KOREA INSTITUTE OF
RADIOLOGICAL & MEDICAL SCIENCES

Forum for Nuclear Cooperation in Asia (FNCA)
2024 Study Panel

Production and Application of Radioisotopes in KIRAMS, Korea

Division of Applied RI
Choong Mo Kang and Kyo Chul Lee

2024.03.11

Introduction of KIRAMS and Division of Applied RI

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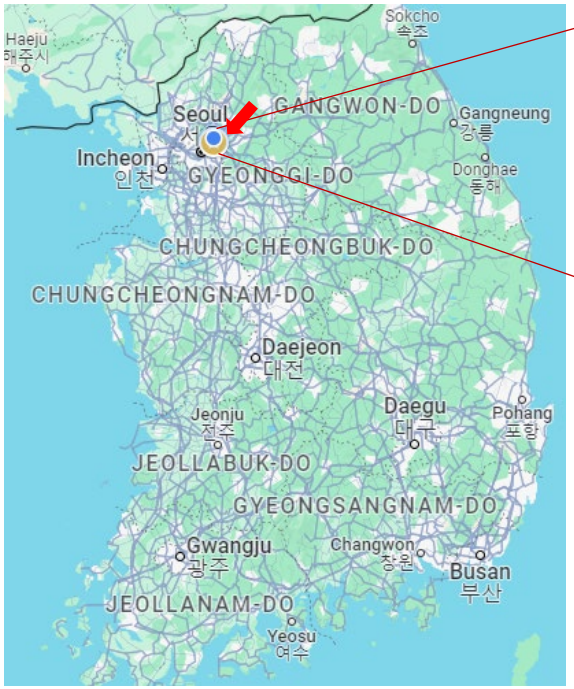


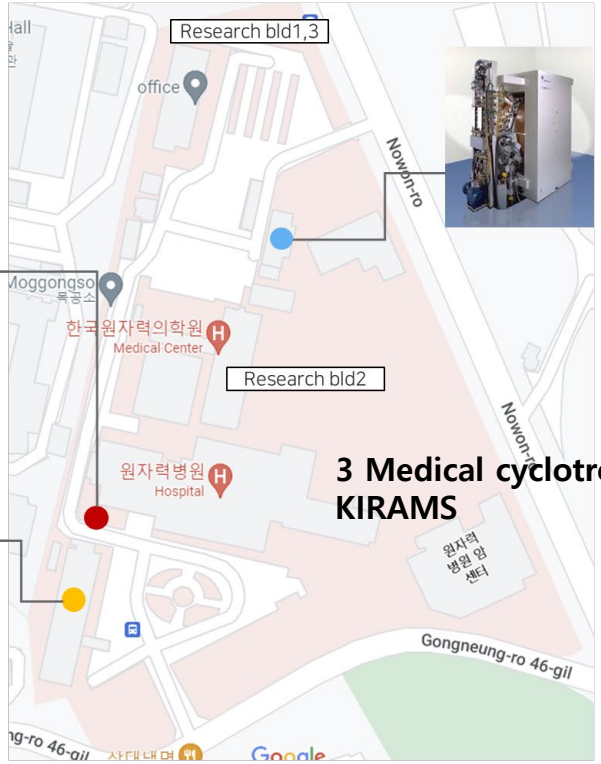
Only one research institute contains hospital in Ministry of Science and ICT

50 MeV Cyclotron (Scanditronix)

- Cu-64
- Zr-89
- I-124
- At-211
- Cu-67
- Sn-117m

30 MeV Cyclotron (IBA)

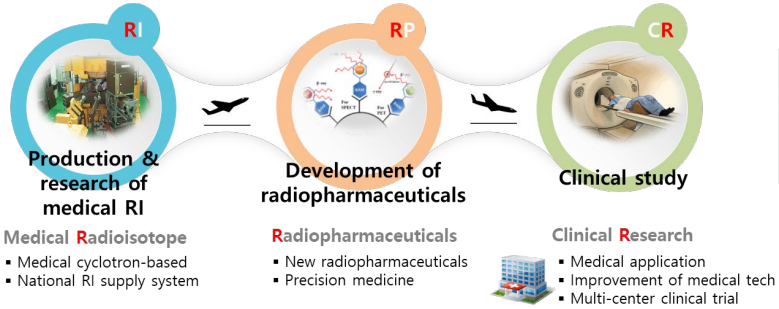
- F-18
- I-123
- Tl-201
- Ac-225



16.5 MeV Cyclotron (GE)

- C-11
- F-18

3 Medical cyclotrons in KIRAMS



Bench to bed research in KIRAMS

Medical Cyclotrons in KIRAMS

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Energy (Proton beam)	Installation	Beam	Target Isotopes
50 MeV	Scanditronix (1985)	Alpha Deuteron Proton	^{64}Cu (PET), ^{124}I (PET), ^{89}Zr(PET), ^{44}Sc(PET), ^{117m}Sn(conversion electron), ^{211}At(alpha), ^{67}Cu(beta), ^{203}Pb(SPECT)
30 MeV	IBA (2000)	Proton	^{18}F(PET), ^{11}C(PET), ^{123}I(SPECT), ^{201}Tl(SPECT), ^{225}Ac(alpha)
16.5 MeV	GE (2018)	Deuteron Proton	^{18}F(PET), ^{11}C(PET), ^{68}Ga(PET)

Regular production; test production; Planned

Research history of KIRAMS-RI

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- 1986; Installation and operation of **MC-50 cyclotron (50 MeV, Scanditronix)**
- 1989; First production and clinic distribution of ^{67}Ga (SPECT, tumor) in Korea
- 1990; First production and clinic distribution of ^{201}Tl (SPECT, myocardiac) in Korea
- 1990; First production and clinic distribution of ^{123}I (SPECT, thyroid) in Korea
- 1992; First development of ^{111}In, ^{22}Na, and ^{51}Cr in Korea
- 1995; First development and production of ^{18}F, ^{11}C in Korea
- 1995; First development and clinic production of [^{18}F]FDG and [^{11}C]methionine in Korea
- 2002; Installation and operation of **Cyclone-30 (30 MeV, IBA)**
- 2003; Mass production and clinic distribution of ^{67}Ga (Korea), ^{201}Tl (Korea), and ^{123}I (Canada)
- 2003; First development and clinic distribution of [^{123}I]mIBG (SPECT, childhood cancer) in Korea
- 2005; First development and research distribution of ^{124}I (PET, thyroid, nanoparticle-labeling) in Korea
- 2007; First development and clinic distribution of ^{64}Cu (PET, tumor) in Korea
- 2007; First development and clinic study (low-level oxygen tumor) of [^{64}Cu]ATSM in Korea
- 2012; First development and research distribution of ^{89}Zr (PET, tumor) in Korea
- 2017; First development and clinic study (PET, breast cancer) of [^{64}Cu]Herceptin in Korea
- 2018; Installation and operation of **PETtrace 800 (16.5 MeV, GE)**
- 2020; First development of ^{211}At (Therapy, tumor) using alpha beam irradiation in Korea
- 2022; First development of ^{67}Cu (Therapy, tumor) using alpha beam irradiation in Korea
- 2022; First development of ^{117m}Sn (Therapy, tumor) using alpha beam irradiation in Korea
- 2023; First development of ^{203}Pb (SPECT, tumor) in Korea in coming Dec.
- 2023; Plan to install the Ga-68 liquid target in Dec. plan to install the Ga-68 liquid target in Dec.

* Red color mark : Regular production

RI Research Trend in Nuclear Medicine

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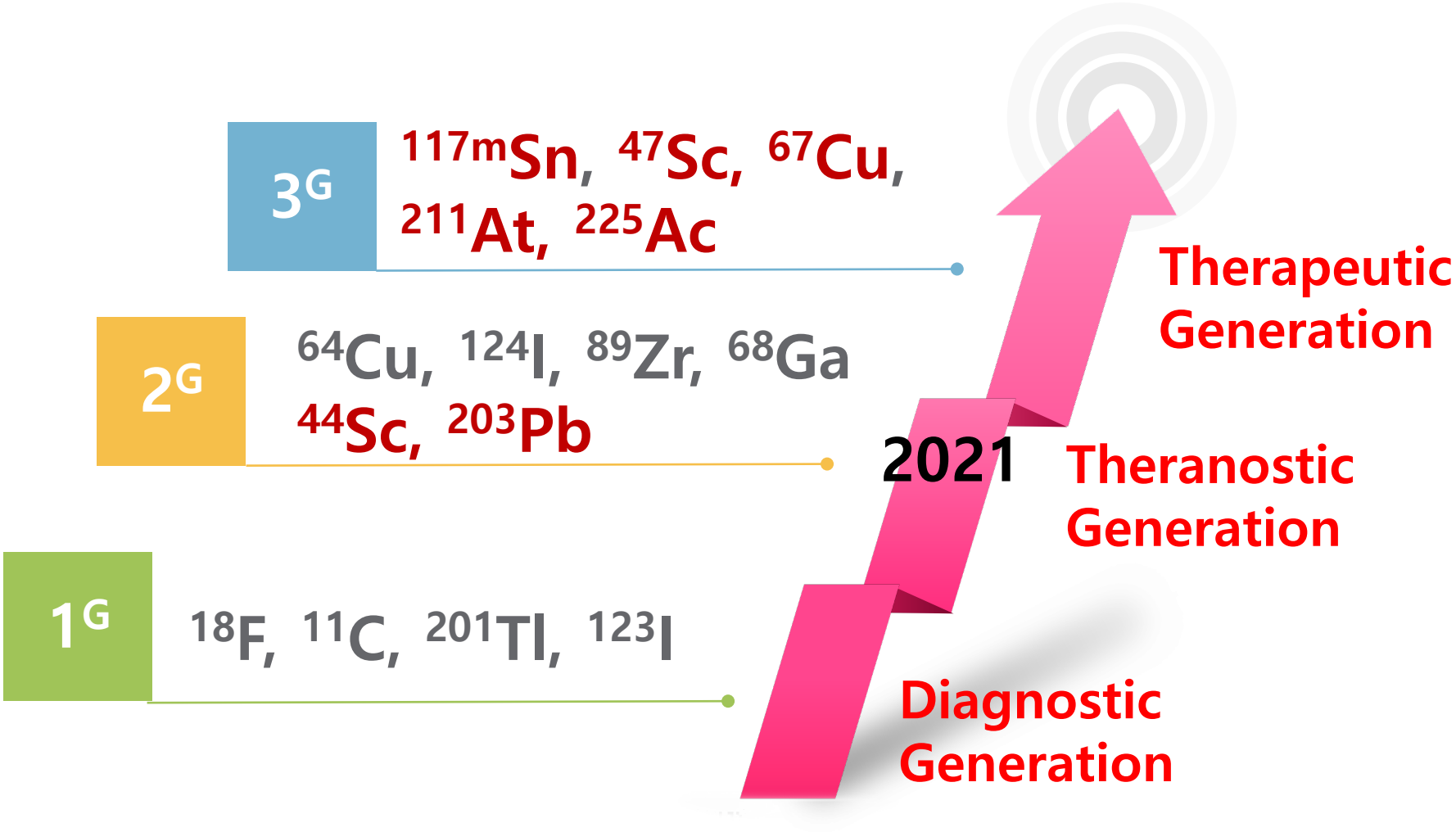

MC-50 Cyclotron Beam Lines

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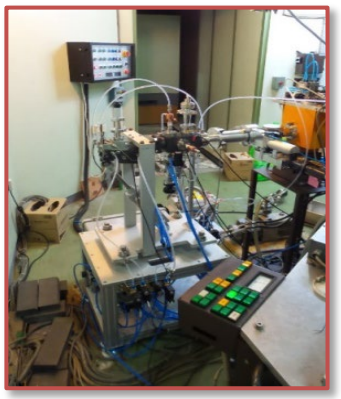

