Nuclear Data for medical RI production by accelerator neutrons

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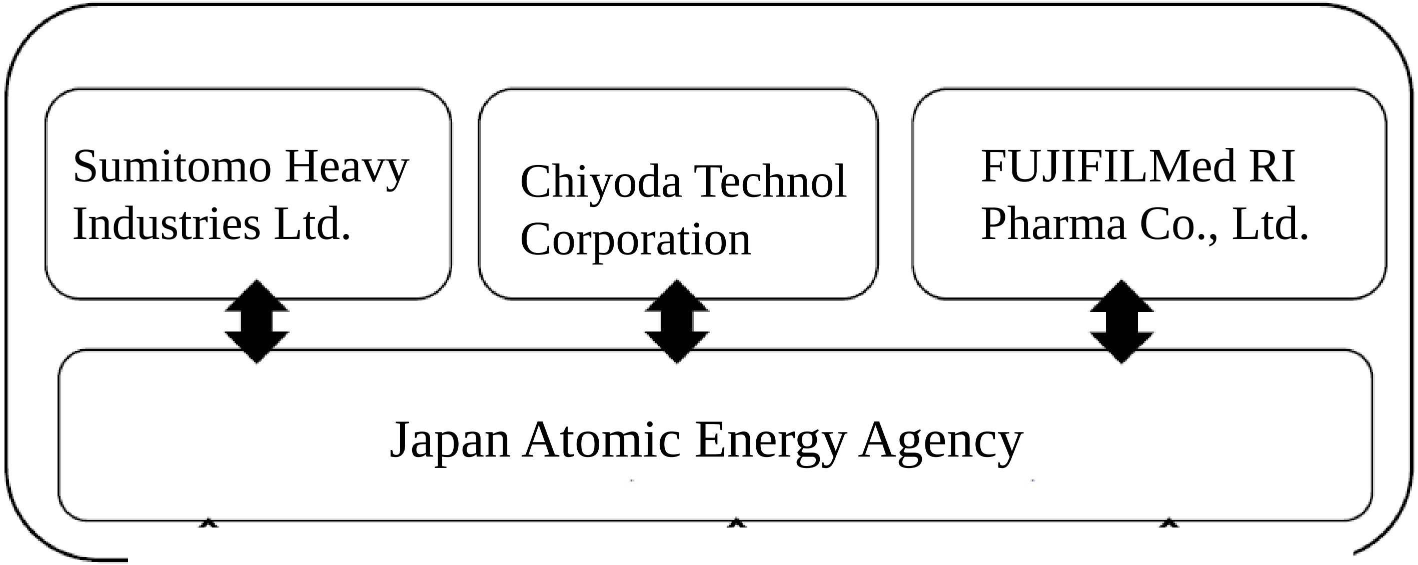
Research Proposal:

Determine the neutron induced reaction cross sections of emerging diagnostic and therapeutic radionuclides as well as the well established and commonly used diagnostic and therapeutic radionuclides.

Our Group

Special Group for RI Generation Technology using Accelerator Neutrons



Sumitomo Heavy Industries Ltd.

Chiyoda Technol Corporation

FUJIFILMed RI Pharma Co., Ltd.

Japan Atomic Energy Agency

Members

1) JAEA:

