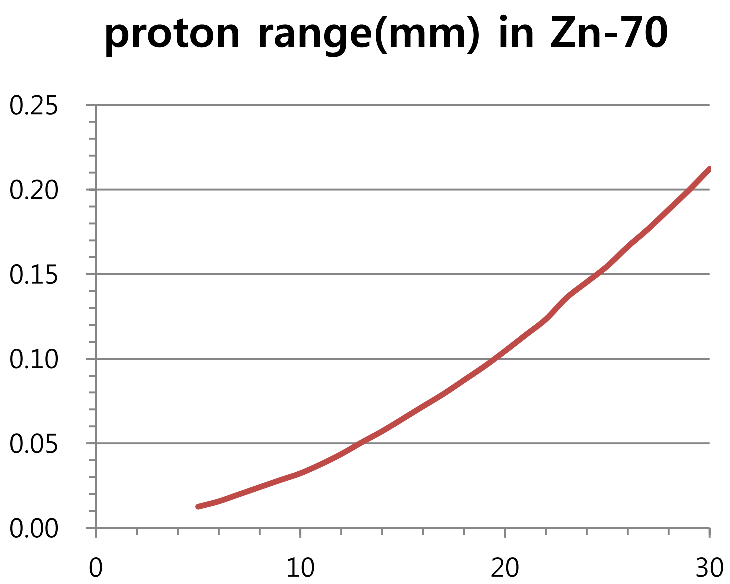
- Cross section data from National Nuclear Data Center (BNL)

단점: alpha particle 의 low beam current → low production yield

- Typical processing sequence of RI production



• ^{70}Zn Target System



Range of protons in Zn−70 target tilted 6°
to the beam direction.

^{70}Zn 농축 표적량 계산 (d=7.39g/cm^3):

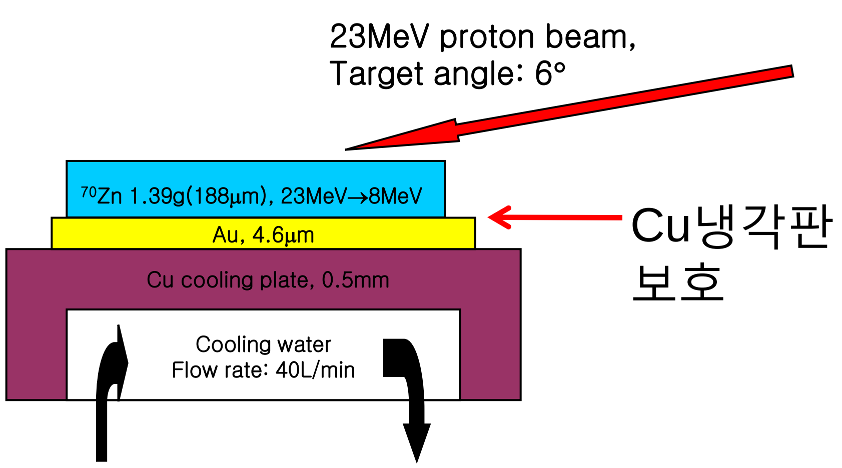
- Proton beam energy : 23 → 8MeV,
- Target thickness calculated with e-loss :

  0.114cm

^{70}Zn target weight (target angle : 6°)

= 0.012cm x10cm^2 x 7.39g/cm^3 = 0.87g

Target에 발생 열량: Watt = ΔE x I
(23MeV x 200μA =4.6 kwatt/10cm^2)



