Industrial Application of Accelerator-Driven Neutron Sources

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- A New Radioisotope Production Method for Radiopharmaceutical
（QST, Nagai Group）
- A new SPECT for γ-ray Imaging
（Kyoto University, Tanimori Group ）
- Future Plan

・A New Radioisotope Production Method for Radiopharmaceutical

Issue

Diagnosis：

- ^{99m}Tc($T_{1/2}$=6.0h)is produced by β-decay of ^{99}Mo($T_{1/2}$=66h).
- Since ^{99}Mo is imported 100% in Japan, troubles of research reactors or airport shut down result in a severe shortage of ^{99}Mo.
- Most of ^{99}Mo is presently produced by neutron induced fission of highly enriched Uranium. Use of low enriched Uranium in future will raise the cost of ^{99}Mo due to increasing of waste and due to required modification of reactors.
- In Japan, the development of domestic production of ^{99}Mo by using the ^{98}Mo(n,γ)^{99}Mo reaction with the JMTR reactor had started. This project had to be stopped due to the governmental decision of the JMTR reactor shut-down.

Therapy：

・The available therapies using radioactive nuclides in japan are limited such as treatments of thyroid cancer (^{131}I), Basedow's disease(^{131}I), lymphatic malignancy(^{90}Y), relief of pain resulted from bone metastasis(^{89}Sr).

・In Japan, since many types of accelerators are in operation, the variety of radionuclides can be produced. But the development of radiopharmaceutical is very slow.

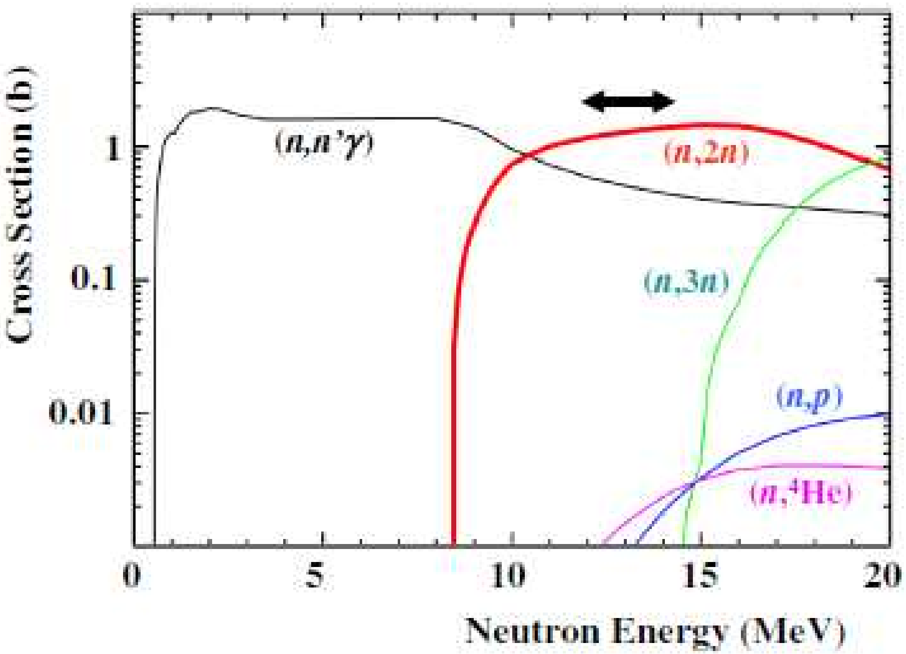
・Proposals for issues

Proposal(1) for the Mo-99 issue by Nagai group.

Production of ^{99}Mo using the $^{100}Mo(n,2n)^{99}Mo$ reaction given by the accelerator neutron.

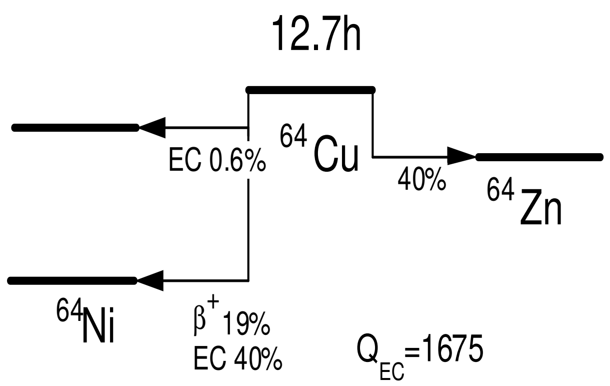
Points

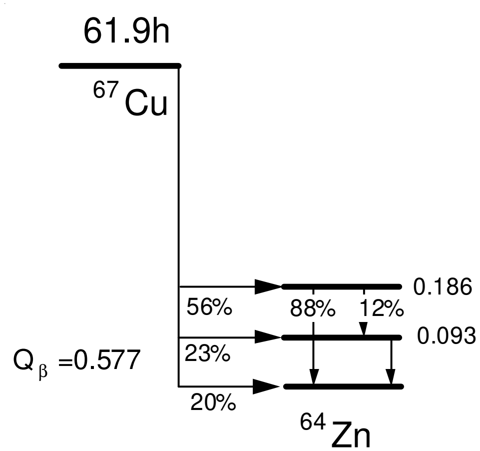
- Small production of unwanted nuclides.
- More than one target can be used at a time.
- Cooling of targets is unnecessary.
- Sublimation technique is applied to chemical separation.