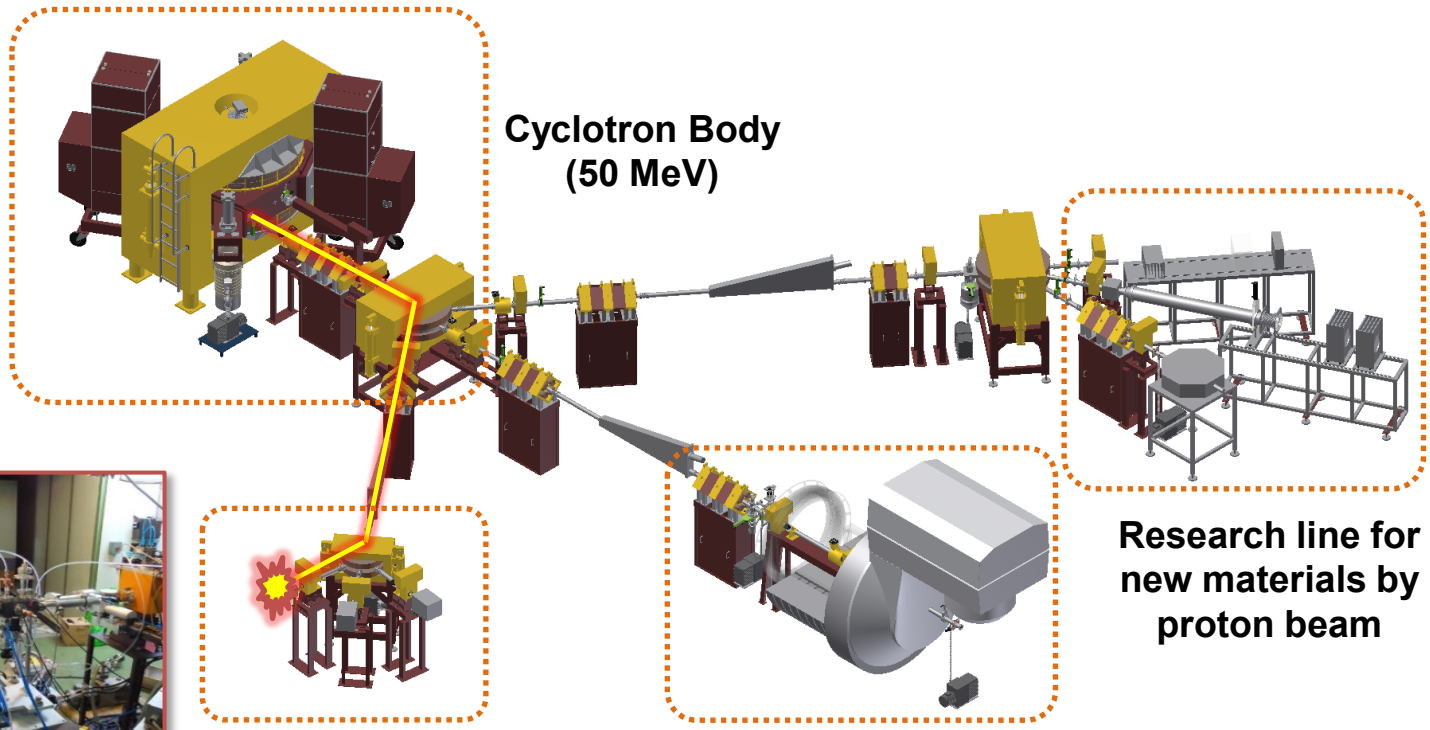

Cyclotron Body
(50 MeV)

Research line for new materials by proton beam

Research line for medical radioisotopes

Research line for Neutron Captured Therapy (NCT)

PET Radioisotopes Development

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50 MeV Cyclotron

Proton Beam (H^+)

Deuteron Beam (D^+)

Alpha Beam (He^{2+})

^{18}F, ^{11}C, ^{44}Sc*

^{64}Cu, ^{124}I, ^{89}Zr

^{117m}Sn*, ^{211}At*, ^{67}Cu*

^{64}Cu Production by Proton Beam

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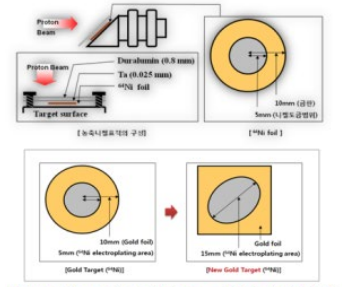
Step 1 Manufacture of enriched ^{64}Ni target

Step 2 Beam irradiation

Step 3 Target-to-solution

Step 4 Chemical purification of ^{64}Cu

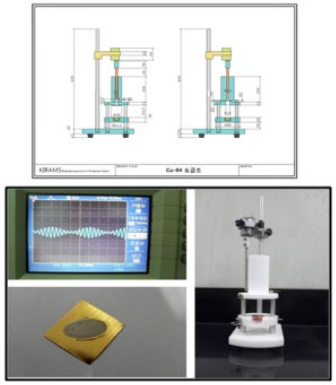
Step 5 Quality control of ^{64}Cu

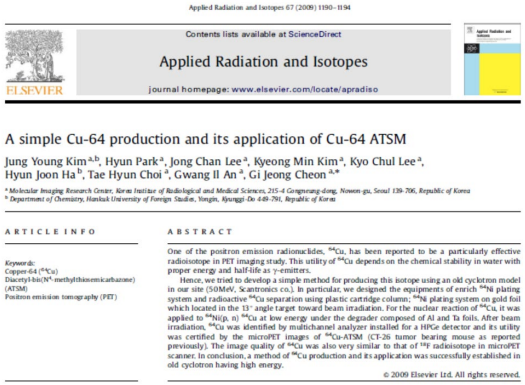


Designed the new target (circle → elliptical) (in 2011)

Ni-64 도금량의 증가 : Cu-64 생산량의 증가 효과

- ^{64}Ni(p, n)^{64}Cu
- Duralumin & Ta as beam degrader
- Irradiation for 4 hrs at about 20-22 MeV





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A simple Cu-64 production and its application of Cu-64 ATSM

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ARTICLE INFO

Keywords:
Copper-64 (^{64}Cu)
Diacetyl-bis(N4-methylthiosemicarbazone) (ATSM)
Positron emission tomography (PET)

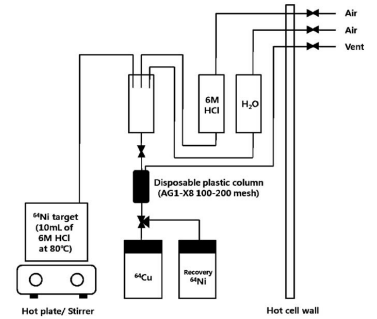
ABSTRACT

One of the positron emission radionuclides, ^{64}Cu, has been reported to be a particularly effective radioisotope in PET imaging study. This utility of ^{64}Cu depends on the chemical stability in water with proper energy and half-life as γ-emitters.

Hence, we tried to develop a simple method for producing this isotope using an old cyclotron model in our site (50MeV, Scantronics co.). In particular, we designed the equipments of enrich ^{64}Ni plating system and radioactive ^{64}Cu separation using plastic cartridge column; ^{64}Ni plating system on gold foil which located in the 13° angle target toward beam irradiation. For the nuclear reaction of ^{64}Cu, it was applied to ^{64}Ni(p, n) ^{64}Cu at low energy under the degrader composed of Al and Ta foils. After beam irradiation, ^{64}Cu was identified by multichannel analyzer installed for a HPGe detector and its utility was certified by the microPET images of ^{64}Cu-ATSM (CT-26 tumor bearing mouse as reported previously). The image quality of ^{64}Cu was also very similar to that of ^{18}F radioisotope in microPET scanner. In conclusion, a method of ^{64}Cu production and its application was successfully established in old cyclotron having high energy.

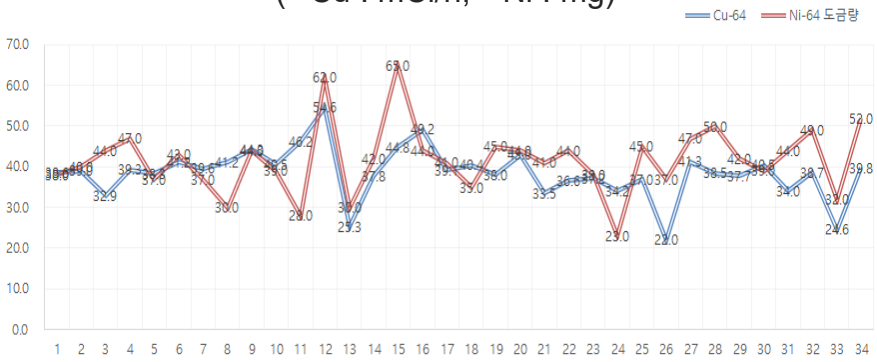
^{64}CuCl$_2$	Copper chloride
Copper-64 (Cu-64)	
Copper-64 is a radiochemical NOT FOR HUMAN USE, ONLY RESEARCH	
Model	KIRAMS-Cu(II)
Package unit	1-50 mCi (1 vial)
Definition	Acidic solution containing copper-64 in the form of copper(II) chloride. Physical properties of copper-64 : Half life 12.7 hours, β⁻ 37.1%, β⁺ 17.9%
Production	Copper-64 is produced by proton irradiation of enriched nickel-64 (purity : 99%). No carrier copper is added.
Characters	Appearance : clear, colorless solution
Identification	Gamma-ray spectrometry : the most prominent gamma photon has an energy of 511 KeV.
Test	pH : lower than 3 Sterility : Not tested for. Bacterial endotoxins :Not tested for.
Radioactive concentration	> 5mCi/mL in glass vial
Radionuclidic purity	Copper-64 : > 99%
Radioactivity	Determine the radioactivity using a calibrated instrument.

한국원자력의학원



^{64}Cu production for ^{64}Ni-electroplating amount

(^{64}Cu : mCi/h, ^{64}Ni : mg)



- ✓ ^{64}Ni : average 41.7 ± 8.5 mg
- ✓ ^{64}Cu : average 38.5 ± 6.3 mCi/h
- ✓ ^{64}Cu : max. 47.3 mCi/h
- ✓ Best production conditions
  - beam stability
  - beam-widespread irradiation
  - homogenous surface on the ^{64}Ni target

^{89}Zr Production by Proton Beam

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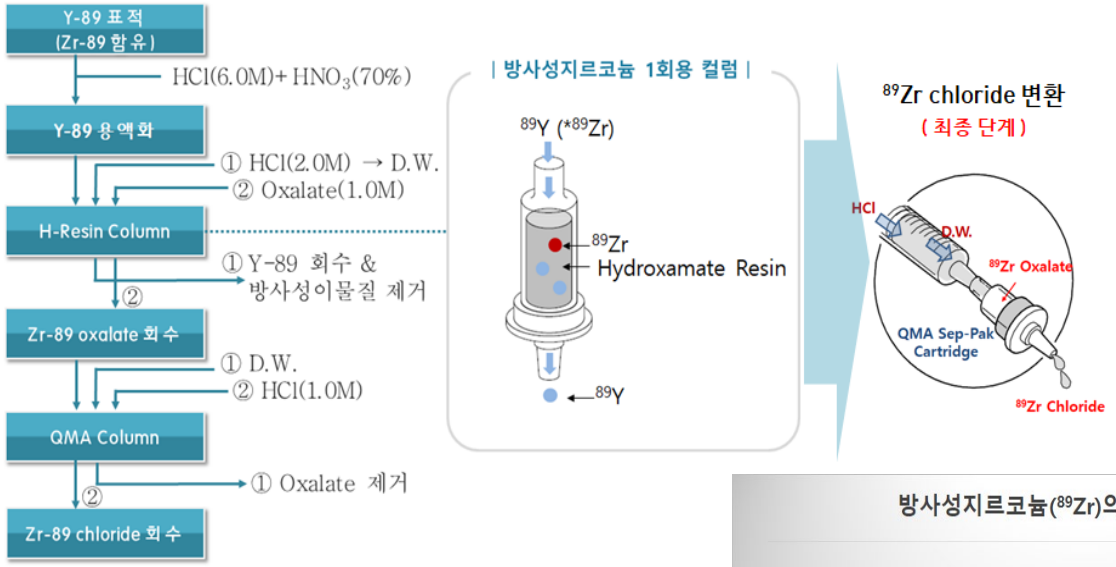
Step 1 Manufacture of enriched ^{89}Y target

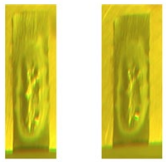
Step 2 Beam irradiation

Step 3 Target-to-solution

Step 4 Chemical purification of ^{89}Zr

Step 5 Quality control of ^{89}Zr

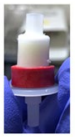




양성자 빔 조사된 Y-Target
두께 0.15mm

Target 녹인 후 vial

1st H-resin
0.34g



2nd H-resin
0.31g

^{89}ZrCl$_4$ Zirconium chloride

Zirconium-89
(Zr-89)
Zirconium-89 is a radiochemical
NOT FOR HUMAN USE, ONLY RESEARCH

Model	KIRAMS-Zr(IV)
Package unit	1-10 mCi (1 vial)
Definition	Acidic solution containing zirconium-89 in the form of zirconium(IV) chloride. Physical properties of zirconium-89 : Half life 3.27 days, β+ 22.3%, EC 76.6%
Production	Zirconium-89 is produced by proton irradiation of enriched yttrium-89 (chemical purity : 99%). No carrier zirconium is added.
Characters	Appearance : clear, colorless solution
Identification	Gamma-ray spectrometry : the most prominent gamma photon has an energy of 511, 909 KeV.
Test	pH : lower than 3 Sterility : Not tested for. Bacterial endotoxins :Not tested for.
Radioactive concentration	> 10.0 mCi/mL in glass vial
Radionuclidic purity	Ziconium-89 : > 99%
Radioactivity	Determine the radioactivity using a calibrated instrument.