nuclear physicist: 3 nuclear data evaluator: 3 radio chemist: 5

radio chemist (technician): 2 accelerator scientist: 3

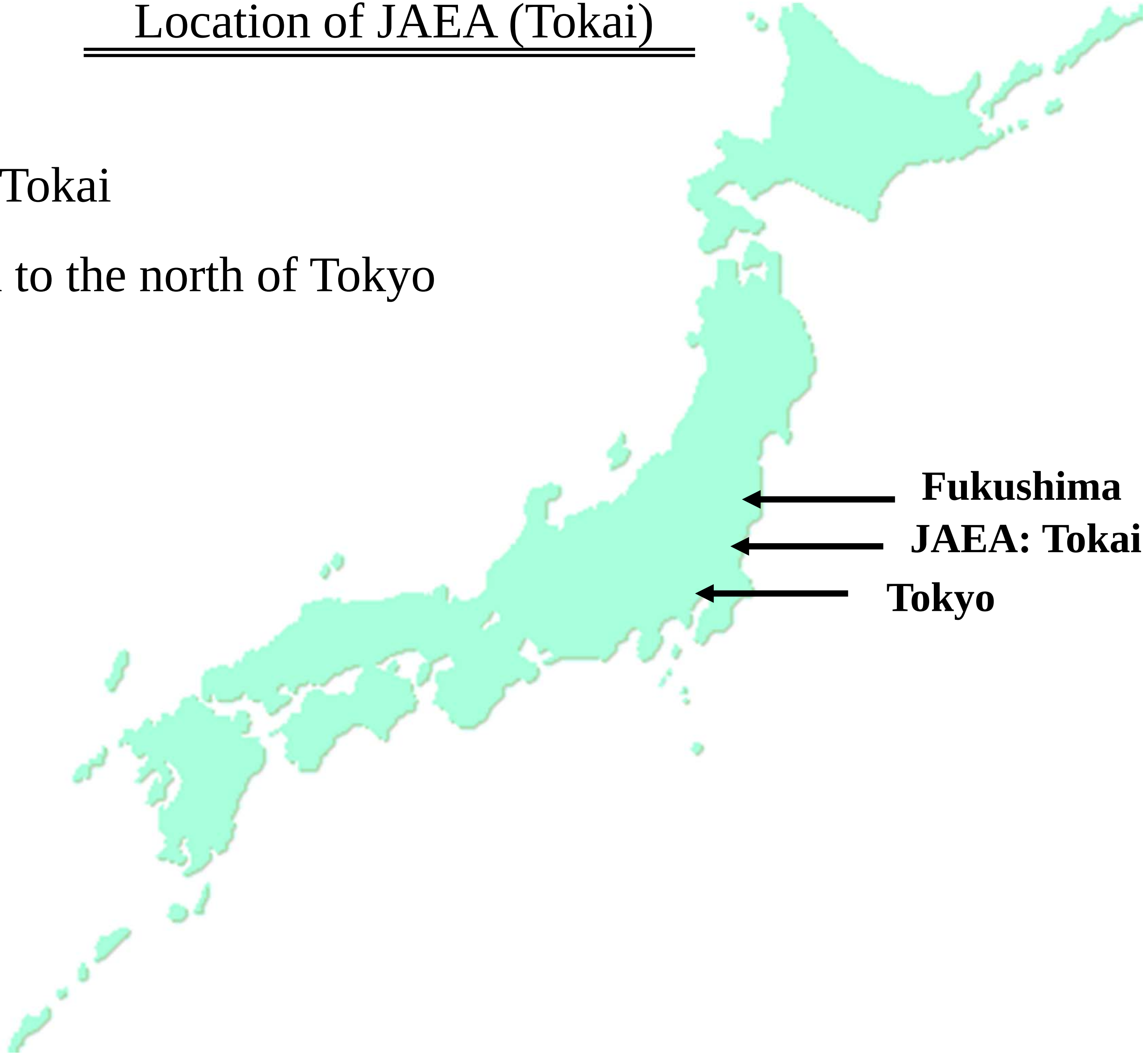
2) Industry

Chiyoda: 5 Sumitomo: 3 FUJIFILM:1

Location of JAEA (Tokai)

JAEA; Tokai

120 km to the north of Tokyo



General background Concerning medical RI production in Japan

♦ in 1995, Japanese government decided to import short-lived radioisotopes

⇒ in fact, most RIs used for nuclear medicine: imported

(141 PET cyclotron facility)

♦ ^{99m}Tc: 0.9 million diagnostic procedures/year

♦ shortage of ^{99}Mo

⇒ Science Council of Japan (2008)