Proposal(2) for New RI production by Nagai group

- Development of new radionuclides for radiopharmaceuticals: ^{64}Cu and ^{67}Cu

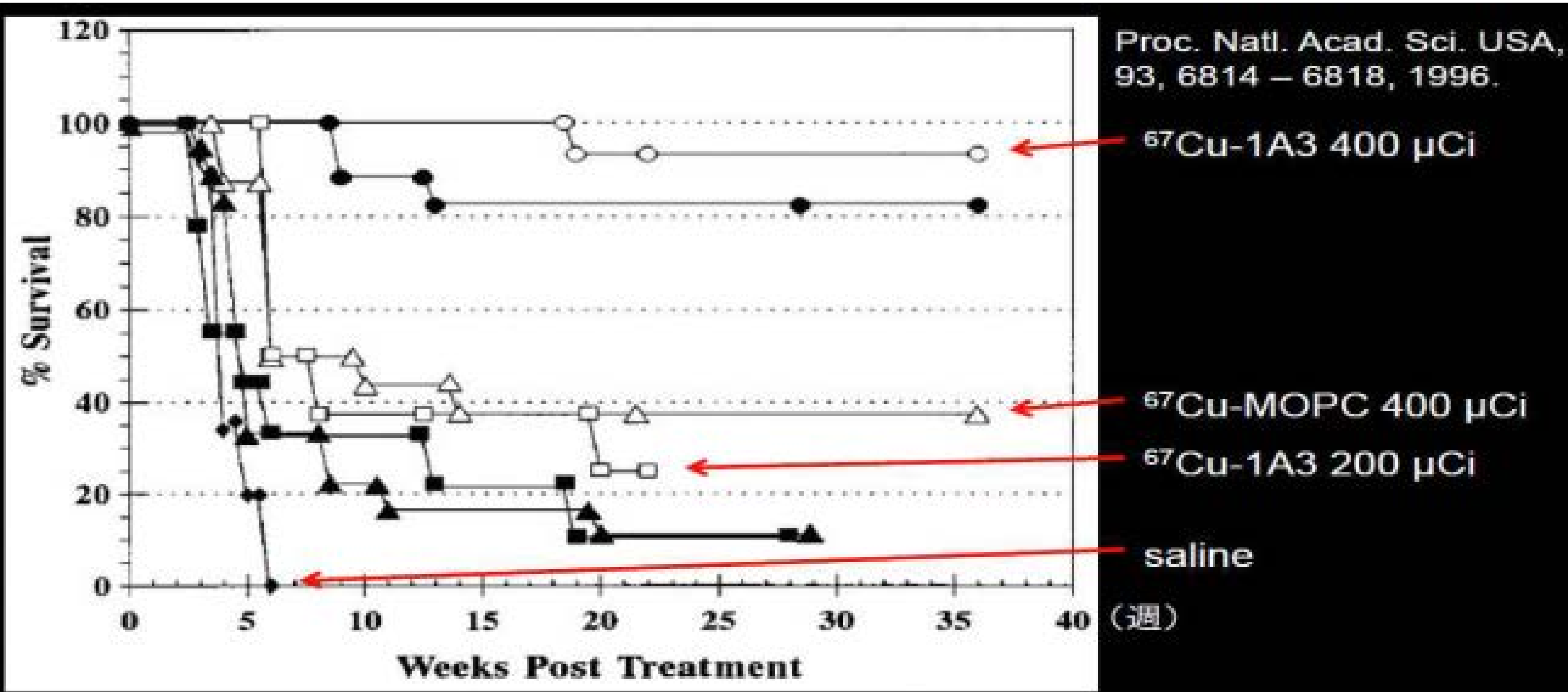




^{64}Cu：PET核種

^{67}Cu：β–γ 核種

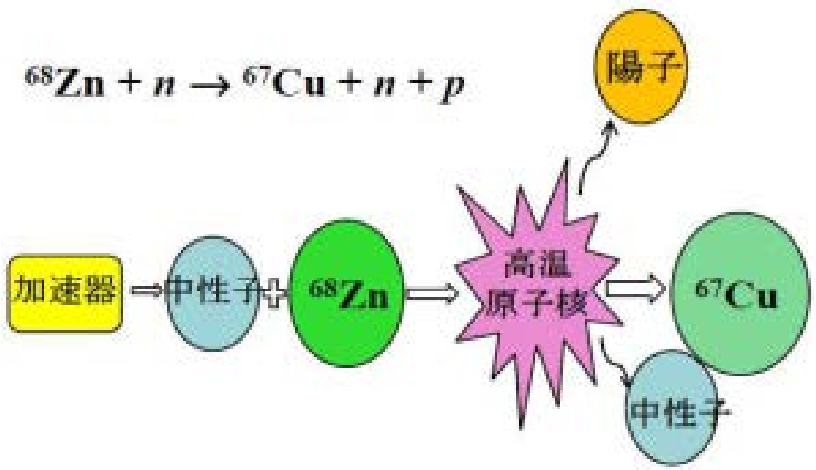
Points
- PET diagnosis by ^{64}Cu and treatment by ^{67}Cu.
- Useful chemical chelates are available.
- Due to small Q_β, mass administration can be used.
- Cu-ATSM concentrate in a low oxygen area of cancer.



ハムスターに、がん細胞(GW39ヒト大腸がん) を移入し、
^{67}Cu標識抗体（^{67}Cu-1A3）を 400 μCi（○、*n* = 15）、
および 200 μCi（□、*n* = 8）投与した。
比較として、親和性のない^{67}Cu標識抗体（^{67}Cu-MOPC）
400 μCi（△、*n* = 16）、生理食塩水（◆、*n* = 28）を投与した。

（飯田先生（鈴鹿医療大学）より）

^{67}Cu production



65Zn 243.7 D	66Zn Stable 27.9 %	67Zn Stable 4.1 %	68Zn Stable 18.8 %	69Zn ★13.8 H 56.4 M	Stable
64Cu 12.7 H	65Cu 30.8 %	66Cu 5.1 M	67Cu 61.8 H	68Cu ★3.8 M 31.1 S	Beta+ /EC decay
63Ni 100.1 Y	64Ni 0.9 %	65Ni 2.5 H	66Ni 54.6 H	67Ni 21 S	Beta- decay

	^{64}Cu	^{67}Ga	^{65}Zn	製造量
Conventionally $^{68}Zn(p,2p)^{67}Cu$	10	2.5	0.1	1
New Method $^{68}Zn(n,x)^{67}Cu$	＜0.016	~0	0.0007	＞30

Small unwanted radionuclides production
^{64}Cu can be produced by the $^{64}Zn(n,p)^{64}Cu$ reaction.
^{64}Zn (49%)

Sato et al., J. Phys. Soc. Jpn. **83** (2014), 073201

Summary

Production

Radio nuclides produced by reactors and accelerators can be produced by accelerator neutrons only.