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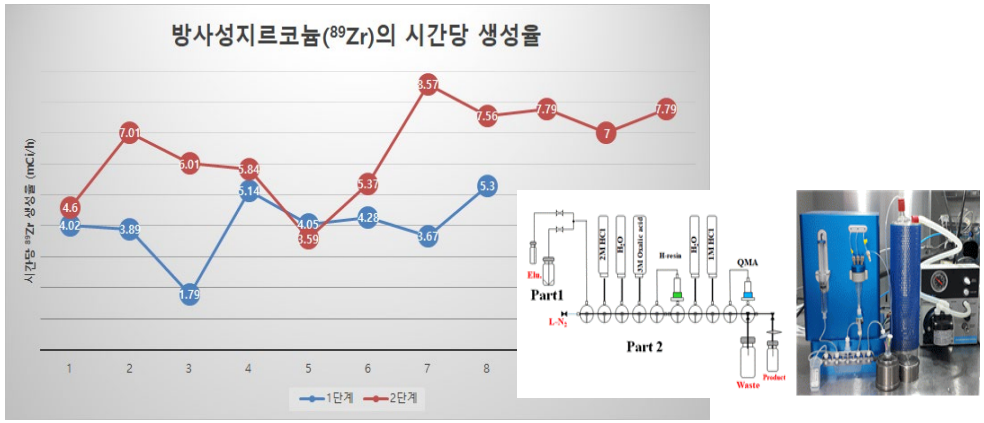
- ✓ ^{89}Zr : average 6.5 ± 1.5 mCi/h
- ✓ ^{89}Zr : max. 8.6 mCi/h
- ✓ Beam : 20 μA, 4 hrs



^{89}Zr Production & Imaging Test

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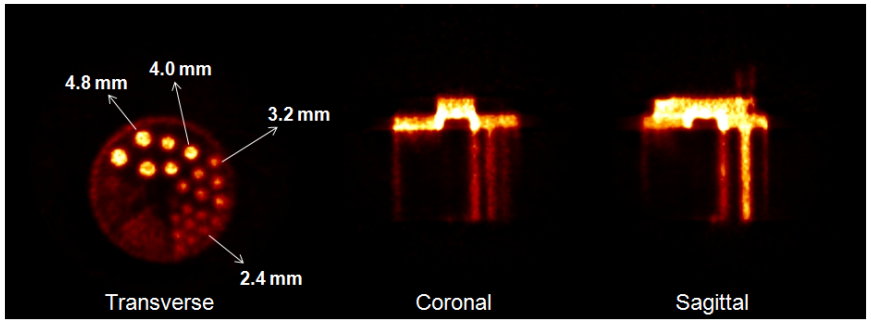
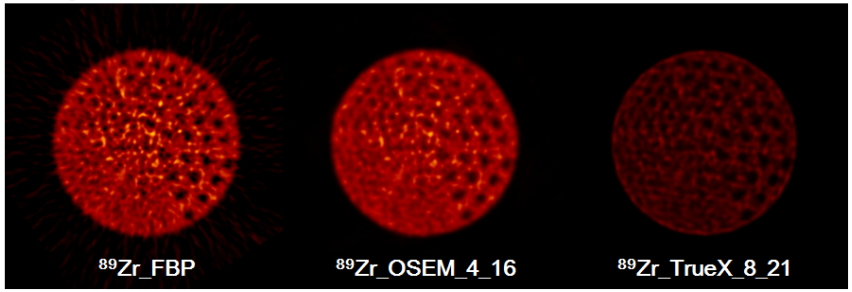


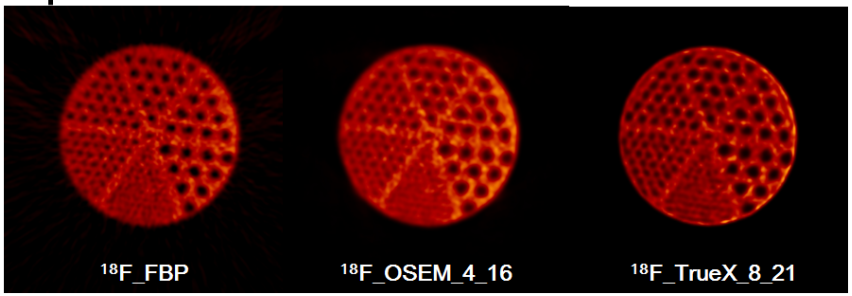
- **Phantom Derenzo :** 100 μCi
- **PET scanner :** Inveon (Siemens)
- **Energy window :** 350-650 KeV
- **Acquisition time :** 80.4 mins
- **Reconstruction :** Derenzo (OSEM 2D)

- **Phantom Jaszczak :** 2,000 μCi
- **PET scanner :** Biograph Truepoint TrueV (Clinical, Siemens)
- **Energy window :** 425-650 KeV
- **Acquisition time :** 10 mins (Brain mode)
- **Reconstruction :** OSEM 2D

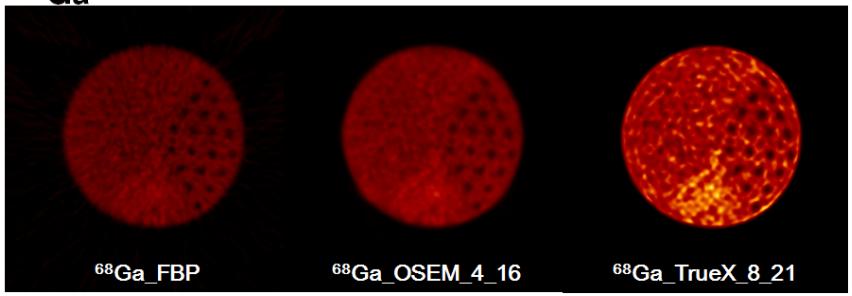
➢ ^{89}Zr



➢ ^{18}F



➢ ^{68}Ga



^{124}I Production by Proton Beam

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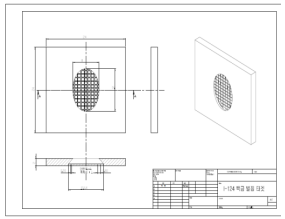
Step 1 ^{125}Te solution on the Pt target body

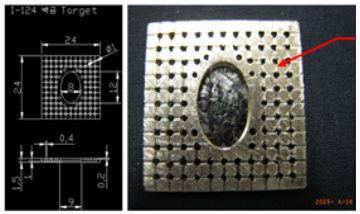
Step 2 Manufacturing of ^{125}Te/Pt target

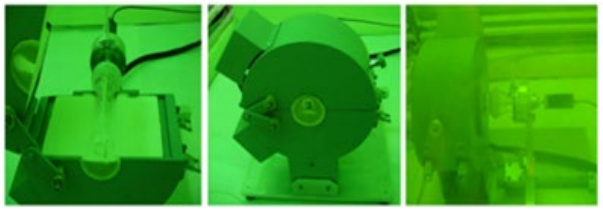
Step 3 Beam irradiation

Step 4 ^{124}I sublimation at 600 ℃

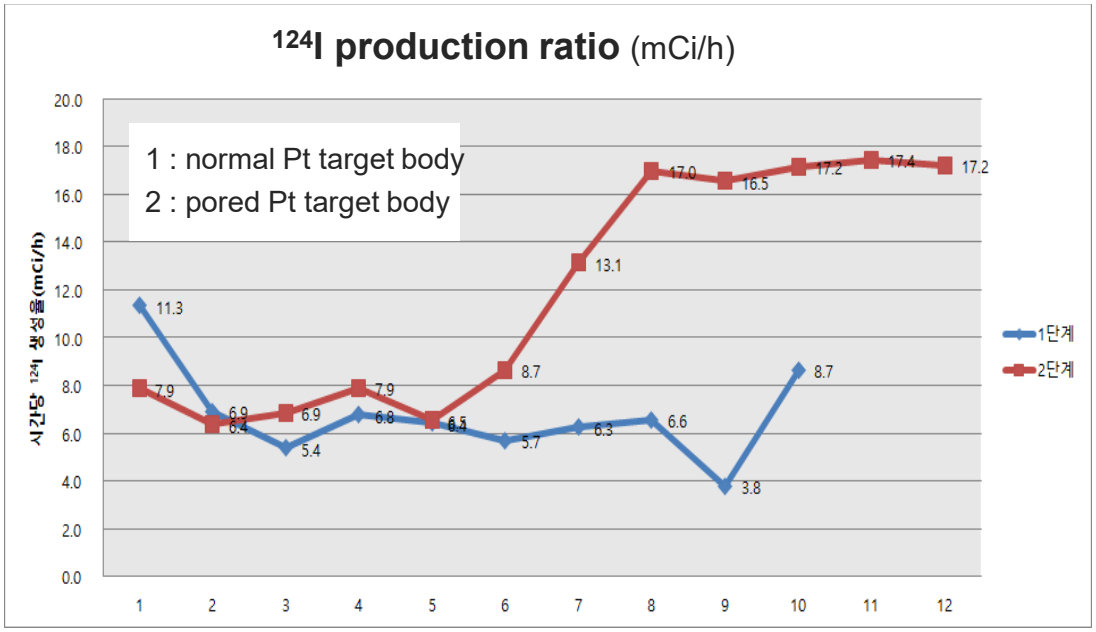
Step 5 Quality control of ^{124}I







^{124}I production ratio (mCi/h)



$Na^{124}I$ Sodium Iodide

Iodine-124
(I-124)
Iodine-124 is a radiochemical
NOT FOR HUMAN USE, ONLY RESEARCH

Model	KIRAMS-Na[^{124}I]
Package unit	1-20 mCi (1 vial)
Definition	A dilute solution of NaOH containing I-124 in the chemical form of iodide ($^{124}I^-$). Physical properties of I-124 : Half life 4.18 days, β^+ 25.6%, EC 74.4%
Production	Iodine-124 is produced by proton irradiation of enriched tellurium-124 or tellurium-125 (chemical purity : over 98%). No carrier iodine (or iodide) is added.
Characters	Appearance : clear & colorless solution
Identification	Gamma-ray spectrometry : the most prominent gamma photon has an energy of 27, 31, 511(major), 603, 723, 1691 KeV.
Test	pH : higher than 9 Sterility : Not tested for. Bacterial endotoxins : Not tested for.
Radioactive concentration	> 2.0 mCi/mL in glass vial
Radionuclidic purity	Iodine-124 : > 99%
Radioactivity	Determine the radioactivity using a calibrated instrument.

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- ✓ ^{125}Te : ~300 mg
- ✓ ^{124}I : average 11.9 ± 4.9 mCi/h
- ✓ ^{124}I : max. 17.4 mCi/h
- ✓ Beam conditions : 20 uA, 3 hrs

^{211}At Production by Alpha Beam

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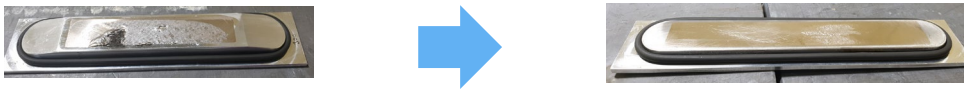
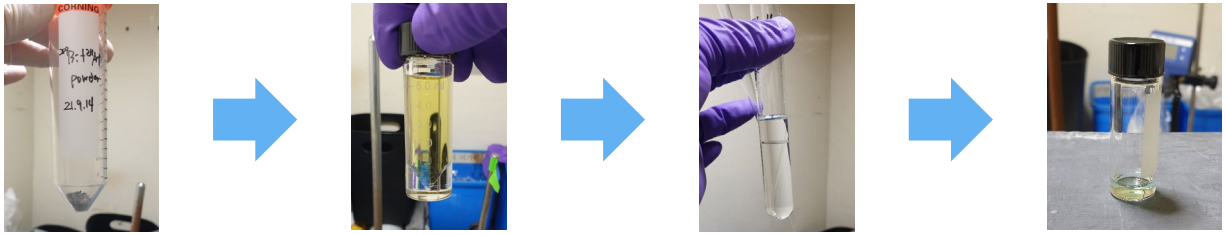
Produced At-211, an alpha particle emitting nuclide for targeted alpha therapy, which has a much better therapeutic effect than existing beta radiation emitting nuclides.

Production volume increased significantly compared to last year through improvements in the target part and purification part. (0.3 μCi → 9.2 mCi).