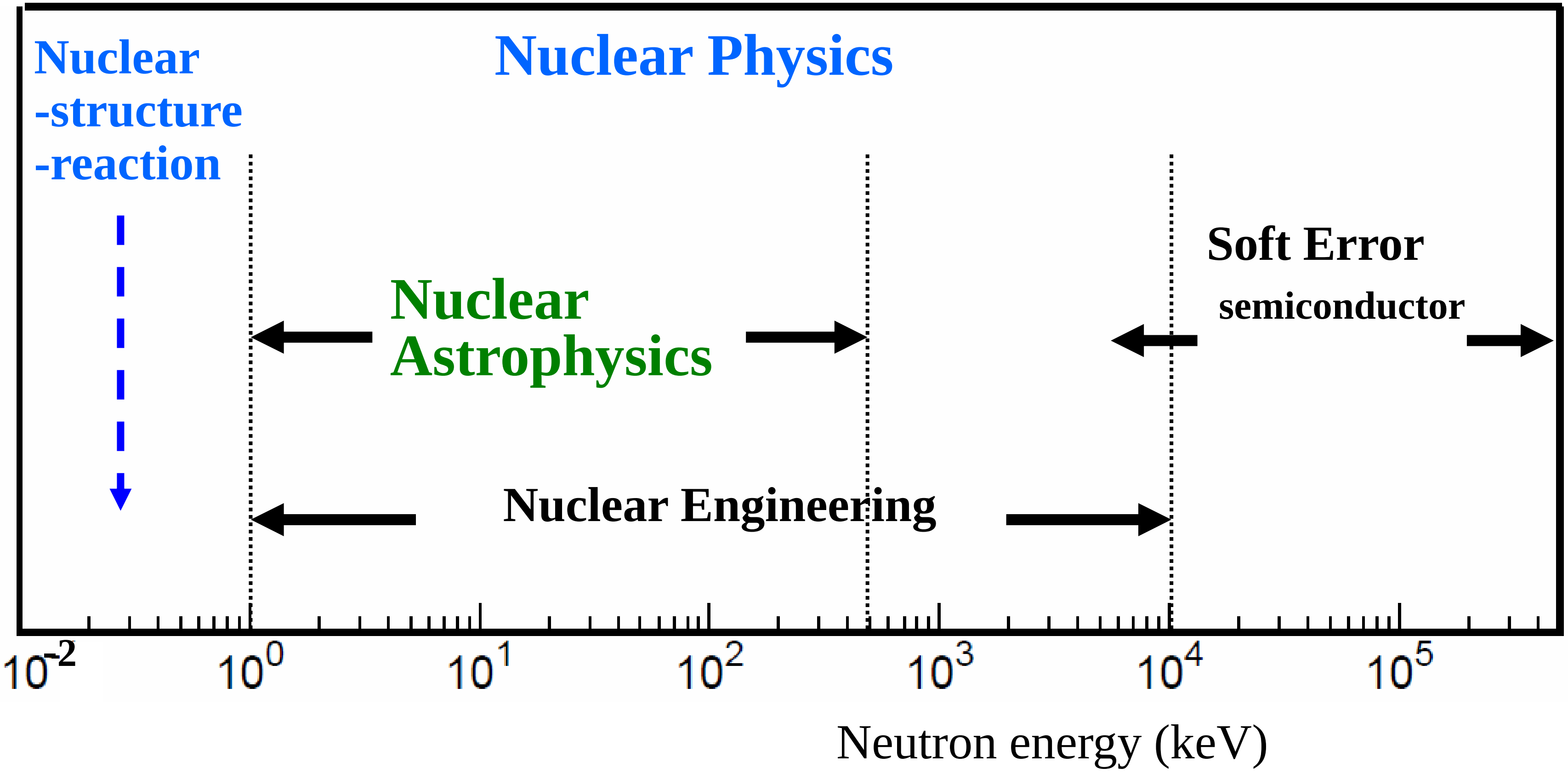
on the reliable & constant supply of RIs