Diagnosis

- For the ^{99}Mo-^{99m}Tc issue can be solved by the ^{99}Mo production with the $^{100}Mo(n,2n)^{99}Mo$ reaction using accelerator neutron and a sublimation technique.

  A dedicated accelerator and a handling facility may contribute largely to this issue.

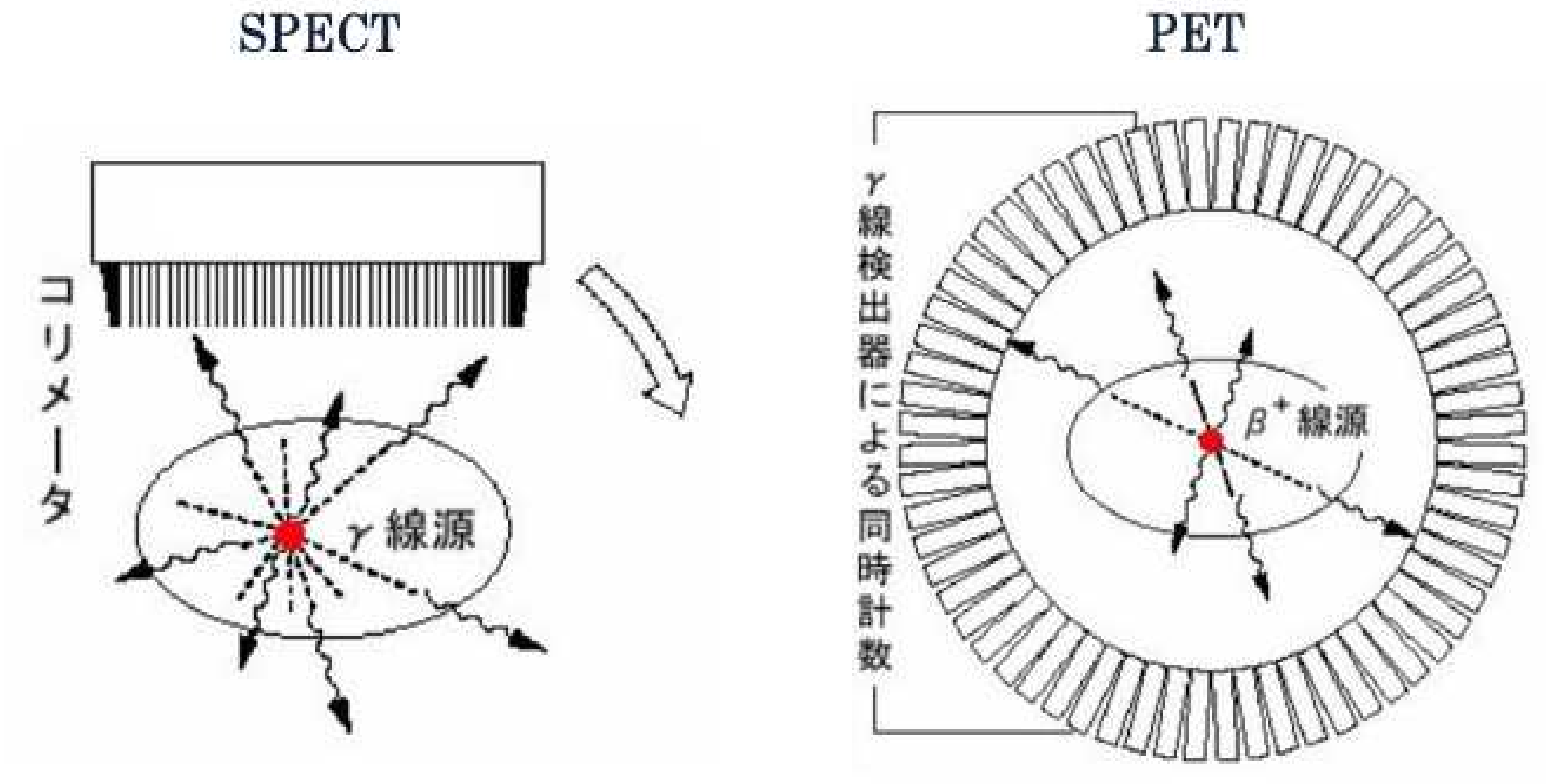
  A 40 MeV 2 mA d-beam can supply about 50 % of the domestic demand.

Treatment

- Fast neutron can produce new radionuclide ^{64}Cu for diagnostic pharmaceutical and ^{67}Cu for therapeutic medicine.
- Diagnostic by PET and treatment by SPECT gives good medical care.

・New SPECT
(Tanimori group, Kyoto University)

Tanimori group developed a γ-ray detection system. The system aimed at to survey stars which emits MeV order γ-rays. The system can measure the direction of the incident γ-ray by observing scattered γ-ray and recoiled electron after Compton scattering.
This method enable to get image of the γ-ray source as the normal camera giving image of material.
They proposed to apply this method to image analysis used in the diagnostic approach: 'New SPECT'
Now, 1496 SPECT systems and 551 PET systems are used in Japan (January 2018).
Since the New SPECT superb functionality compared with present SPECT and PET, thus all theses systems may be replaced by the New SPECT



Imaging Method

Issues of SPECT and PET

SPECT

・Spatial resolution of SPECT(8～12 mm) is inferior to PET(2～5mm).

・Since SPECT use collimators, efficiency(0.0001～0.02%) of SPECT is worse than PET(0.1～1%).

・Since SPECT gets an image by analyzing images obtained by rotating 180 or 360 deg, it is impossible to get moving image.

PET

・Number of accidental coincidences is large.