Beam irradiation and Improvement of target production



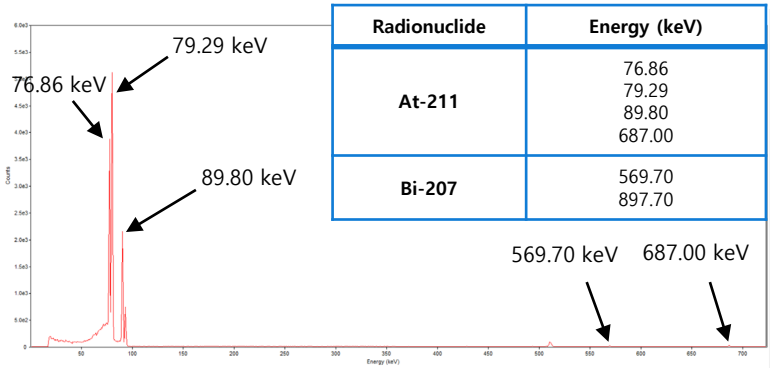
Wet extraction method for purification



Approximately 72.7% of the target radioactivity can be obtained through the ^{211}At separation and purification process using wet extraction.

At-211 5-15 mCi obtained as a NaAt form in 4 M sodium hydroxide solution.

Quality control



Gamma detector analysis

Radionuclide	Energy (keV)
At-211	76.86 79.29 89.80 687.00
Bi-207	569.70 897.70

Isotope	Concentration (ppm (μg/g))
Bi-209	2.12±1.62
Al-27	1.37±1.50

ICP-MS analysis

^{211}At Production by Alpha Beam

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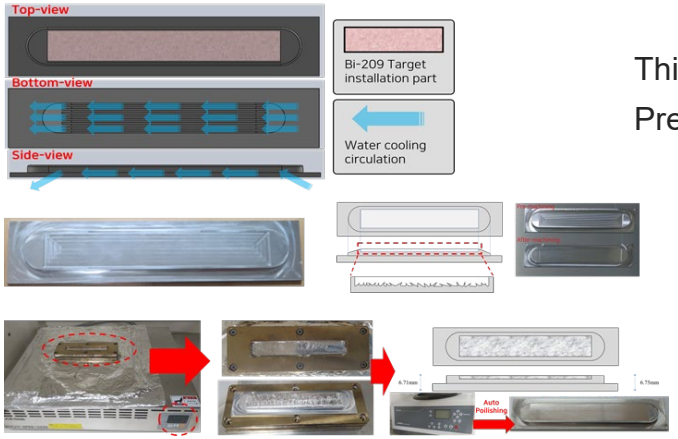
Improved targets and coolant systems to increase At-211 production

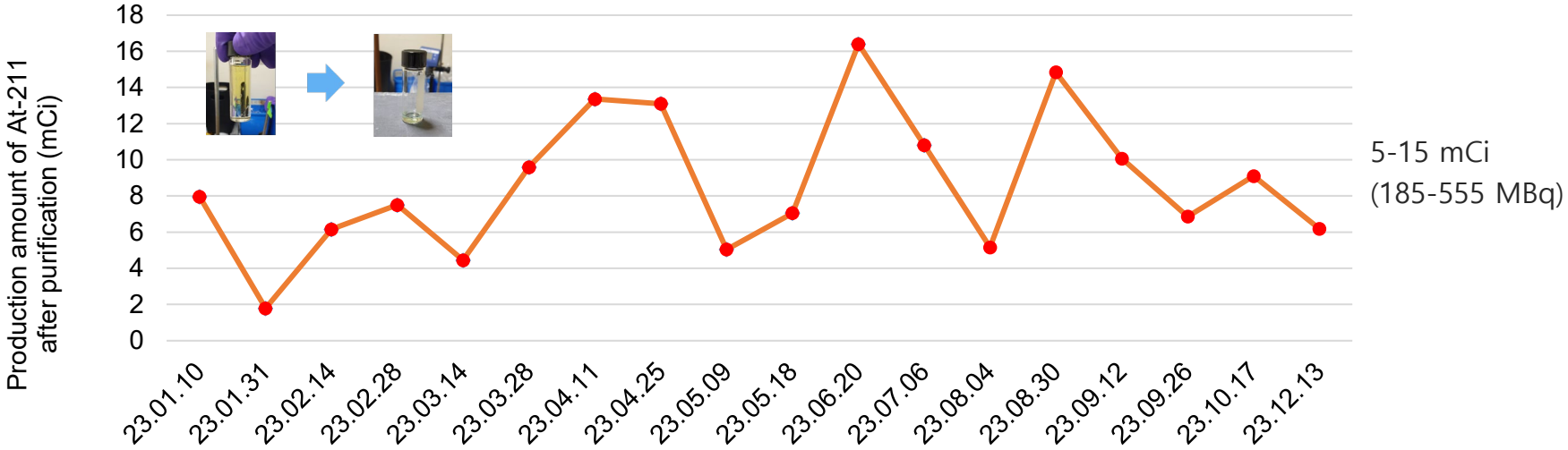


Thickness of Al target body set to 7 mm for efficient cooling of Bi-209.
Pressure of coolant was increased to over 10 bar.

Surface reprocessing to improve Al target body adhesion and cooling efficiency of Bi-209

Bi-209 plated at a thickness of 120-150 μm

- Changes in production volume of At-211 separated and purified by wet extraction method



5-15 mCi
(185-555 MBq)

Production record of At-211 in

^{211}At Production by Alpha Beam

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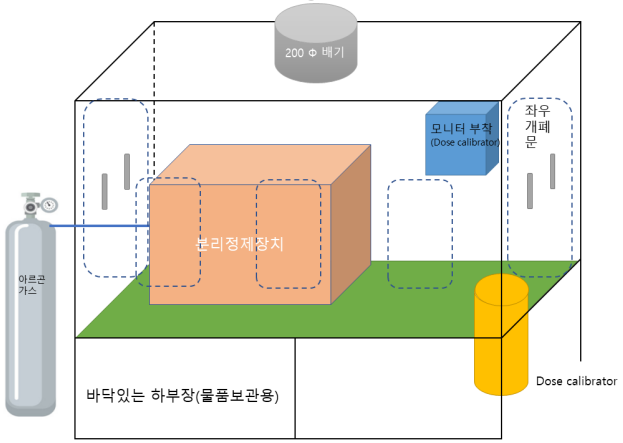
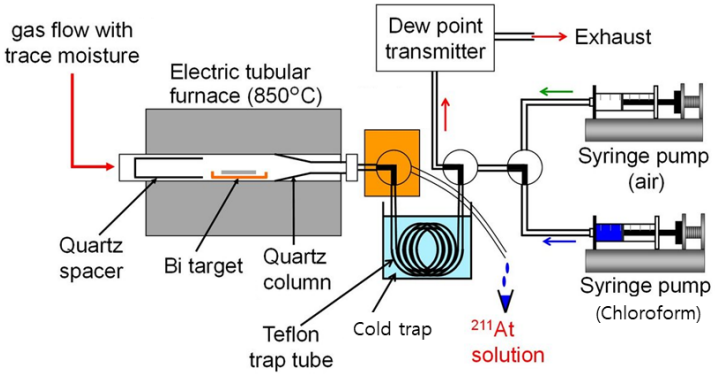
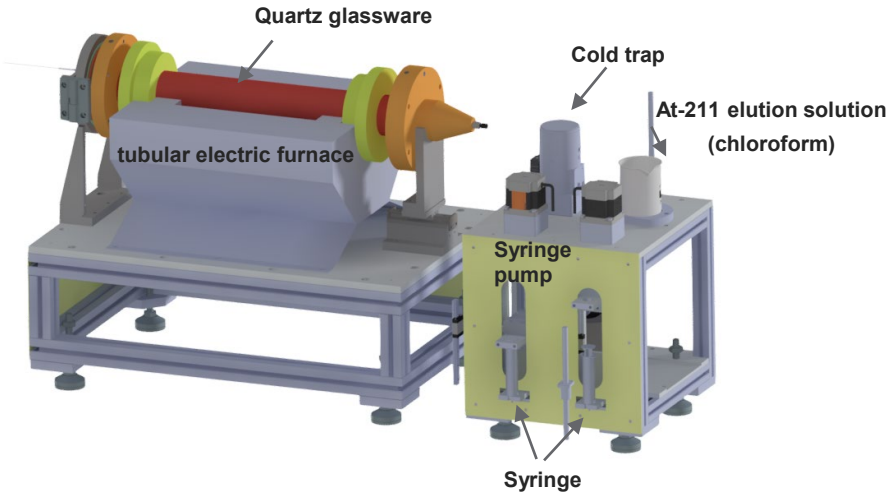
Installation of automatic separation and purification equipment (dry distillation method) for At-211 (in progress)



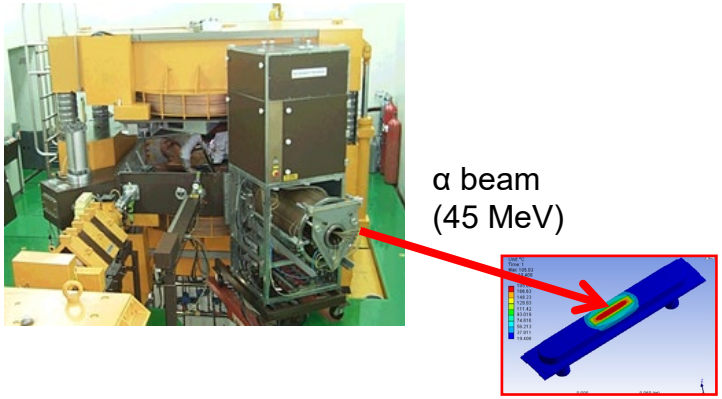
Glove box concept diagram for dry distillation device installation

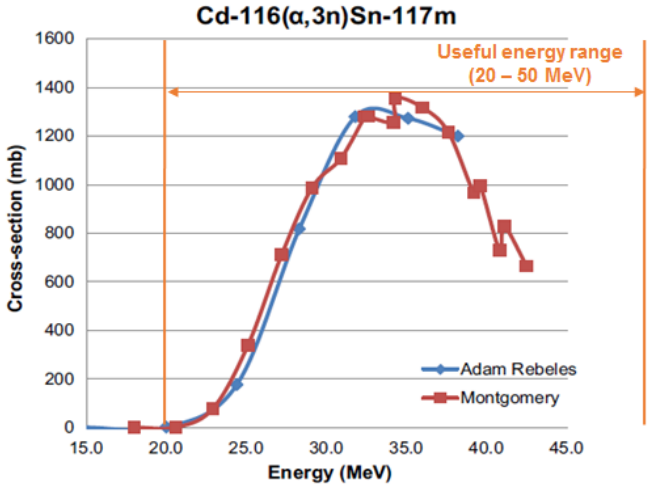




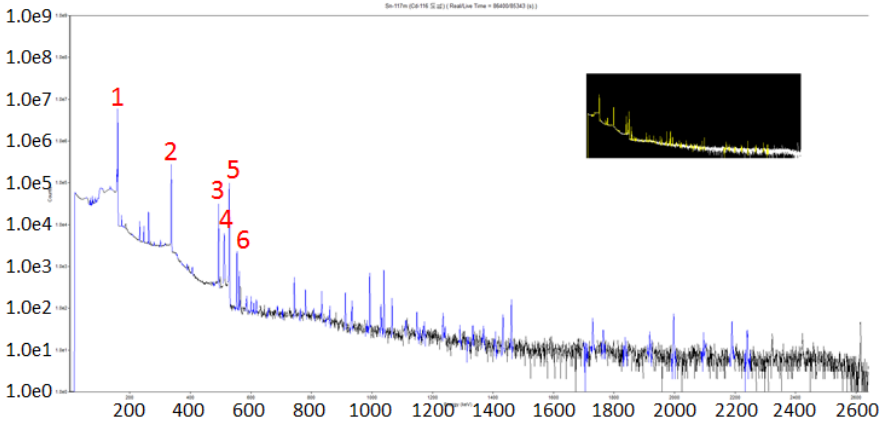
Concept and design of prototype dry distillation device

^{117m}Sn Production by Alpha Beam





Cd-116(α, 3n)Sn-117m



Confirmation of production of Sn-117m from gamma rays of 158.56 keV energy

In-115m at 336.24 keV energy

Cd-115g at 492.3 keV enegy

Cd-115g at 527.9 keV energy

} Toxic impurity

In-117g was also produced at 552.9 keV energy

In the case of In-115m and In-117g, the half-life is very short at 4.49 h and 43.2 m, respectively.