⇒ consider a possibility of

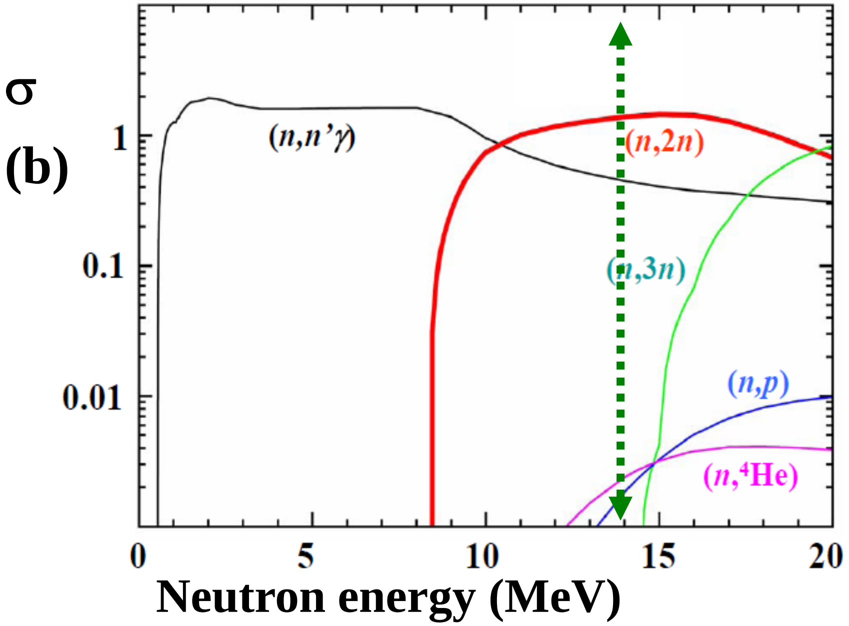
domestic production of RIs

提　言

我が国における放射性同位元素の
安定供給体制について


Nuclear
-structure
-reaction
Nuclear Physics
Nuclear
Astrophysics
Soft Error
semiconductor
Nuclear Engineering
10^{-2}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
10^{5}
Neutron energy (keV)

^{99}Mo production using accelerator neutrons



^{99}Mo production using

^{100}Mo(n,2n)^{99}Mo

Y. Nagai & Y. Hatsukawa:
J.Phys. Soc. Jpn. 3 (2009) 033201

Characteristic points:

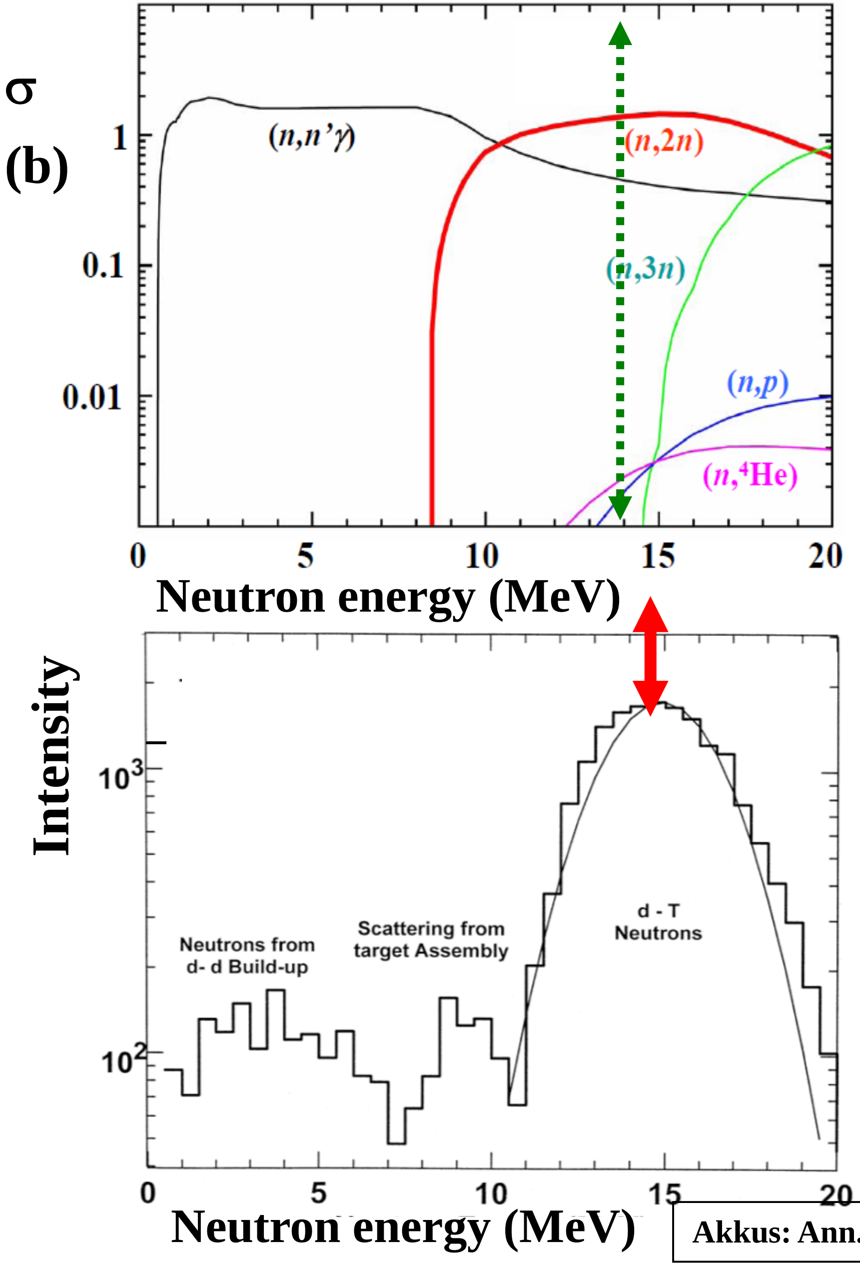
♦ **$\sigma(n,2n)$: large at E_n ~ 14 MeV, 10-times larger than that of ^{98}Mo(n,γ)^{99}Mo.**

♦ **$\sigma(n,X)$: radioactive waste production are quite small.**

♦ **intense $\phi(n)$: obtained using an accelerator.**

♦ **^{100}Mo sample of over 200 g: used. (reused) {enrichment of ^{100}Mo ~90%}**

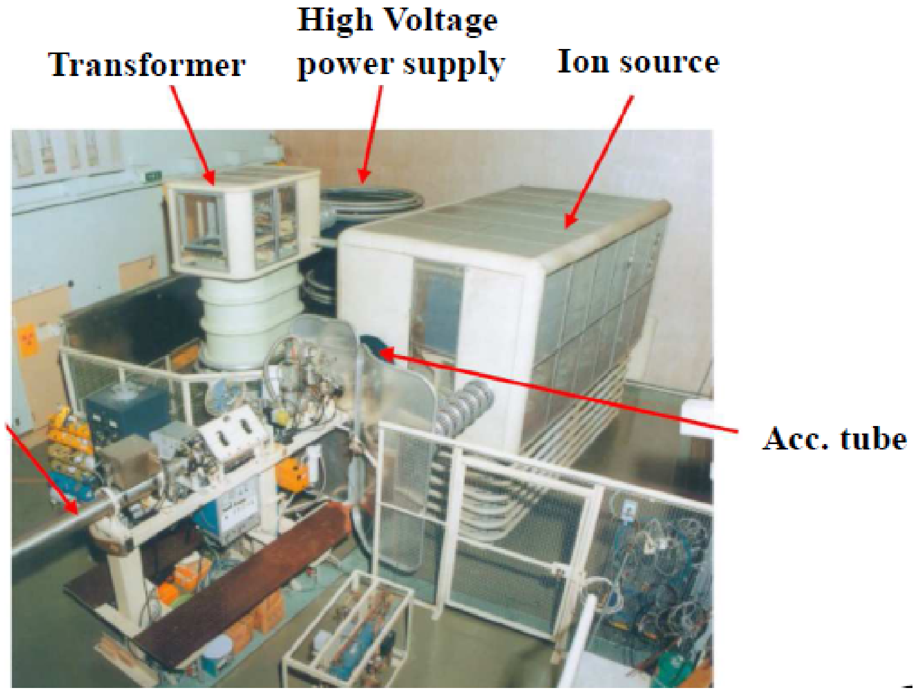
14 MeV neutrons



Akkus: Ann. Nucl. Energy (2001)