・Except FDG, radionuclides have to be produced by a cyclotron in the hospital.

・ The spatial resolution of New SPECT is similar to PET

・ The New SPECT can give moving image.

Due to these advantages, all PET and SPECT can be replaced by the New SPECTs.

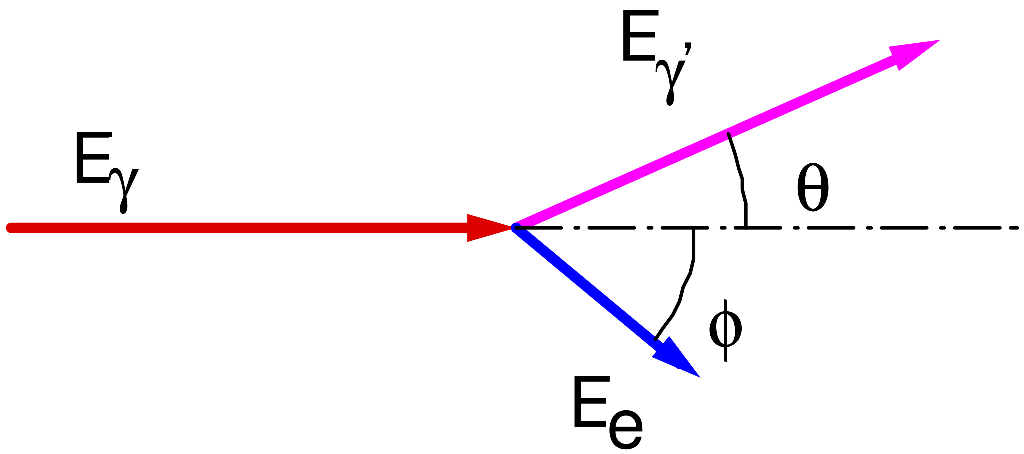
Experiment to improve the spatial resolution of SPECT

（頭部SPECT用フルデジタル高解像度検出器における画像処理ソフトウェアの開発と生の比較
賀久和弥（奈良先端科学技術大学院大学情報科学研究科修士論文）

Collimator for high spatial resolution SPECT

	Test Device			東芝製SPECT GCA-7200A
Collimator	Normal	High res.	Hyper res.	LEHR
Hole size(mm)	1.22	0.8	0.8	1.11
Thickness (mm)	30	30	50	24
Wall(mm)	0.18	0.18	0.18	0.16
Efficiency(%)	0.00906	0.00342	0.00121	0.0119

コンプトン散乱



$$E_{\gamma'} = \frac{E_\gamma}{1 + E_\gamma(1-\cos\theta)/mc^2} = \frac{E_{\gamma'} + E_e}{1 + (E_{\gamma'} + E_e)(1-\cos\theta)/mc^2}$$

Energies of the scattered γ-ray and recoiled electron determine θ

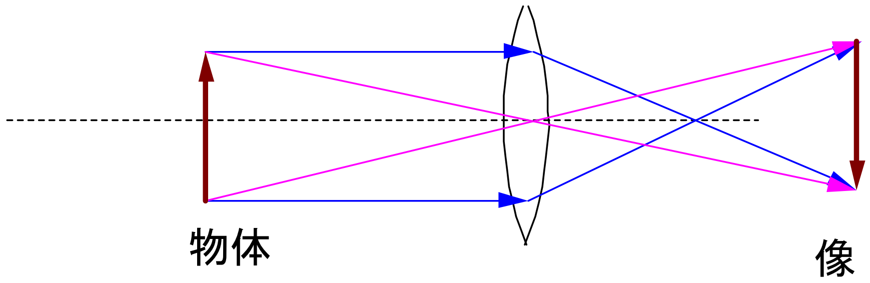
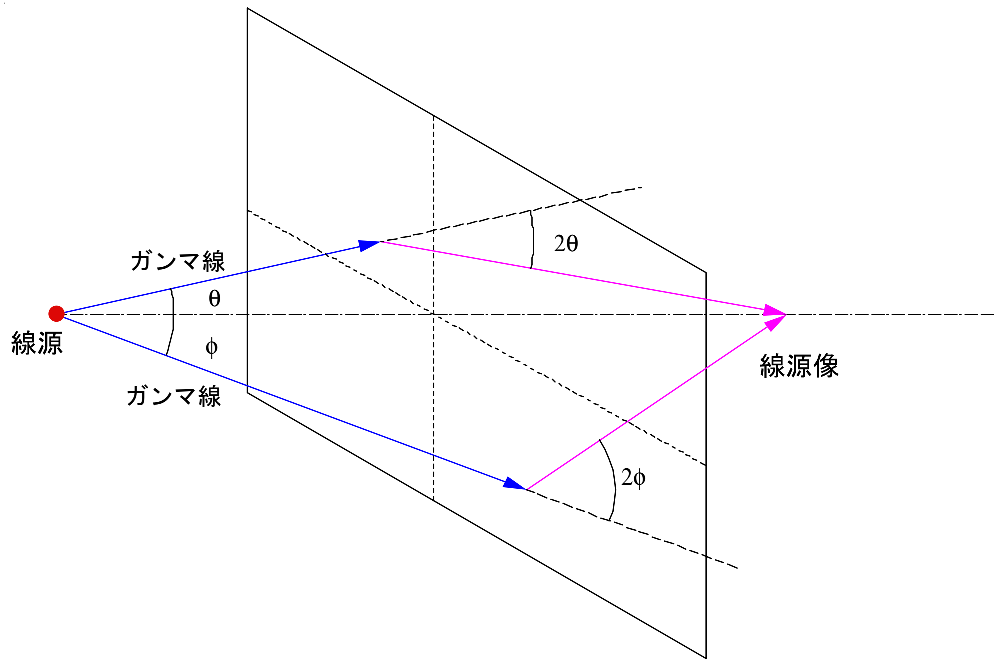
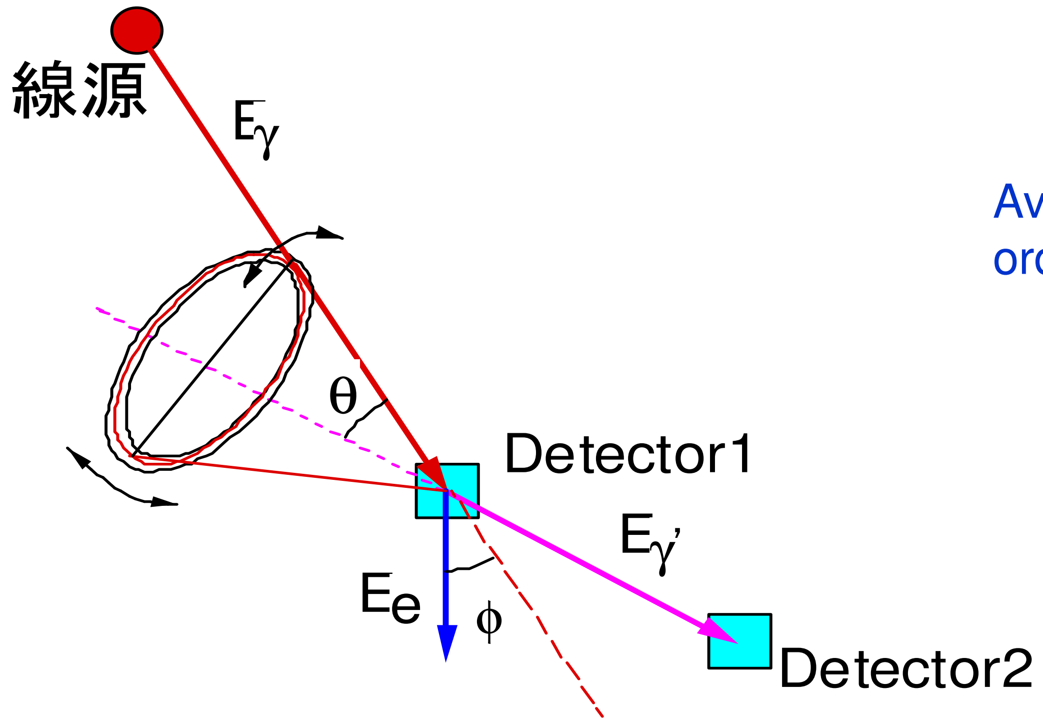