^{67}Cu Production by Alpha Beam

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Particle	Reaction
Proton	^{68}Zn(p,2p)^{67}Cu
	^{70}Zn(p,α)^{67}Cu
Alpha	^{64}Ni(α,p)^{67}Cu

```
  Sample Title:          Cu-67 20220929
  Nuclide Library Used: C:\GENIE2K\CAMFILES\CU-67.NLB

.....................    IDENTIFIED NUCLIDES     ....................

Nuclide     Id          Energy     Yield      Activity      Activity
Name     Confidence     (keV)       (%)     (Bq /unit)   Uncertainty

CU-67      1.000        91.27*      7.00   1.75067E+005  4.06369E+003
                        93.31*     16.10   1.77405E+005  3.69719E+003
                       184.58*     48.70   1.67598E+005  3.20814E+003
                       208.95*      0.12   1.97426E+005  1.95146E+004
                       300.22*      0.80   1.85884E+005  6.68784E+003
                       393.53*      0.22   1.64289E+005  1.15812E+004
```

- **29 MeV 10 μA/8 h, 960 μCi (35 MBq) : 1 time**
- **29 MeV 10 μA/4 h, ave. 250 μCi (10 MBq) : 5 times**

Future radioisotope production plans (Pb-203)

$^{203}Pb/^{212}Pb$ Theranostic Pair

Isotopes of the same element have identical chemistries

- **^{203}Pb – diagnostic**

  ^{203}Pb -> ^{203}Tl (stable)
  279 keV gamma (SPECT; ***I*** = 81%)
  $T_{1/2}$ = 52 h

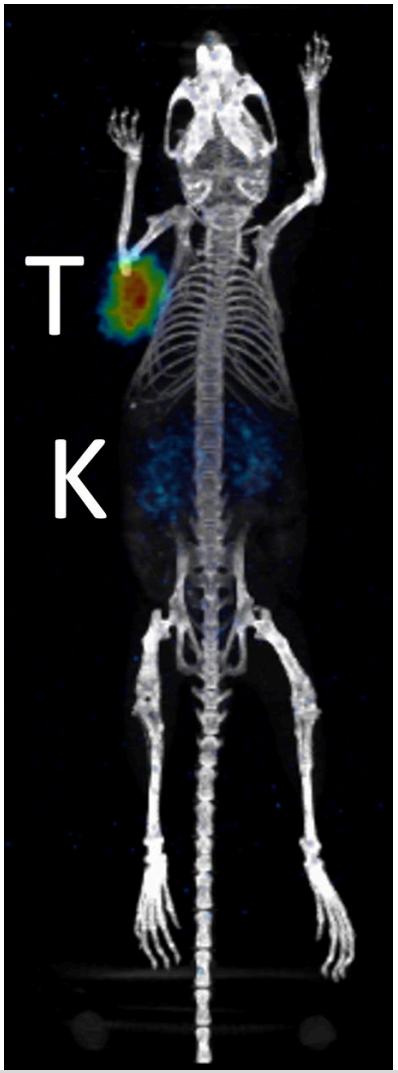
- **^{212}Pb – therapeutic**

  ^{212}Pb -> ^{212}Bi $T_{1/2}$ = 11 h **(peptides, fast PK)**
  Two α's in "*series*" (^{212}Bi and ^{212}Po)

Li *et al.*, *Curr Med Chem 2020*

^{203}Pb

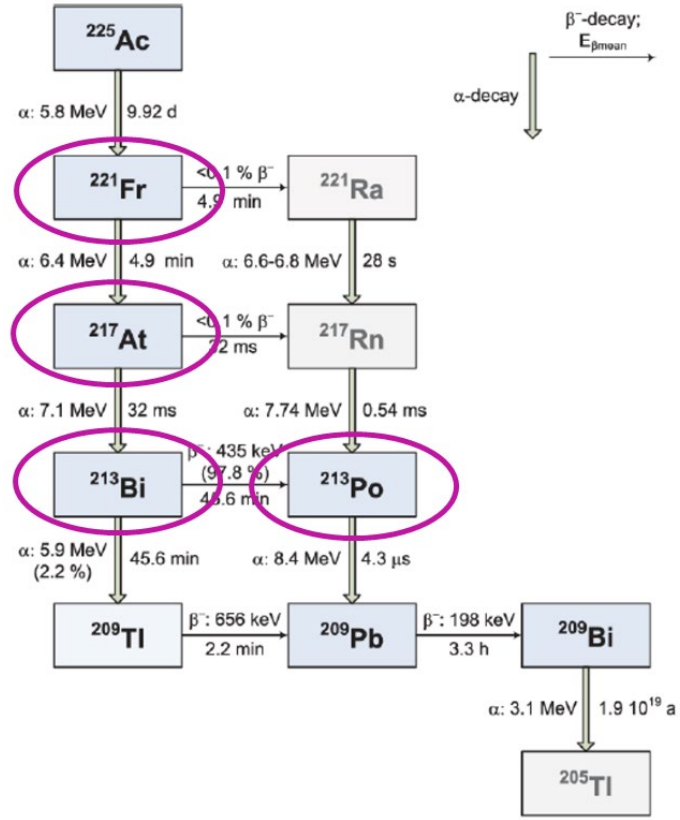
SPECT/CT



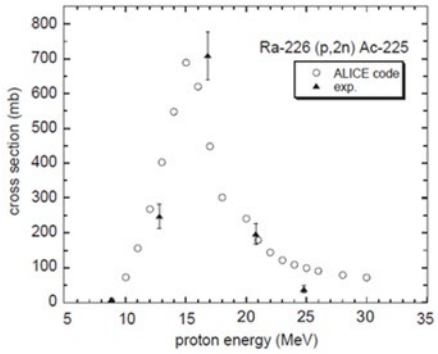
by Prof. Michael Schultz

Future radioisotope production plans (Ac-225)

^{225}Ac Decay Series



- ^{229}Th ($t_{1/2}$: 7340 y) ⟶ ^{225}Ac **Generator**
  - Up to now, the main process used to produce the ^{225}Ac for preclinical and clinical studies
  - Limitation of stock of ^{233}U
- ^{232}Th $\xrightarrow{(P, x)}$ ^{225}Ac **High energy accelerator (> 100 MeV)**
  - High energy protons are required
  - ^{227}Ac ($t_{1/2}$: 21.8 y) can be produced
- ^{226}Ra $\xrightarrow{(P, 2n)}$ ^{225}Ac **Cyclotron (30 MeV)**
  - Recycling of ^{226}Ra used for brachytherapy
  - Handling of ^{222}Rn (gas) produced from ^{226}Ra

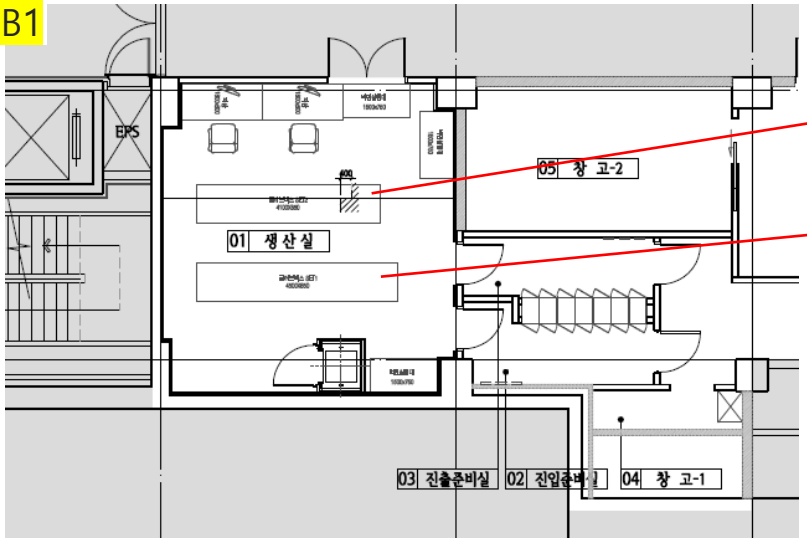


Appl Radat Isot 2005;62(3):383-387

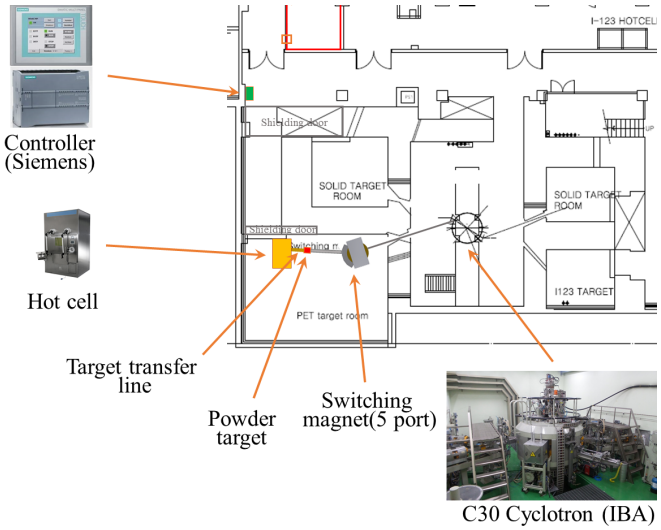
Future radioisotope production plans (Ac-225)

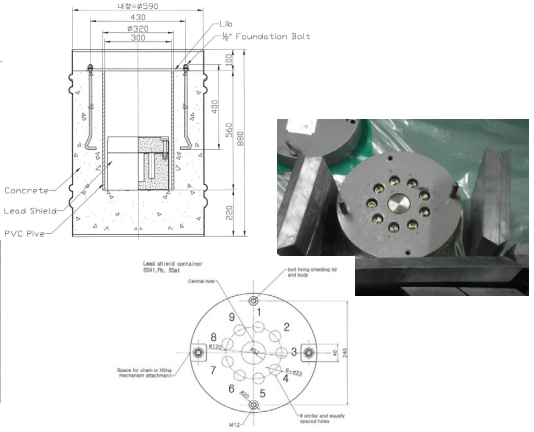
KIRAMS KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

B1



B2





Ra-226 source

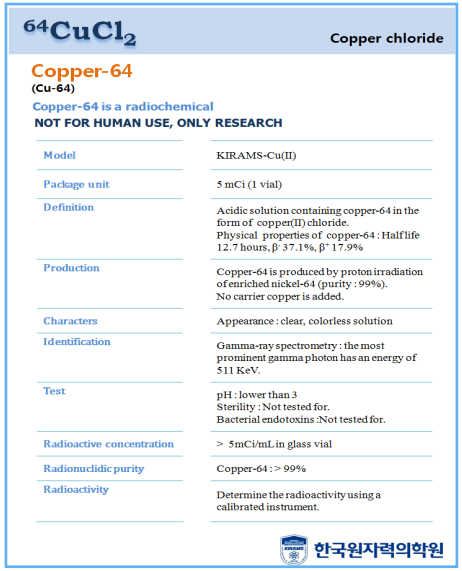
Medical application of radioisotopes

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Clinical Study

- **^{64}Cu-ATSM** (FDA approved, research); Diagnostic study of tumor bearing low level oxygen (KIRAMS)
- **^{64}Cu-DOTA-Trastuzumab & ^{64}Cu-NOTA-Trastuzumab** (FDA approved, research) ; Metastatic breast cancer (Surgery-Nuclear medicine, KIRAMS)

Production License by KINS



$^{64}CuCl_2$ Copper chloride

Copper-64
(Cu-64)
Copper-64 is a radiochemical
NOT FOR HUMAN USE, ONLY RESEARCH

Model	KIRAMS-Cu(II)
Package unit	5 mCi (1 vial)
Definition	Acidic solution containing copper-64 in the form of copper(II) chloride. Physical properties of copper-64 : Half life 12.7 hours, β- 37.1%, β+ 17.9%
Production	Copper-64 is produced by proton irradiation of enriched nickel-64 (purity : 99%). No carrier copper is added.
Characters	Appearance : clear, colorless solution
Identification	Gamma-ray spectrometry : the most prominent gamma photon has an energy of 511 KeV.
Test	pH : lower than 3 Sterility : Not tested for. Bacterial endotoxins :Not tested for.
Radioactive concentration	> 5mCi/mL in glass vial
Radionuclidic purity	Copper-64 : > 99%
Radioactivity	Determine the radioactivity using a calibrated instrument.