^{70}Zn target assembly

• ^{70}Zn target (Au, ^{70}Zn plating) fabrication

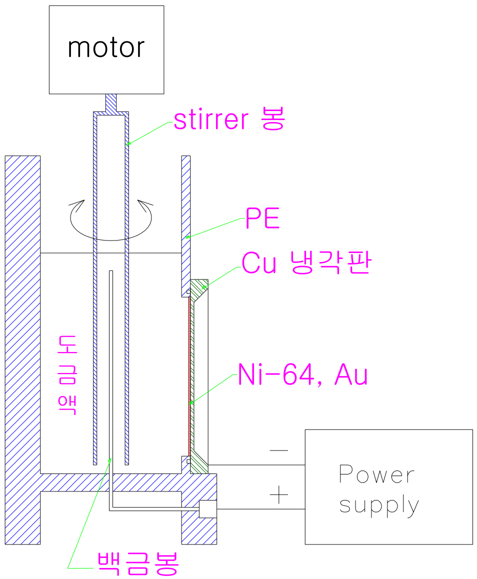
1) Au Plating : 0.3g $KAu(CN)_2$/3g EDTA/
   2g phosphate buffer in 500mL H_2O
   thickness: ~ 8mg/cm²
   Area: 12cm²(1.2cm x 10.2cm)

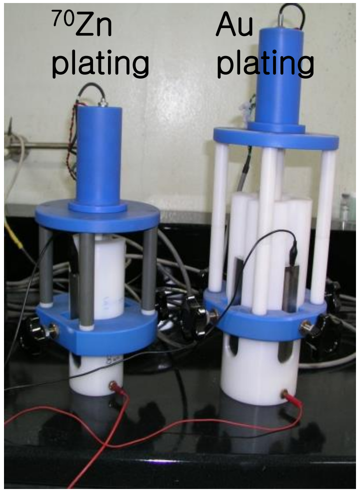
2) ^{70}Zn plating:
   Electrolyte: 1.2g ^{70}Zn+0.5g boric acid+
   1.0g NaCl in 80ml DM water

- Tracer: ^{65}Zn
- Current: constant 200mA on 10cm² target surface
- Time: 6 hr, Cathode efficiency: 71.7%
- Target thickness: 105mg/cm²

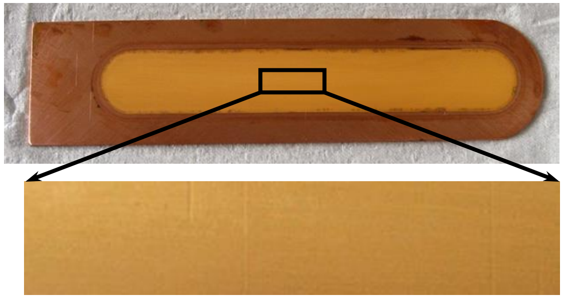
− Recovery with cation resin

^{70}Zn electro-plating device



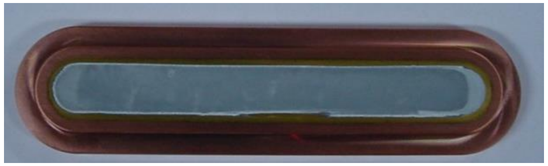


Au plating on Cu cooling plate



10 배 확대

^{70}ZnTarget



표적 안전성 평가를 위한 burning test (350°C heating/bending test)

Power supply

• ^{70}Zn 표적 (Au, Zn plating) 제작 기술

1) Au 도금: 0.3g $KAu(CN)_2$/3g EDTA/2g KH_2PO_4 buffer in 500mL H_2O

3) Zn plating

(1) $ZnCl_2$: 2g, NH_4Cl: 20g, 2ml hydrazine in 80ml H_2O
constant voltage : 1.4V, current: 100mA for 4hr
heater: 40°C, stirrer speed: 700rpm
surface: sponge, bad

(2) $ZnCl_2$:2g, boric acid: 1.5g, NaCl: 5g in 80ml H_2O
const. voltage: 3V, current: 120mA for 5hr
heater: 60°C, stirrer speed: 700rpm
surface: very good, but 630mg 도금 후 다시 녹음
pH adjustment (pH 0.5 → 3) with c-NaOH

(3) $ZnCl_2$: 2g, boric acid: 1.5g, NaCl: 5g in 80ml H_2O
constant current : 100mA, voltage: 3.5 → 2.9V
pH adjustment (pH 0.5 → 3) with c-NaOH
surface: micro-crystal, not bad
Zn amount: 495mg → 441mg plating