Image obtained by light

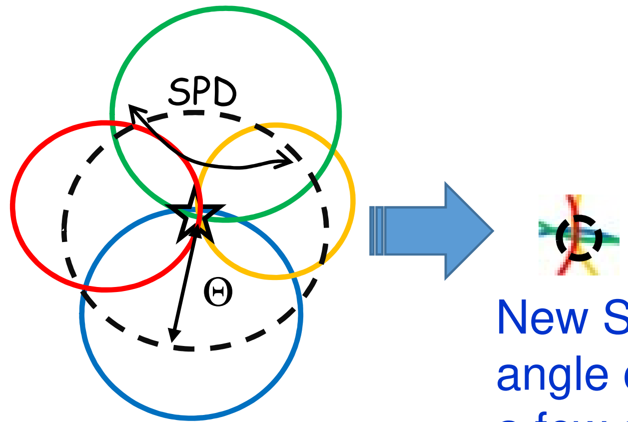


Once the direction of γ-ray is given at each point on the detection plain, the image of the γ-ray source can be obtained.

Image obtained by γ-ray



Average angle of view is 50 deg for ordinary Compton Camera.

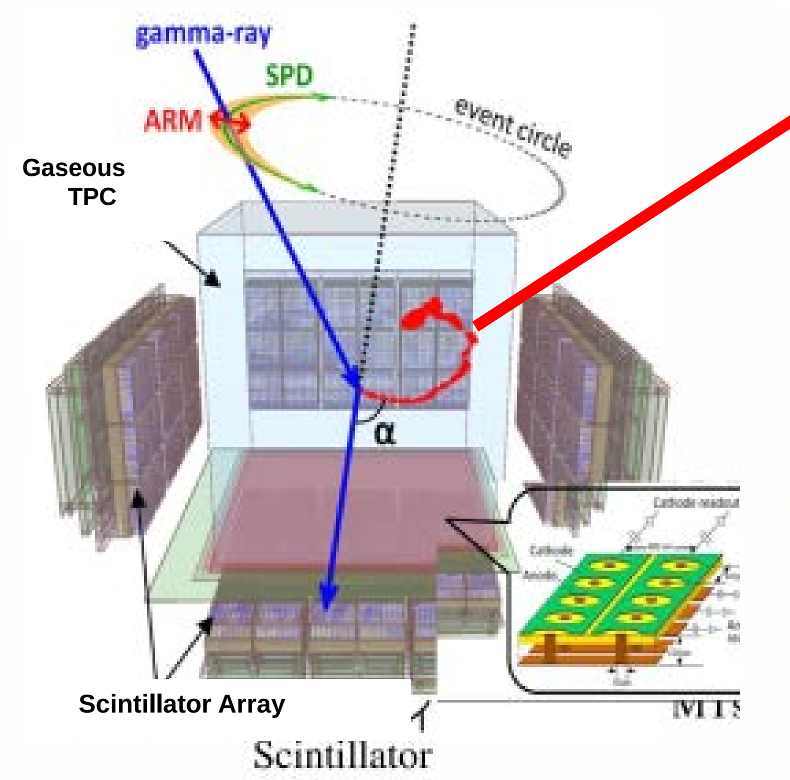


New SPECT :
angle of view is about a few deg.