FNS (Fusion Neutronics Source, JAEA)

3×10^{12} n/s



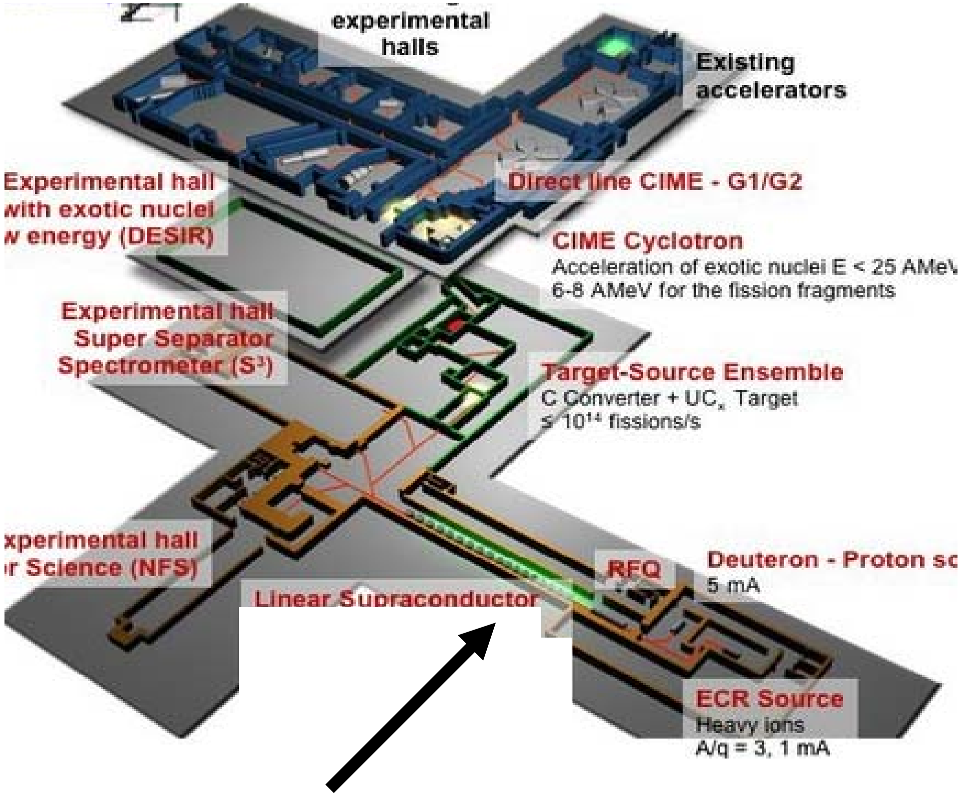
- **Production of 14 MeVneutrons**

$^{3}H(d,n)^{4}He \quad Ed=0.35$ MeV

Intense 14 MeV neutrons

Intense neutrons from C(*d*,*n*) reaction at $E_d = 40$ MeV :
one of the most intense ones, available by a current accelerator technology.

France (SPIRAL2)



40 MeV 5 mA deuteron beam (Super conducting linac) $\Rightarrow$ 10×10^{13} n/(cm^2 sec)

Neutrons from C(*d*,*n*) reaction

Emitted neutrons from the reaction peak at forward angles with respect to the deuteron beam direction, and have an energy spectrum with a most probable energy of 14 MeV.