- Isotopic abundance of the enriched ^{70}Zn target (ISOFLEX)

Isotope	^{64}Zn	^{66}Zn	^{67}Zn	^{68}Zn	^{70}Zn
Content (%)	0.054	0.047	0.005	0.361	99.533

* ^{67}Ga 계산 생산량: 0.361% x 8mCi/μA/h x 200μA x 10h = 57mCi

- **Proton beam irradiation on ^{70}Zn target**

^{70}Zn target after 200μA, 23 MeV proton beam irradiation

Beam irradiation condition

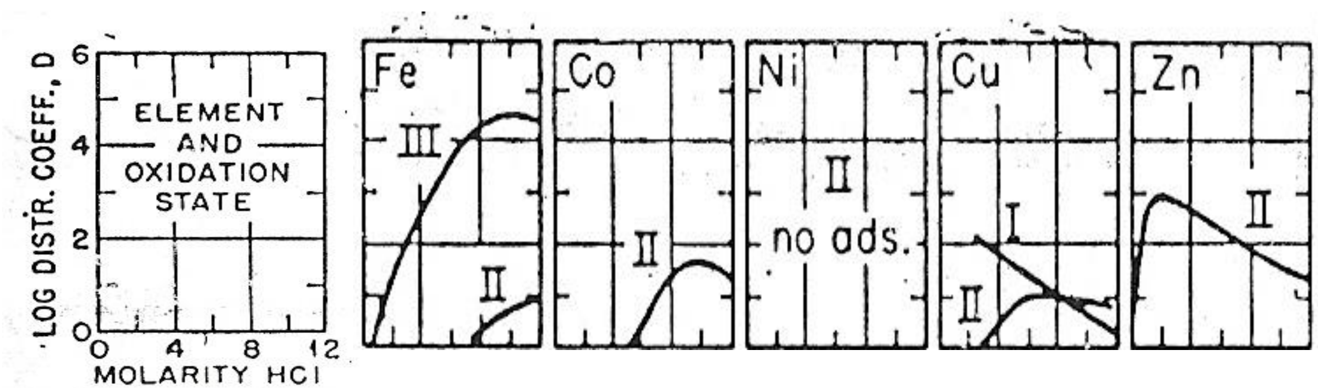
- Energy: 23MeV
- Beam current: 200μA
- Time: 2hr

Zn의 thermal conductivity: 116W/m/k
Ni의 thermal conductivity: 90.9W/m/k

- **Chemical separation :**

  1) Solvent extraction with 0.01% dithizone in
     CCl_4–0.5N HCl (vol. ratio, aq:org=1:1/10)
     org. phase: ^{67}Cu
     Aq. phase: ^{67}Ga, ^{70}Zn등 impurity RI