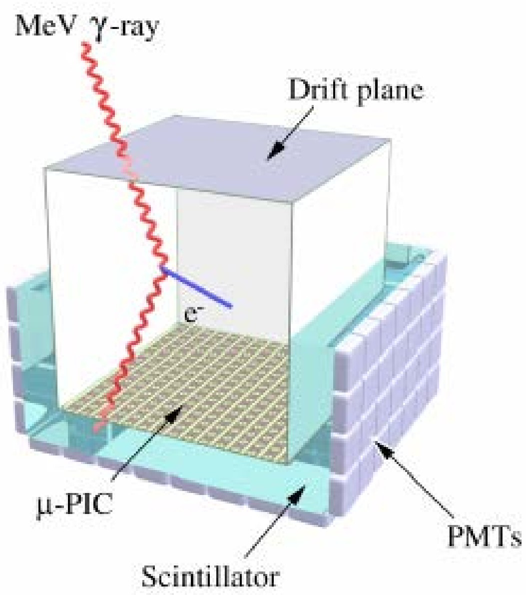
Ordinary Compton camera shows that the direction of incident γ-ray is somewhere on the cone shape.

ETCC:Electron-Tracking Compton Camera(New SPECT)

- Ordinary CC＋Electron tracking

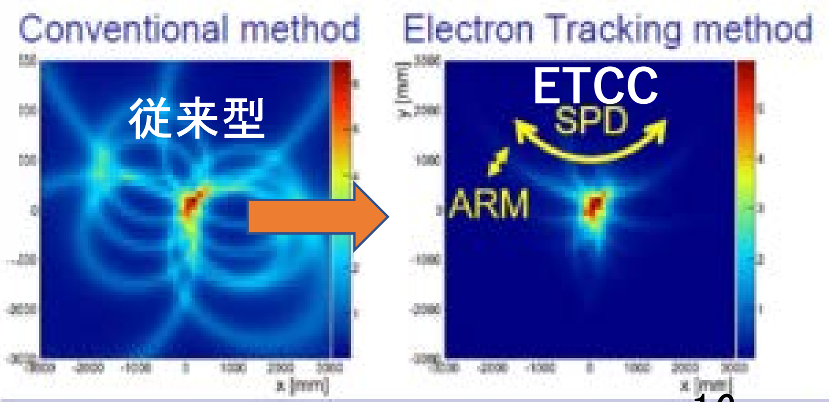


Outline of New SPECT



TPC

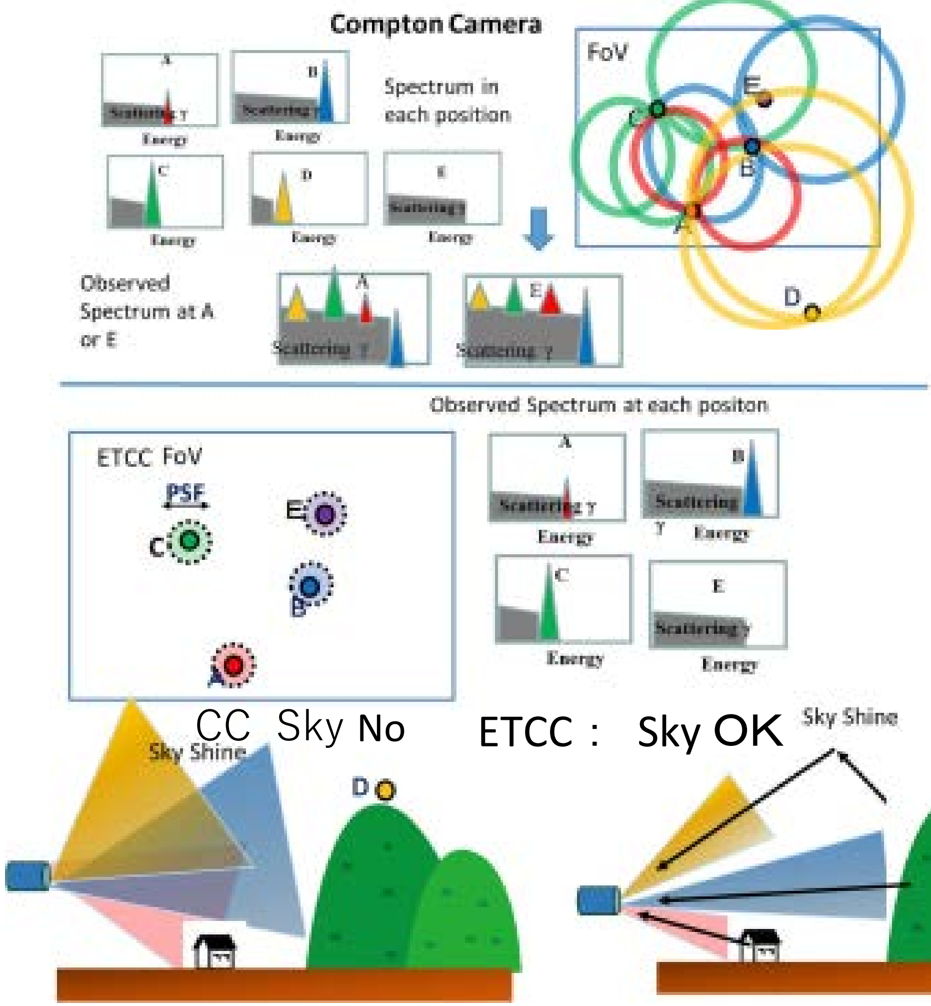
- **Technic developed by Tanimori group.**
- **ETCC can determine the point of incident γ-ray in the diagram and not like circles given by ordinary CC.**
- **ETCC is developed for astronomy, then they started medical application.**