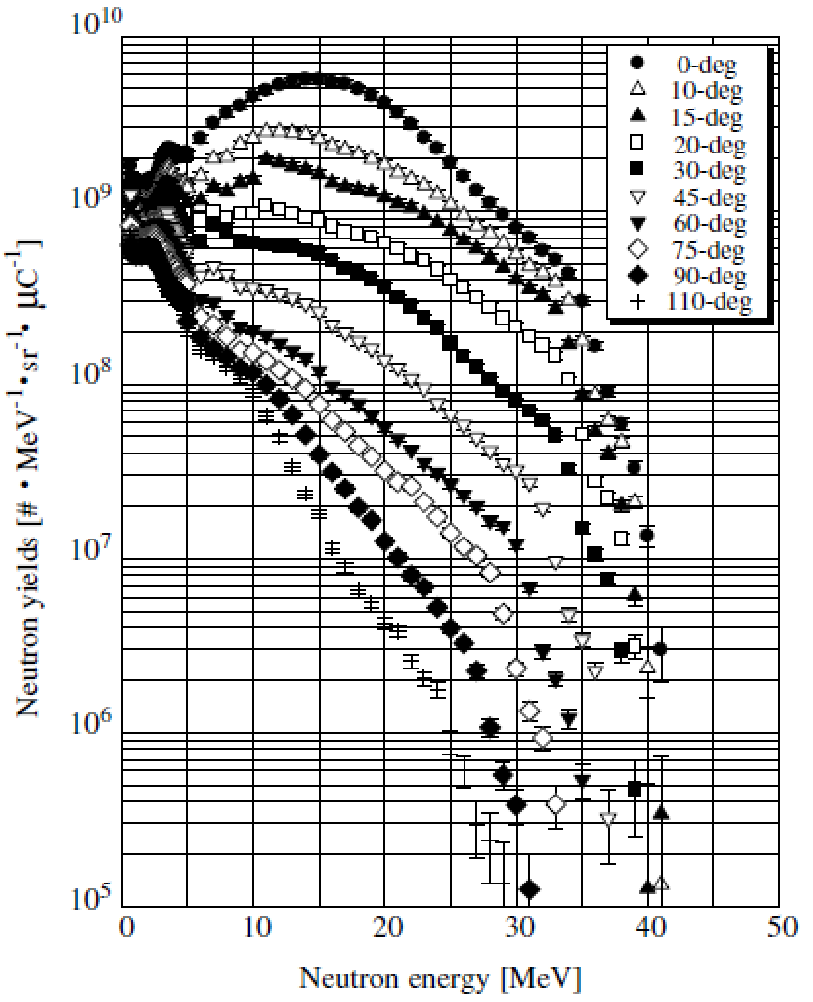


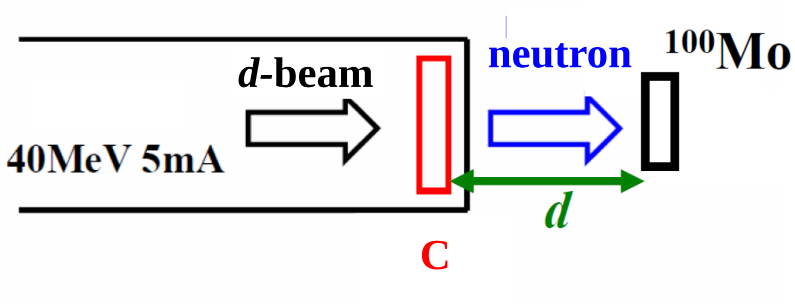
Fig. 2. Neutron energy spectra from a thick carbon target bombarded by 40 MeV deuterons at 10 laboratory angles.