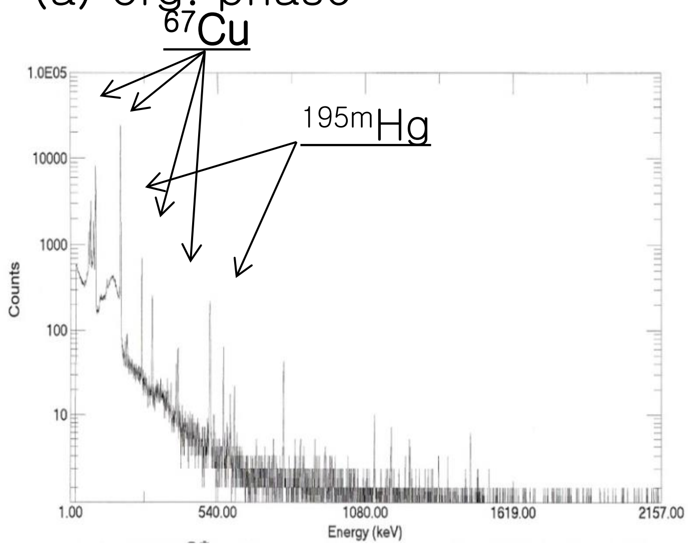
  2) Anion resin (AG1x) 분배계수: 이동상 HCl



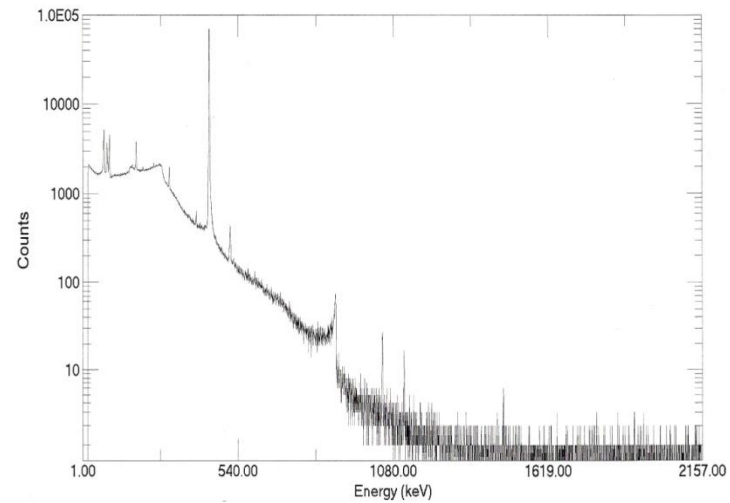
• ^{67}Cu separation from irradiated ^{70}Zn enriched target

^{67}Cu separation from proton irradiated ^{70}Zn target
by solvent extraction (0.01% dithizone in CCl_4 – 0.5N HCl)