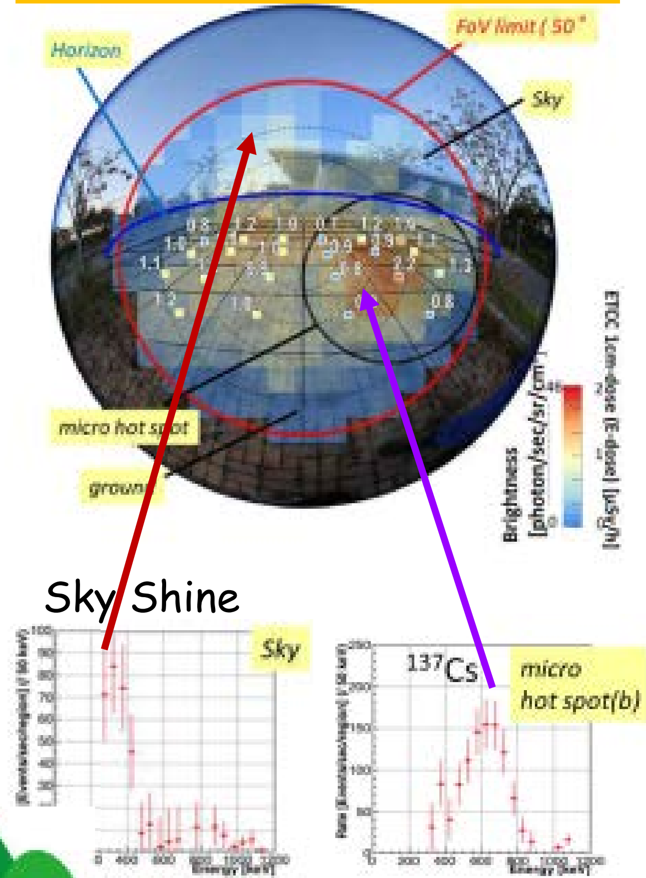


核ガンマ線イメージング分光を福島で実現

CC = 画像内の各点のスペクトルが混合する。
ETCC =画像内の各点のスペクトルが分離

福島除染地域の撮像
僅かな取残しCsのラインと空からのスカイシャインがよく判明できる





世界で初めてスカイシャインの撮像、スペクトル観測に成功

Points of the new SPECT

- Scattering γ-ray from collimator does not show up.
- Since the direction of γ-ray can be determined, scattered γ-rays are easily rejected.
- Detection efficiency is ten times of ordinary SPECTs.
- Total administrated dose of RI is less than 50MBq about 1/5 of amount for present diagnostic.
- Moving image can be obtained.
- Wide energy range of γ-ray can be used as 130keV～1300keV
- Cost of new SPECT will be ½ of ordinary SPECT.
- Spatial resolution

SPECT: ～10 mm at 140 keV
New SPECT: ～10 mm at 140 keV
～6 mm at 300 keV
> 5 mm at 500 keV

・Future Plan

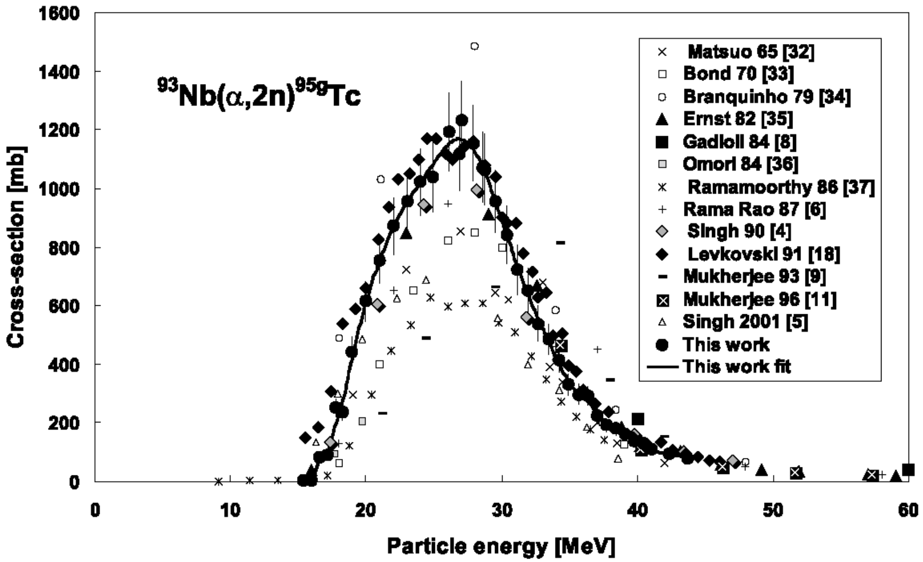
Dignosis

- New SPECT gives better spatial resolution for higher energy γ-rays.
- Since ^{99m}Tc is used for variety of diagnosis, Tc is good candidate.
- Following radioactive Tc are available.

  ^{92}Tc(4.4m)、^{93}Tc(2.7h)、^{93m}Tc(43m)、^{94}Tc(4.9h)、^{94m}Tc(52m)、
  ^{95}Tc(20h)、^{95m}Tc(61d)、^{96}Tc(4.3d)、^{96m}Tc(52m)

- ^{93}Nb（abundance 100%) is target nucleus for (α, xn) reaction for production of radioactive Tc.