한국원자력의학원

SCI Journal

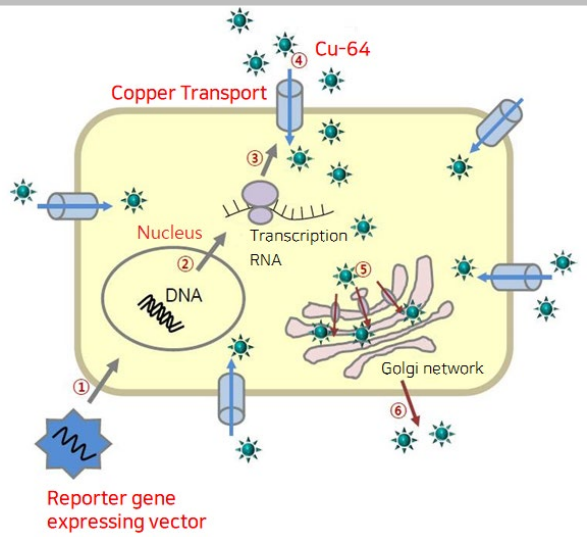
PET-RI	Cu-64 (32)	I-124 (11)	Zr-89 (2)
2016년 (13)	Amino Acids(2) J. Nucl. Med.(2) Nucl. Med. Commun.(1) Biochem. Biophy. Res. Comm.(1) Nucl. Eng. Tech. (1) Nucl. Med. Commun.(1) Cancer Biother. Radiopharm. (2)	Appl. Radiat. Isot. (1) Mol. Imaging Biol. (1)	Mol Pharm.(1)
2015년 (9)	EANMMI Res, (1) PloS One (1) Nucl. Med. Commun.(1) Int. J. Oncol.(1) Inorg. Chem. (1) ACS Med. Chem. Lett.(2)	Biochem. Biophy. Res. Comm.(1)	Cancer Biother. Radiopharm. (1)
2014년 (6)	J. Nucl. Med.(1) Nucl. Med. Biol. (1) J. Med. Chem. (1) ACS Med. Chem. Lett.(1) Bioconjug. Chem.(1)	ACS Med. Chem. Lett.(1)	
2013년 (4)	Nucl. Med. Biol. (1) Biomaterials(2) Bioconjug. Chem.(1) ACS Med. Chem. Lett.(1)		
2012년 (5)	Nucl. Med. Biol. (1) Bioconjug. Chem.(2)	Bioorg. Medi. Chem.(1) J. Korean Med. Sci (1)	
2010년 (3)	Nucl. Med. Mol. Imaging(1) Appl. Radiat. Isot. (1)	Appl. Radiat. Isot. (1)	
2008년 (1)		Angewandte Chemie(1)	
2007년 (2)		J. Med. Chem. (1) J. Label. Como. Radiopharm(1)	
2005년 (1)		J. Nucl. Med.(1)	
RI 개발 년도	2009년	2005년	2014년

Radioisotopes application (KIRAMS)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Diagnosis and therapy for tumor cell by copper transporter

Working process of copper transport



- Korean patent : 10-2013-0073311 (2013.06.25)
- KBS news, YTN news, etc. (2014.08.20)

Journal of Nuclear Medicine, 2014

Detection of Increased ^{64}Cu Uptake by Human Copper Transporter 1 Gene Overexpression Using PET with $^{64}CuCl_2$ in Human Breast Cancer Xenograft Model

Kwang Il Kim[1], Su Jin Jang[1], Ju Hui Park[1], Yong Jin Lee[1], Tae Sup Lee[1], Kwang Sun Woo[1], Hyun Park[1], Jae Gol Choe[2], Gwang Il An[1], and Joo Hyun Kang[1]

[1]*Molecular Imaging Research Center, Korea Institute of Radiological and Medical Sciences, Seoul, Korea; and* [2]*Department of Nuclear Medicine, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea*

Copper is an essential cofactor for a variety of biochemical processes including oxidative phosphorylation, cellular antioxidant activity, and elimination of free radicals. The copper transporter 1 is known to be involved in cellular uptake of copper ions. In this study, we evaluated the utility of human copper transporter 1 (*hCTR1*) gene as a new reporter gene for ^{64}Cu PET imaging. **Methods:** Human breast cancer cells (MDA-MB-231) were infected with a lentiviral vector constitutively expressing the *hCTR1* gene under super cytomegalovirus promoter, and positive clones (MDA-MB-231-hCTR1) were selected. The expression of *hCTR1* gene in MDA-MB-231-hCTR1 cells was measured by reverse transcription polymerase chain reaction, Western blot, and ^{64}Cu uptake assay. To evaluate the cytotoxic effects induced by hCTR1 expression, the dose-dependent cell survival rate after treatment with cisplatin (Cis-diaminedichloroplatinum (II) [CDDP]) was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and trypan blue dye exclusion. Small-animal PET images were acquired in tumor-bearing mice from 2 to 48 h after an intravenous injection of ^{64}Cu. **Results:** The *hCTR1* gene expression in MDA-MB-231-hCTR1 cells was confirmed at the RNA and protein expression and the cellular ^{64}Cu uptake level. MTT assay and trypan blue dye exclusion showed that the cell viability of MDA-MB-231-hCTR1 cells decreased more rapidly than that of MDA-MB-231 cells after treatment with CDDP for 96 or 72 h, respectively. Small-animal PET imaging revealed a higher accumulation of ^{64}Cu in MDA-MB-231-hCTR1 tumors than in MDA-MB-231 tumors. With respect to the biodistribution data, the percentage injected dose per gram of ^{64}Cu in the MDA-MB-231 tumors and MDA-MB-231-hCTR1 tumors at 48 h after ^{64}Cu injection was 2.581 ± 0.254 and 5.373 ± 1.098, respectively. **Conclusion:** An increase in ^{64}Cu uptake induced by the expression of *hCTR1* gene was demonstrated in vivo and in vitro, suggesting the potential use of *hCTR1* gene as a new imaging reporter gene for PET with $^{64}CuCl_2$.

Key Words: hCTR1; reporter gene; ^{64}Cu; PET; cisplatin

J Nucl Med 2014; 55:1692–1698
DOI: 10.2967/jnumed.114.141127

Received Apr. 3, 2014; revision accepted Jul. 11, 2014.

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E-mail: kang2325@kirams.re.kr
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E-mail: gwangil@kirams.re.kr

Published online Aug. 4, 2014.

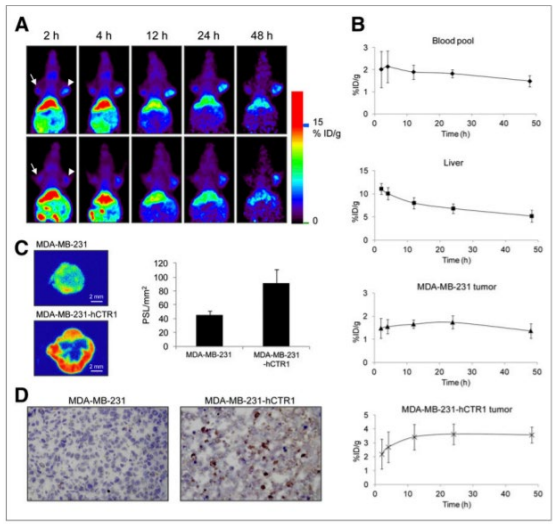


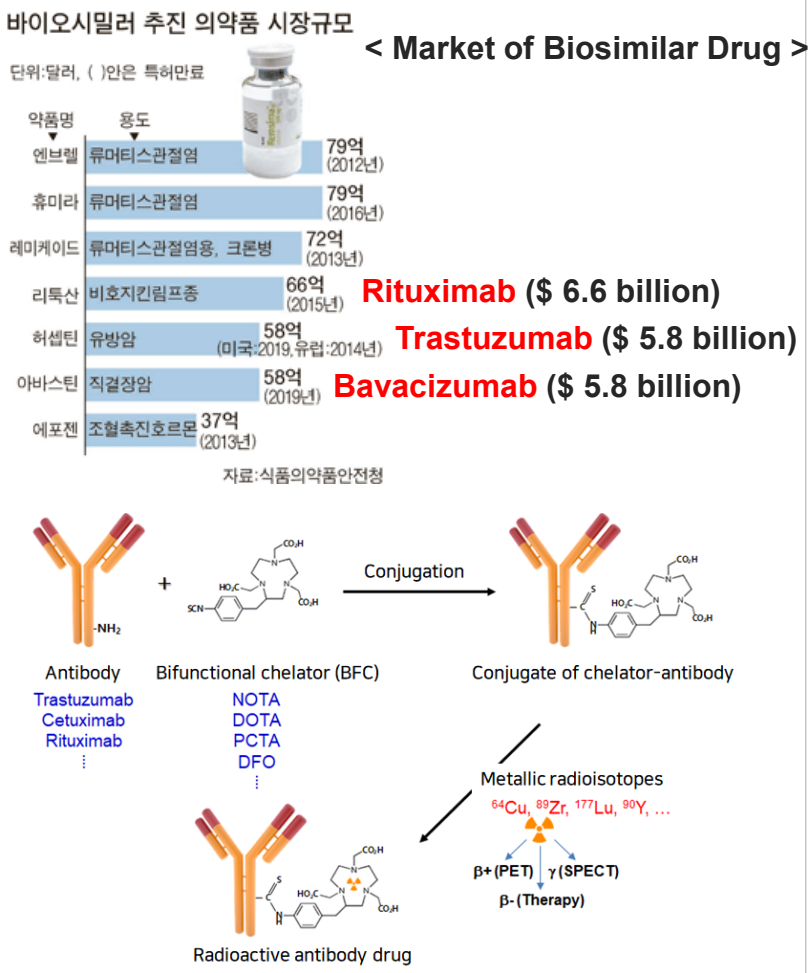
FIGURE 4. Small-animal PET images and autoradiographs of MDA-MB-231 and MDA-MB-231-hCTR1 tumors after injection of ^{64}Cu. (A) Representative PET images of xenografted mice bearing MDA-MB-231 (arrow) and MDA-MB-231-hCTR1 (arrowhead) tumors after tail vein injection of ^{64}Cu (n = 3). PET images were obtained at 2, 4, 12, 24, and 48 h after ^{64}Cu injection. (B) Time–activity curves of blood pool, liver, MDA-MB-231 tumor, and MDA-MB-231-hCTR1 tumor were calculated on PET images. Blood-pool activity was obtained from ROI of heart region. Time course of radioactivity was obtained by ROI analysis and presented as %ID/g. (C) Autoradiopraphs of MDA-MB-231 and MDA-MB-231-hCTR1 tumors. After acquisition of PET images, mice were euthanized. Tumor sections were exposed to image plate for scanning and quantification of ROI. (D) Anti-CTR1 immunohistochemistry of slices from MDA-MB-231 (left) and MDA-MB-231-hCTR1 (right) tumor tissues (original magnification, ×400).

Radioisotopes application (KIRAMS)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Clinical study for metastatic breast cancer using radioactive trastuzumab

Preparation of RI-antibody conjugate



^{64}Cu-DOTA (or NOTA)-trastuzumab,2017

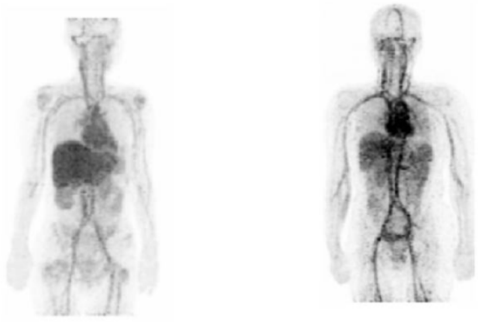
서울신문

조직검사 없이 난치성 유방암 정확히 집어낸다

입력 2017.11.06. 11:26 댓글 0개

Clinical study for metastatic breast cancer by KFDA

[서울신문]여성암 중 하나인 유방암은 발병 원인을 아직 정확하게 모르기 때문에 유방암 발병 확률을 정확히 어렵다는 문제가 있다.



유방암 환자에게 방사성동위원소 구리-64를 주사해 유방암 발병과 치료효과를 정밀하게 영상으로 확인할 수 있는 기술을 개발했다.한국원자력의학원 제공

또 유방암 5년 생존율은 0기 암의 경우 100%에 가깝지만 4기의 경우는 20% 미만으로 떨어진다. 이 때문에 유방암 생존율을 높일 수 있는 방법은 조기 발견인데 정확한 진단을 위해서는 조직검사를 해야 하기 때문에 조기진단이 쉽지 않다는 문제가 있다.

한국원자력의학원 유방암 연구팀은 방사성동위원소인 구리-64(Cu-64)를 이용한 양전자방출단층촬영(PET-CT)로 유방암의 표적치료 효과와 진단을 예측하는 기술을 개발했다고 6일 밝혔다.