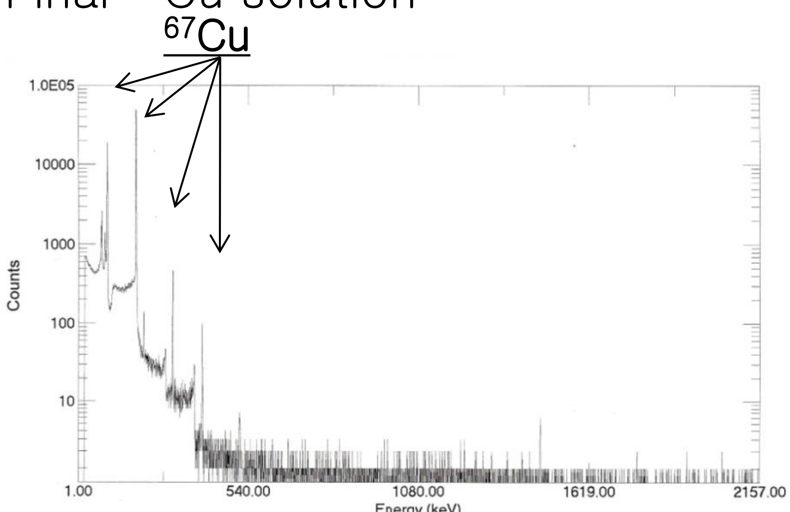
(a) org. phase



(b) aq. phase



Final ^{67}Cu solution

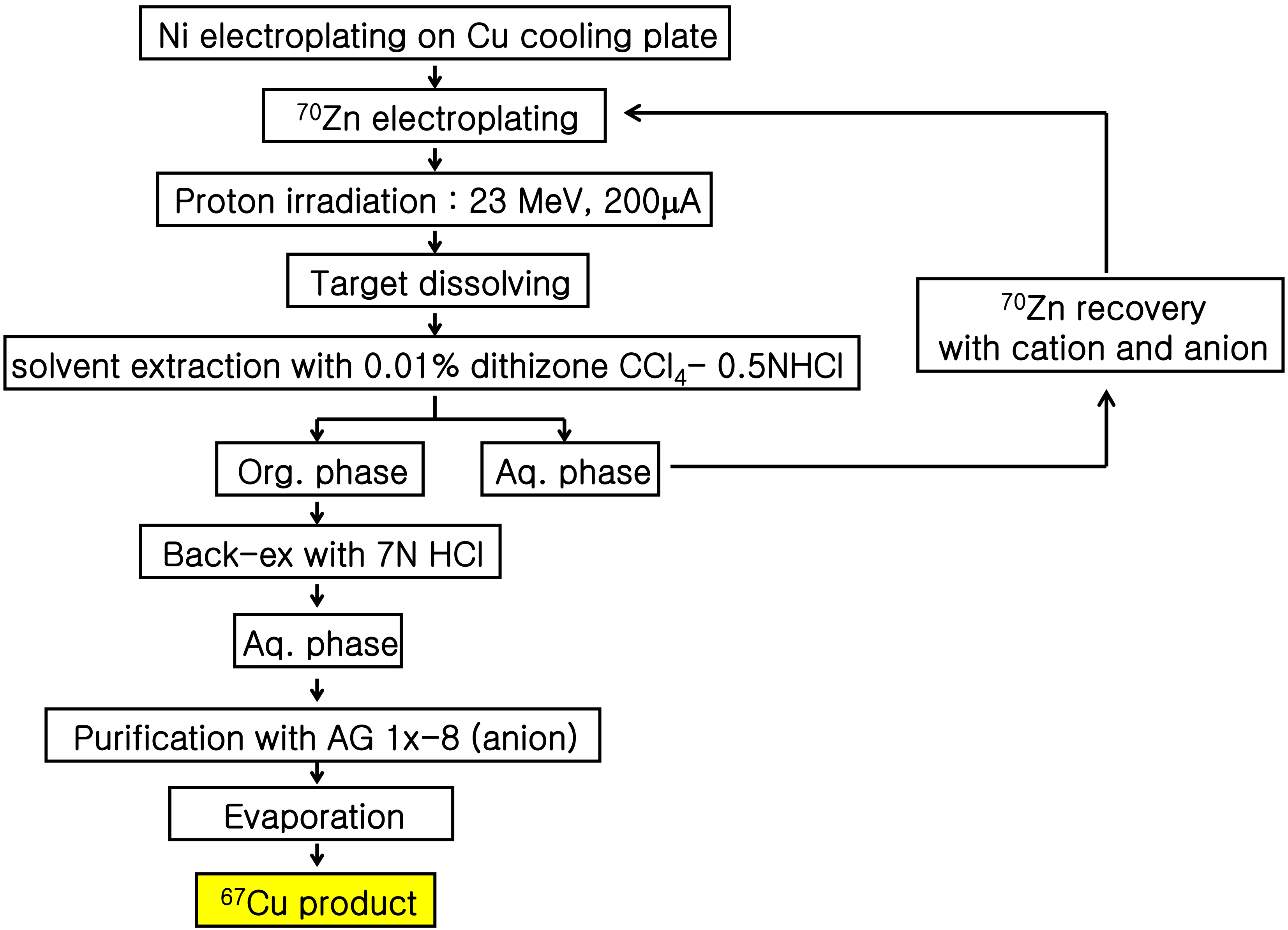


Final solution은 anion resin후 product임.
^{195m}Hg는 anion으로 제거하였음.