  ^{93}Nb(α,n)^{96m}Tc、^{93}Nb(α,2n)^{95}Tc、^{93}Nb(α,3n)^{94,94m}Tc


$^{93}Nb(\alpha,2n)^{95g}Tc$
Cross-section [mb]
Particle energy [MeV]
Matsuo 65 [32]
Bond 70 [33]
Branquinho 79 [34]
Ernst 82 [35]
Gadioli 84 [8]
Omori 84 [36]
Ramamoorthy 86 [37]
Rama Rao 87 [6]
Singh 90 [4]
Levkovski 91 [18]
Mukherjee 93 [9]
Mukherjee 96 [11]
Singh 2001 [5]
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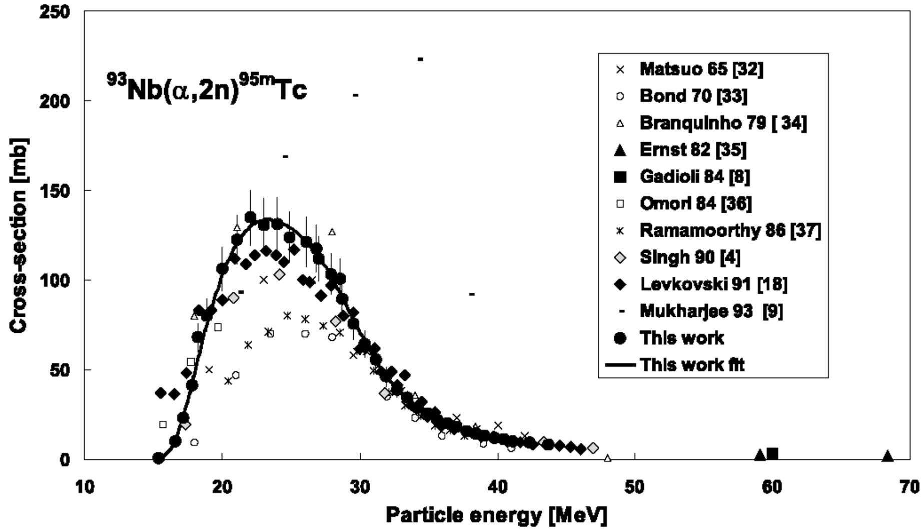
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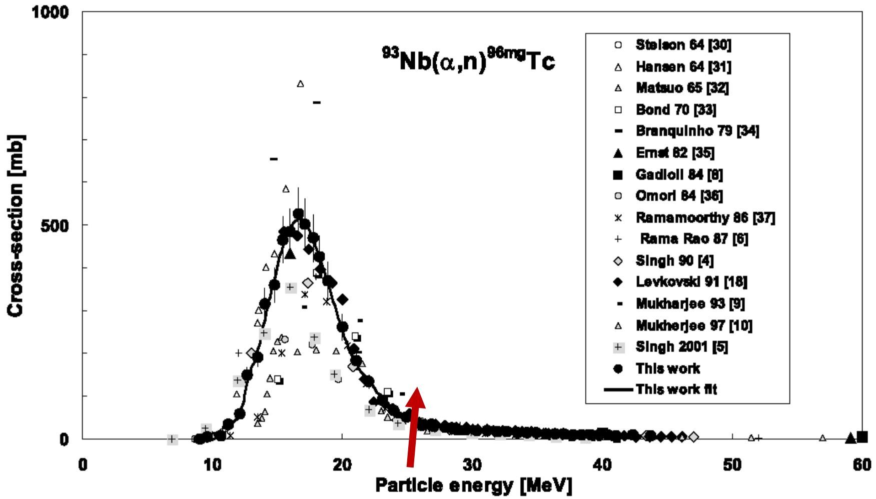
$^{93}Nb(\alpha,n)^{96mg}Tc$
Cross-section [mb]
Particle energy [MeV]
Stelson 64 [30]
Hansen 64 [31]
Matsuo 65 [32]
Bond 70 [33]
Branquinho 79 [34]
Ernst 82 [35]
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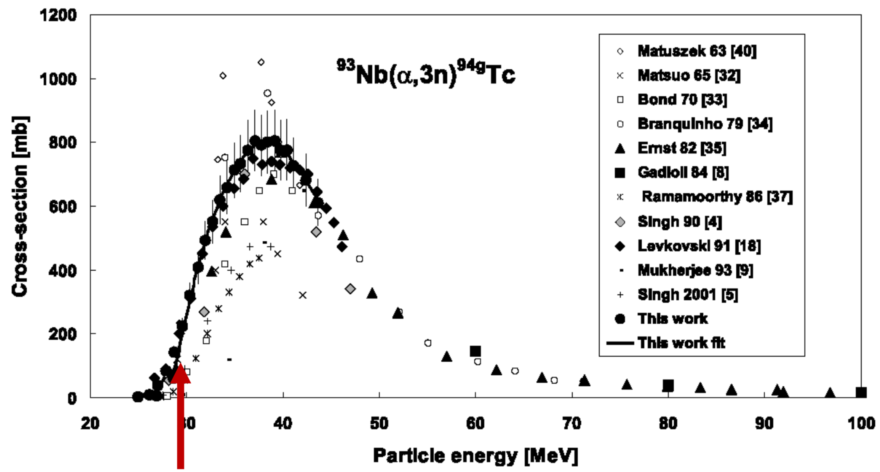
$^{93}Nb(\alpha,3n)^{94g}Tc$
Cross-section [mb]
Particle energy [MeV]
Matuszek 63 [40]
Matsuo 65 [32]
Bond 70 [33]
Branquinho 79 [34]
Ernst 82 [35]
Gadioli 84 [8]
Ramamoorthy 86 [37]
Singh 90 [4]
Levkovski 91 [18]
Mukherjee 93 [9]
Singh 2001 [5]
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^{95}Tc Production

- α particle beam of 30 MeV, 30μA is available by a cyclotron at RIKEN.
- The amount of 4.25 GBq of ^{95}Tc can be obtained under the following assumptions, 24 hours irradiation, 24 hours for chemical separation and delivery, and 50% for chemical handling efficiency.
- The production amount of ^{95}Tc during 1 week is 25.5 GBq assuming 6 days irradiation and 24 hours irradiation/day. The annual number of diagnosis is 2550, assuming 50 MBq for each diagnosis.
- Now 900,000 diagnosis are carried out each year in Japan. To cover this number, a particle beam of 10 mA is needed.

Cost of 95Tc for diagnosis

- Since the operating cost of the AVF cyclotron in RIKEN is 640,000 yen for 24 hours. The cost of 50 MBq of ^{95}Tc for one diagnosis is 7,500 yen.

Future plan

Diagnosis

1st phase

Construction of the New SPECT by optimization of ETCC for medical diagnosis.

2nd phase

The requirement of ^{99m}Tc in Japan can be produced by one cyclotron using high efficiency of New SPECT. The construction of the cyclotron facility is important and necessary.

3rd phase

Development of ^{95}Tc

4th phase

Development of cyclotron for high intensity α beam.

Medical treatment

Development of radiopharmaceutical using ^{64}Cu and ^{67}Cu

END