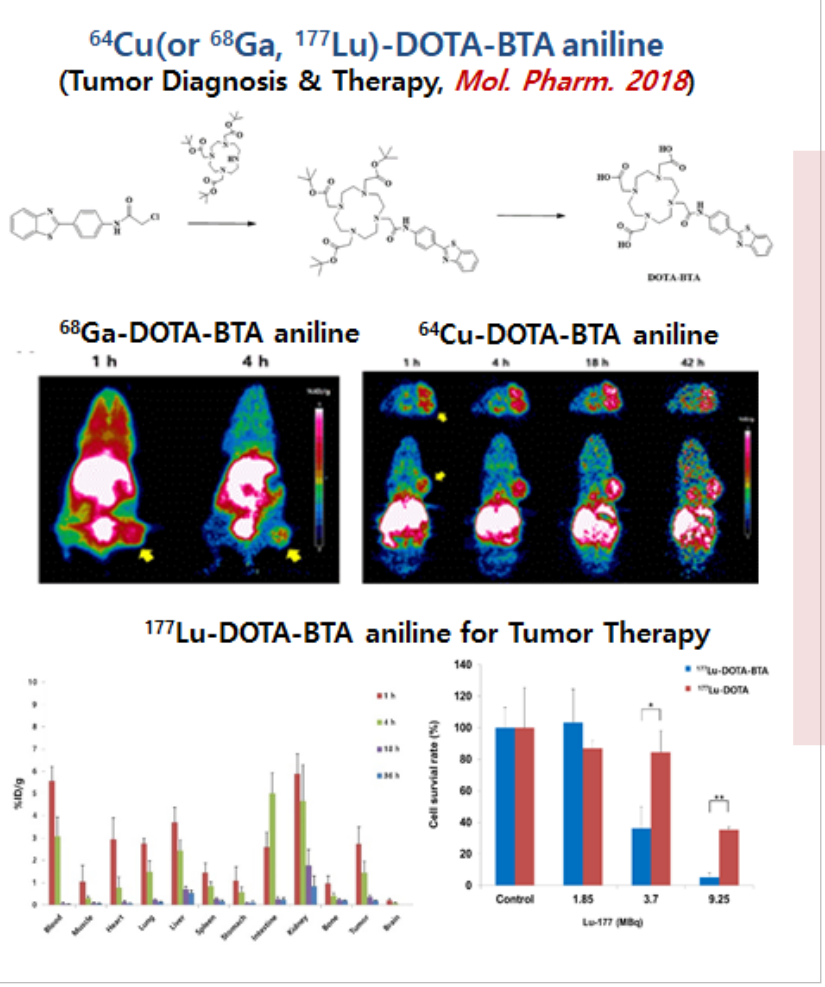
PET-CT는 암조기진단과 치료에 사용되는 영상진단검사법 중 하나로 암세포 주변에 조영제인 방사성의약품이 집중되도록 해 암의 위치, 크기, 전이 및 성장정도를 파악하는 기술이다.

Radioisotopes application (KIRAMS)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Diagnosis and therapy for cervical cancer (targeting HeLa cells)

^{64}Cu-DOTA-BTA aniline



Introduction to TV news, TYN

Radioisotopes application (KIRAMS)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Success of ^{89}Zr-PET imaging & Diagnosis for Rheumatoid Arthritis using ^{89}Zr oxalate

First Production of ^{89}Zr in Korea

암 진단용 방사성동위원소, 국내 생산 가능해졌다

[2017-09-28 10:26:35] 목록 | 프린트

국내 연구진이 그동안 수입에 의존했던 암 치료용 방사성동위원소의 국내 양산 시스템을 구축하는 데 성공했습니다.

한국원자력의학원은 지르코늄-89 양산시스템을 구축하고, 다음 달부터 국내 의료기관에 공급할 예정이라고 밝혔습니다.

지르코늄-89는 다른 방사성동위원소와 달리 반감기가 3.3일로 길어 정확한 암 진단이나 장시간의 약물반응 관찰이 가능하지만, 대량생산이 어려워 그동안 수입에 의존해왔습니다.

연구팀은 특수 흡착제를 이용해 불순물을 제거하는 방식으로 순도 99.9%의 지르코늄-89를 분리 정제하는 데 성공했다고 설명했습니다.

의학원은 사전 수요조사를 통해 서울대병원 등 14개 연구팀에 다음 달부터 지르코늄-89를 제공하기로 했습니다.

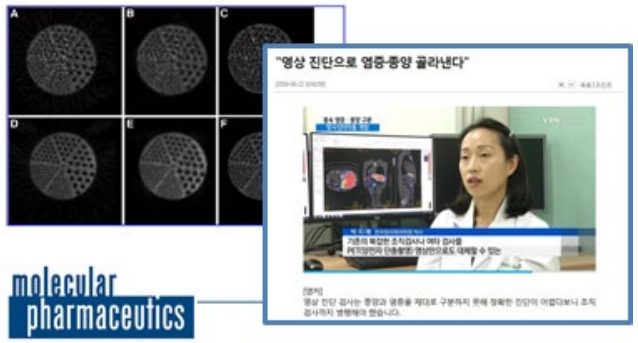
양훼영 [hwe@ytn.co.kr]

Rheumatoid Arthritis, ^{89}Zr oxalate

CANCER BIOTHERAPY AND RADIOPHARMACEUTICALS
Volume 30, Number 1, 2015
© Mary Ann Liebert, Inc.
DOI: 10.1089/cbr.2014.1709

Spatial Resolution and Image Qualities of Zr-89 on Siemens Biograph TruePoint PET/CT

Young Sub Lee,[1,2] Jin Su Kim,[1] Jung Young Kim,[1] Byung Il Kim,[1] Sang Moo Lim,[1] and Hee-Joung Kim[2]

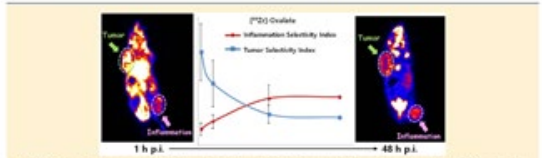


molecular pharmaceutics

Evaluation of [^{89}Zr]-Oxalate as a PET Tracer in Inflammation, Tumor, and Rheumatoid Arthritis Models

Ji-Ae Park,[†] Yong Jin Lee,[†] Ji Woong Lee,[†] Ran Ji Yoo,[†] Un Chol Shin,[†] Kyo Chul Lee,[†] Byung il Kim,[‡] Kyeong Min Kim,[†] and Jung Young Kim*[,†]

[†]Molecular Imaging Research Center, Korea Institute of Radiological & Medical Science, Seoul 139-706, Republic of Korea
[‡]Department of Nuclear Medicine, Korea Institute of Radiological and Medical Sciences, Seoul 139-706, Republic of Korea



ABSTRACT: To obtain an additional pharmacological agent for the diagnosis of inflammation, we investigated the medical use of ^{89}Zr-oxalate as a positron emission tomography (PET) probe for the in vivo imaging of inflammation and compared its efficacy to that of 2-deoxy-2-[^{18}F]fluoro-D-glucose ([^{18}F]FDG) and sodium [^{18}F]fluoride. ^{89}Zr-oxalate exhibited observable higher uptake in a macrophage cell line than in tumor cells. The inflammatory lesions and tumors were clearly visualized by PET imaging and autoradiography using ^{89}Zr-oxalate. Compared to [^{18}F]FDG and sodium [^{18}F]fluoride, ^{89}Zr-oxalate demonstrated a high selectivity index to the tumor at an early time point after injection and to inflammation at a delayed time point after injection (24 h). Through histological examination, large numbers of macrophages and neutrophils were observed in the tumor lesions with the highest ^{89}Zr-oxalate uptake. In a rheumatoid arthritis (RA) mouse model, ^{89}Zr-oxalate demonstrated a high level of accumulation in inflammatory lesions. ^{89}Zr-oxalate is a new strategic tool for tumor imaging and inflammatory processes.

KEYWORDS: *^{89}Zr-oxalate, inflammation, tumor, rheumatoid arthritis, PET*

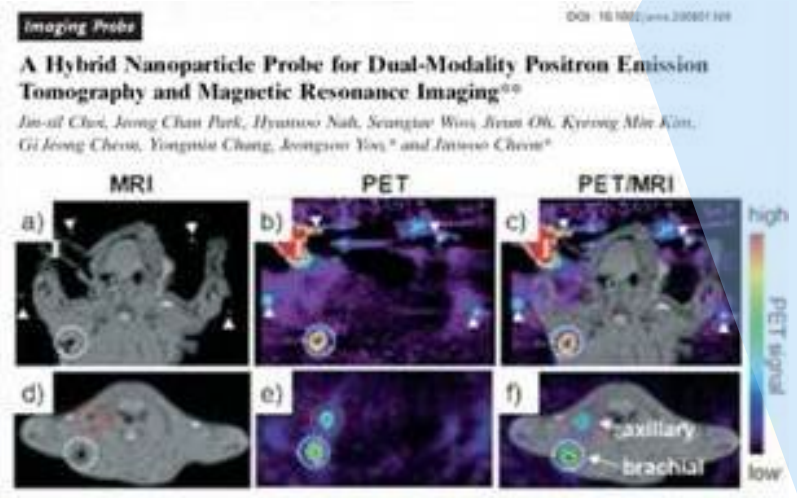
Radioisotopes application (collaboration)

Multi-modal probe using nanoparticles and ^{124}I for tumor imaging

Co-work with Univ.

PET-MRI hybrid Imaging agent

- Dr. Yoo (K.P. Univ.)& Dr. Ahn (KIRAMS)
- Angewandte Chemie. 47:6259-62, 2008 (IF=11.261)



Multi-modal imaging agent for metastatic tumor cell

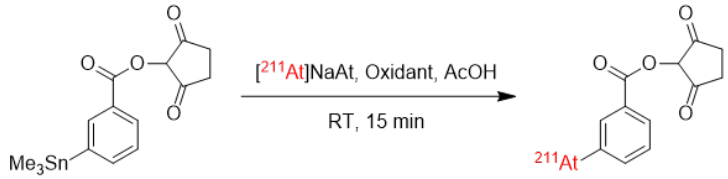
- Dr. Yoo (K.P. Univ.)& Dr. Ahn (KIRAMS)
- First development of multi-modal agent for PET-MRI-Optical instruments
- Small 6(24):2862-8, 2010 (IF=8.349)

Radioisotopes application (KIRAMS)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Labeling experiment using produced At-211

Small molecules

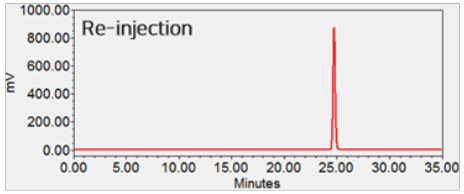


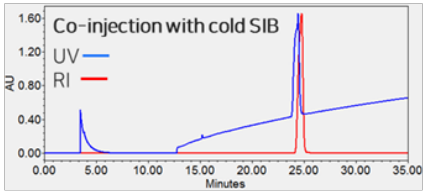
STB

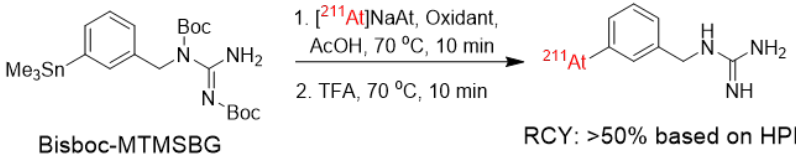
STB=N-succinimidyl 3-(trimethylstannyl)benzoate

RCY: 45.4% based on HPLC

[211At]SAB



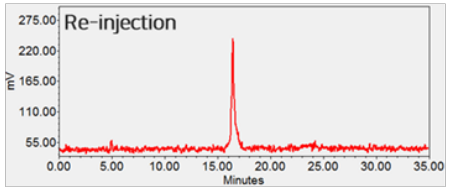


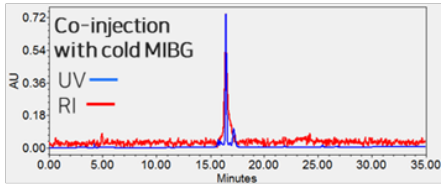


Bisboc-MTMSBG

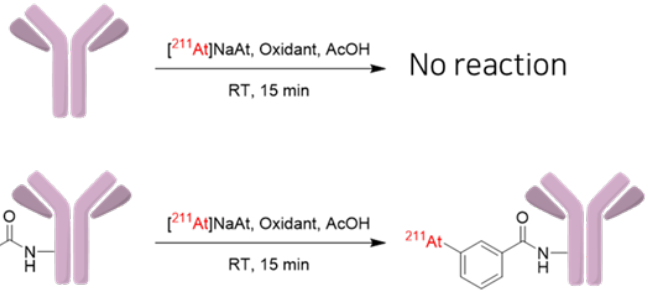
RCY: >50% based on HPLC

[211At]MABG





Antibody Conjugation

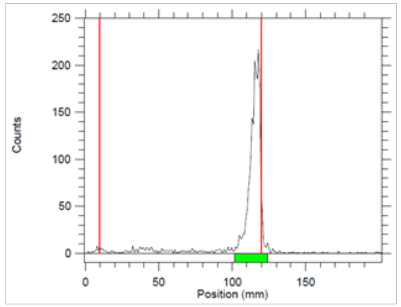


Pre-conjugated antibody with STB (TB-trastuzumab)