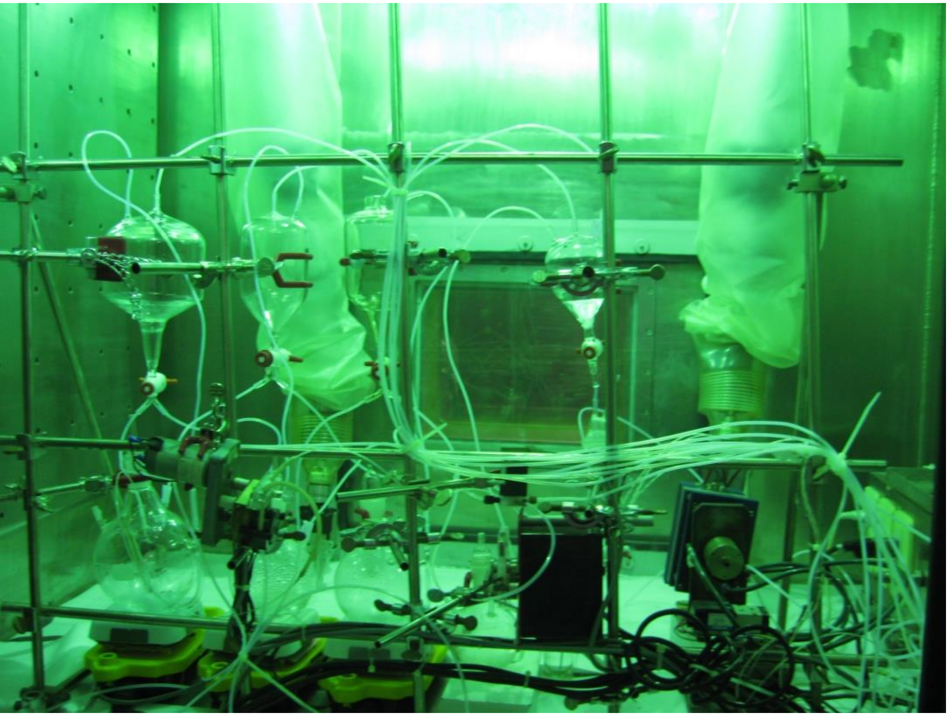
- Radionuclides in proton beam irradiated ^{70}Zn target

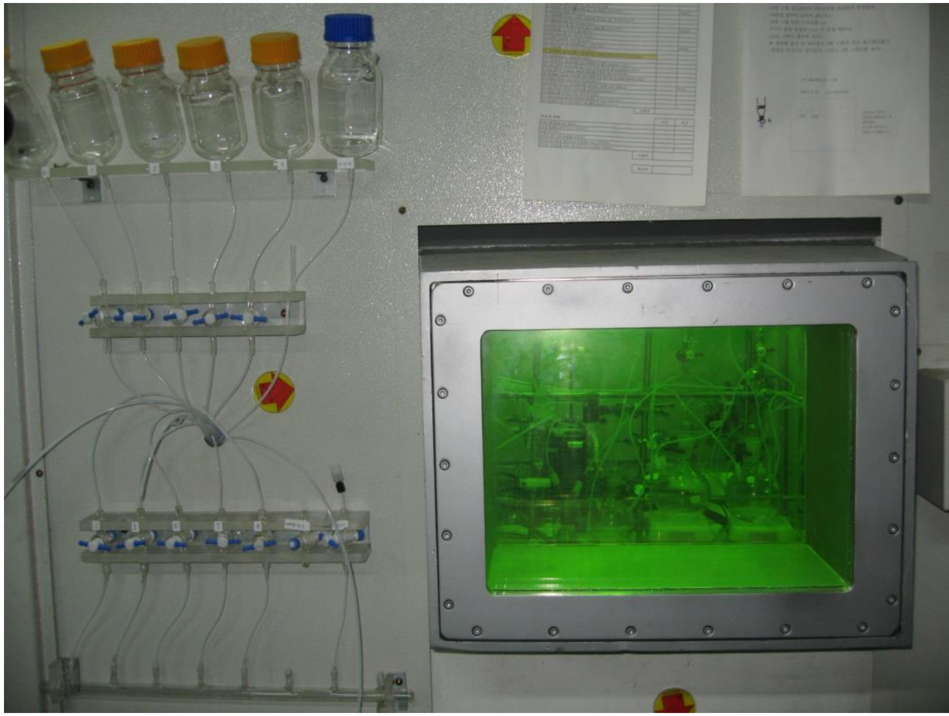
Nuclide	Half-life	Gamma-ray	Nuclear reaction
^{67}Cu	61.83h	91(7), 93(16.1),184(48.7) 208(0.12), 300(0.80)	**$^{70}Zn(p,\alpha)^{67}Cu$**
^{67}Ga *	78.28h	91(3), 93(38.8),184(21.4), 208(2.5),300(16.6),393(4.6)	**$^{68}Zn(p,2n)^{67}Ga$**
^{62}Zn	9.19h	507(14.8), 548(15.3),596(26)	$^{64}Zn(p,3n)^{62}Ga \rightarrow {}^{62}Zn$
^{69m}Zn	13.76h	438(94.8)	$^{70}Zn(p,pn)^{69m}Zn$
^{195m}Hg	41.6 h	261(31),560(7.1)	$^{197}Au(p,3n)^{195m}Hg$
^{195}Hg	10.53 h	585(2.04),599(1.8),1111(1.5)	$^{197}Au(p,3n)^{195m}Hg$