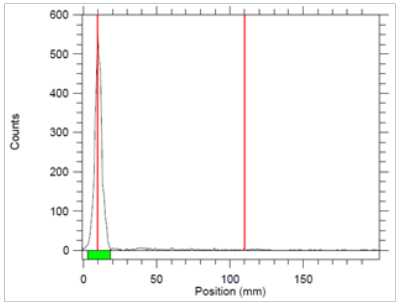
[211At]AB-trastuzumab

RCY: 62.3-83.1% based on PD-10

Radio-TLC



Free 211At



[211At]AB-trastuzumab

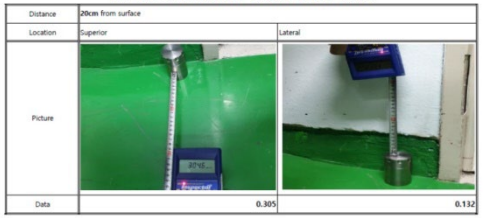
Tungsten shields for RI supply

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Zr-89

- Radioactivity: 10 mCi (370 MBq)
- 두께: 텅스텐 10 mm
- Gamma Energy: 511 keV(22.6%), 909 keV(99.9%), 1657(0.1%), 1713(0.77%), 1744(0.13%)
- 광자반응: MCPLIB84
- 시뮬레이션 코드: MCNP6.1
- 운반용기 차폐체 모델링

Zr-89 container Dose rate test



I-124

- Radioactivity: 50 mCi (1,850 MBq)
- 두께: 아크릴 10 mm, 텅스텐 19 mm
- Gamma Energy: 511 keV(22.5%), 602.7 keV(63%). 722.8(10.4%), 1509.5(3.1%), 1691(10.9%)
- 광자반응: MCPLIB84
- 시뮬레이션 코드: MCNP6.1
- 운반용기 차폐체 모델링

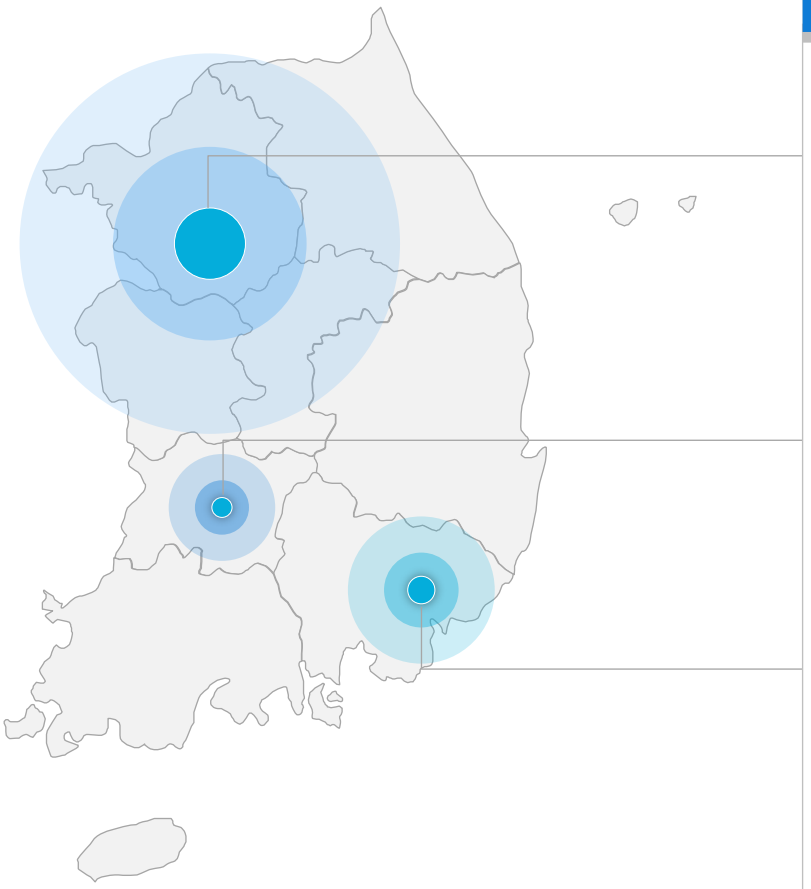
I-124 container Dose rate test

Cu-64

- Radioactivity: 100 mCi (3,700 MBq)
- 두께: 아크릴 5 mm, 텅스텐 8 mm
- Gamma Energy: 511 keV(42.63%), 1346 keV(0.47%)
- 광자반응: MCPLIB84
- 시뮬레이션 코드: MCNP6.1
- 운반용기 차폐체 모델링

Cu-64 container Dose rate test

RI supply from KIRAMS



Partner Institutions

(1) Seoul National Univ. Hospital

(2) Asan Medical Center

(3) Samsung Medical Center

(4) Severance Hospital

(5) A-Ju Univ. Hospital

(6) Kyungpook National Univ. Hospital

(7) Kyungook Univ.

(8) Chonnam National Univ. Hosptial

(9) Yonsei Univ.

(10) KIRAMS researchers

(11) Singapore Univ. (International co-work)

The record of RI supply (50 MeV cyclotron)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

Cu-64
I-124
Zr-89
At-211

✓ KIRAMS supply radioactivity (2023.06.)

Radioisotopes	2021	2022	2023
Cu-64	3,705.5 mCi	4,437.1 mCi	2,356 mCi
I-124	129.4 mCi	177.4 mCi	75.3 mCi
Zr-89	69 mCi	85 mCi	16 mCi
At-211	-	58 mCi	52.5 mCi

✓ KIRAMS I-124 : [I-124]NaI in NaOH solution

✓ KIRAMS Cu-64 : [Cu-64]$CuCl_2$ in HCl solution

✓ KIRAMS Zr-89 : [Zr-89]$ZrCl_4$ in HCl solution

Radioisotopes produced by 50 MeV cyclotron is for pre-clinical or clinical researches.

The record of RI supply (30 MeV cyclotron)

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES

F-18 FDG
Tl-201
I-123
I-123 mIBG

✓ KIRAMS supply radioactivity (2022.12.)

Radioisotopes	2019	2020	2021	2022
F-18 FDG	23,110 mCi	20,710 mCi	22,455 mCi	19,455 mCi
Tl-201	29,055 mCi	20,900 mCi	24,788 mCi	21,717 mCi
I-123	14,688 mCi	10,581 mCi	12,357 mCi	11,316 mCi
I-123 mIBG	12.060 mCi	7,674 mCi	2,166 mCi	10,119 mCi

Radioisotopes produced by 30 MeV cyclotron is for sale.

International PET-RI Supply by KIRAMS

KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES


NUCLEAR LIGHT INDUSTRY

NLI-RIC-^{89}Zr

Type "A" Tungsten Shielded Container for radioactive substances transportation

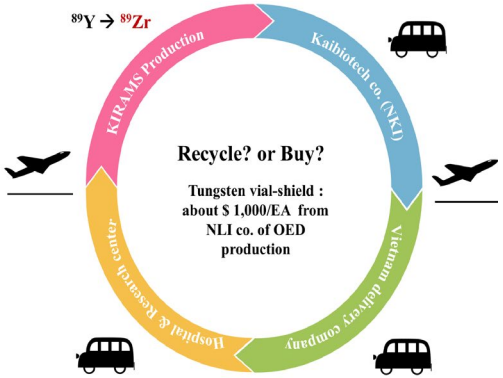
Features

- Manufactured in conformity with the law of Korean Nuclear Safety and Security, "Technical Standards according to Regulations on Packaging and Transportation of Radioactive Materials, etc."
- Air-tight ensured by O-ring sealing device on the top of container
- Three types of containers available for optimum shielding effect depending on each nuclide.
- Minimized pollution possibility with neat finish and easy-to-open structure by rotating the cap on the top of container.
- Provided with Certificate for Type A Container
- Shielding evaluation method in accordance with MCNP code

Specifications

- External dimensions : Ø46 x H79 mm
- Internal dimensions : Ø26 x H57 mm
- Weight : 1.75Kg
- Tungsten shielding : 10mm (W:94.83%, Ni:3.15%, Fe:2.02%)
- Density : 18.85g/cm^3
- Maximal transportable activity : 10mCi
- Max dose ratio on the surface : 0.23mSv/hr (Distance 20cm)

NUCLEAR LIGHT INDUSTRY CO., LTD.
Maunggi-ro 5en-gil, Incheon, Republic of Korea
Tel : +82 2 2682 6571 Fax : +82 2 2682 4929 E-mail : info@nli.com Web : http://www.nli.com



원자력의학원, 방사성의약품 국제 컨퍼런스·협약식

입력 2019.03.08. 14:21 댓글 0개

한국원자력의학원이 최근 방사선의학연구소 제3연구동에서 몽골과 베트남의 관계자를 초청해 방사성항체의약품 관련 국제 컨퍼런스를 개최하고 공동연구협약을 체결했습니다.

컨퍼런스는 의학원의 의료용 방사성동위원소 개발, 표지기술과 방사성항체의약품을 이용한 풍부한 임상경험을 몽골과 베트남의 전문가와 공유하고 관련 분야의 최근 동향과 주요 이슈를 논의하는 장으로 마련됐습니다.

의학원은 행사에 참여한 베트남 하노이방사선조사센터·108육군병원, 몽골 국립병원과 국제협약을 체결하고 의료용 방사성동위원소, 표지기술 공급, 의약품의 임상시험 수행, 임상데이터 제공 등 방사성항체의약품 공동연구를 위한 발판을 마련했습니다.

[이상범 기자 / boomsang@daum.net]

MEMORANDUM OF UNDERSTANDING

FOR COOPERATION IN RESEARCH AND DEVELOPMENT ON MEDICAL ISOTOPES AND ITS APPLICATIONS

BETWEEN 108 MILITARY CENTRAL HOSPITAL (108 MCH) AND KOREA INSTITUTE OF RADIOLOGICAL & MEDICAL SCIENCES (KIRAMS)

Korea Institute of Radiological and Medical Sciences (KIRAMS) and 108 Military Central Hospital (108 MCH), is hereinafter referred to as "the Parties".
Considering the Parties' common interests in the fields of research and development on Medical Isotopes and its Applications, and relying on the mutual benefits derived from the Parties' cooperation, Parties herein have agreed to implement the following items.

Article 1 GUIDING PRINCIPLE

1.1 The Parties promote their cooperation in the fields of research and development on "Medical Isotopes and its Applications".
1.2 The Parties shall implement the cooperation on the basis of mutual benefit, equality, and reciprocity in accordance with the relevant laws and regulations of their respective countries.
1.3 Whenever the Parties agree to undertake cooperation, they shall produce an appendix to the Memorandum of Understanding (MOU) that specifies details of the intended cooperation, and the appendix will be signed by appropriate representatives of the Parties.

Article 2 SCOPE OF COOPERATION

The cooperation mentioned in Article 1 of this MOU shall include the following:
2.1 The exchange of expertise and experience on medical isotopes applications (^{89}Zr-mAb, etc.).
2.2 The exchange and support of experts training.
2.3 The sharing of scientific results of preclinical and clinical studies.

Article 3 COORDINATION

3.1 Each Party will appoint a coordinator to implement the cooperation under the MOU. Each Party will, upon signing this MOU, notify name and contact address of the other coordinator.

3.2 All the requests made and the information provided under this MOU would be made or provided to the coordinators. Meetings between the Parties will be arranged through the coordinators.
3.3 The Parties will determine the cost of collaboration activities by mutual agreements.

Article 4 SETTLEMENT OF DISPUTES AND DISAGREEMENTS

Any dispute or disagreement related to the implementation of this MOU will be settled cordially by mutual negotiations and agreements between the Two Parties.

Article 5 FINAL PROVISIONS

This MOU will come into effect since its signing date and remain valid for a period of a one-year. Three months before the end of this duration if none of the Two Parties suggests expiration, this MOU will be automatically extended for another continuing period of a one-year.

5.1 Any amendment and supplement to this MOU is subject to mutual written agreements of the Two Parties.

5.2 This MOU sets the basic direction of potential collaboration between the Parties hereto and creates no legal rights or obligations of Parties. Any activity on collaboration carried out by the Parties under the MOU must comply with the existing laws and regulations in the place where the activity takes place.

The undersigned authorized institutional representatives concur in this Memorandum of Understanding.

Mi Sook Kim, M.D., Ph.D.,
President,
Korea Institute of Radiological & Medical Sciences(KIRAMS)

Date: 2019 4 9

Mai Hong Bang, M.D., PhD., Director
108 Military Central Hospital(108 MCH)

Date: 2019 4 9

Thank for your attention!

ck190@kirams.re.kr

Accompanied Growth of Radiochemistry

KOREA INSTITUTE OF
RADIOLOGICAL & MEDICAL SCIENCES