- Flow chart of ^{67}Cu production with ^{70}Zn enriched target



- Chemical process unit in hot-cell





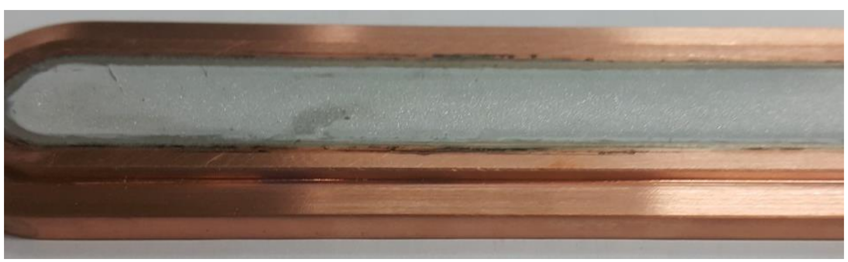
- Zn target on Ni coated Cu cooling plate.

- Ni plating on Cu cooling plate.

Electrolyte : $NiCl_2$ 4.3g, boric acid 0.5g, NaCl 2g
in 500ml H_2O
200mA constant current

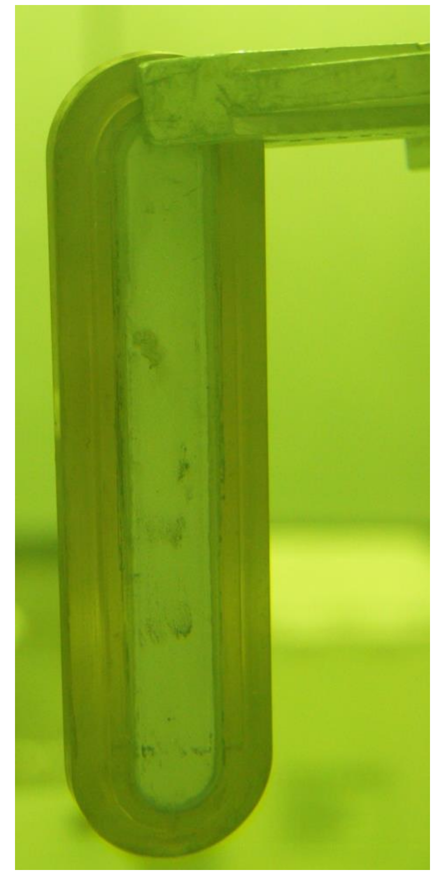
↓

- Zn plating on Ni coated Cu cooling plate.



Electrolyte : $ZnCl_2$ 4.2g, boric acid 1.0g, NaCl 1g
in 90ml H_2O
100mA constant current
200mg Zn plating

- 200μA proton beam irradiation
No melting on Zn target



• Conclusions

- ^{67}Cu mass production:

  Cyclone-30 (<30MeV): $^{70}Zn(p,\alpha)^{67}Cu$

  100MeV LINAC (>70MeV): $^{68}Zn(p,2p)^{67}Cu$ + $^{70}Zn(p,\alpha)^{67}Cu$,

- ^{67}Cu expected yields:

  23MeV : 330mCi at EOB with 200μA for 10hr irradi.

  dual beam irradiation : 660mCi (= 330mCi x 2)

- ^{70}Zn Target : Ni coated Cu plate,

  no melting at 200uA proton beam irradiation

- Separation method (Solvent extra. + chromato.)
  - solvent extraction: 0.01% dithizone in CCl_4-HCl
  - ion chromatography: AG1x-8