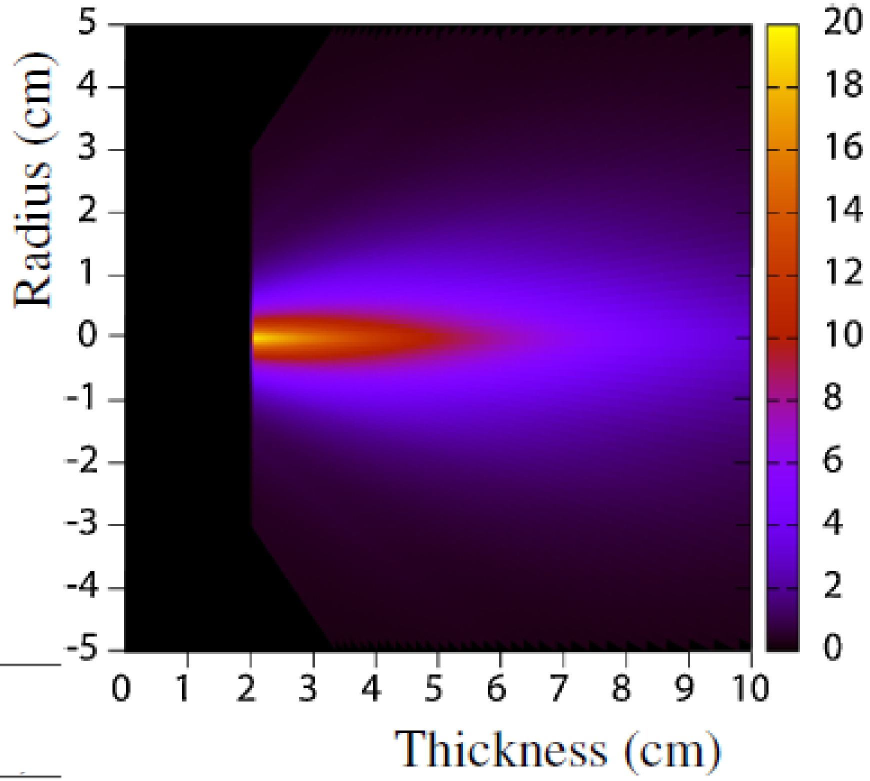
M. Hagiwara et al. (2004)

^{99}Mo production using neutrons from C(*d*,*n*) reaction

◆ **40 MeV 5 mA *d*-beam**

◆ **^{99}Mo yield distribution**





♦ at EOI for 2 days

Sample Mass (g)	Act. (TBq) *d* = 1 cm	2 cm	4 cm
63	5.9	4.1	2.2
126	7.7	5.5	3.1
251	8.6	7.1	5.0
503	12.2	10.2	7.2

F. Minato and Y. Nagai:
J. Phys. Soc. Japan, (2010)

99Mo requirement in Japan: 2250 Ci/week (domestic production)

40 MeV 5 mA *d* ＋C ⇒ ~20% of the demand in Japan (^{100}Mo : *d*=2 cm)

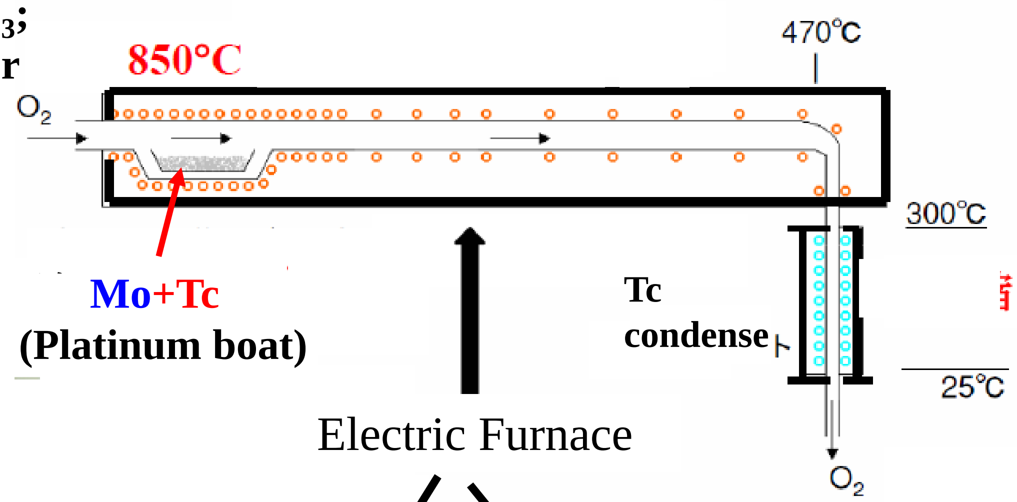
Exp. study of ^{99}Mo production using neutrons from ^{3}H(*d*,*n*)

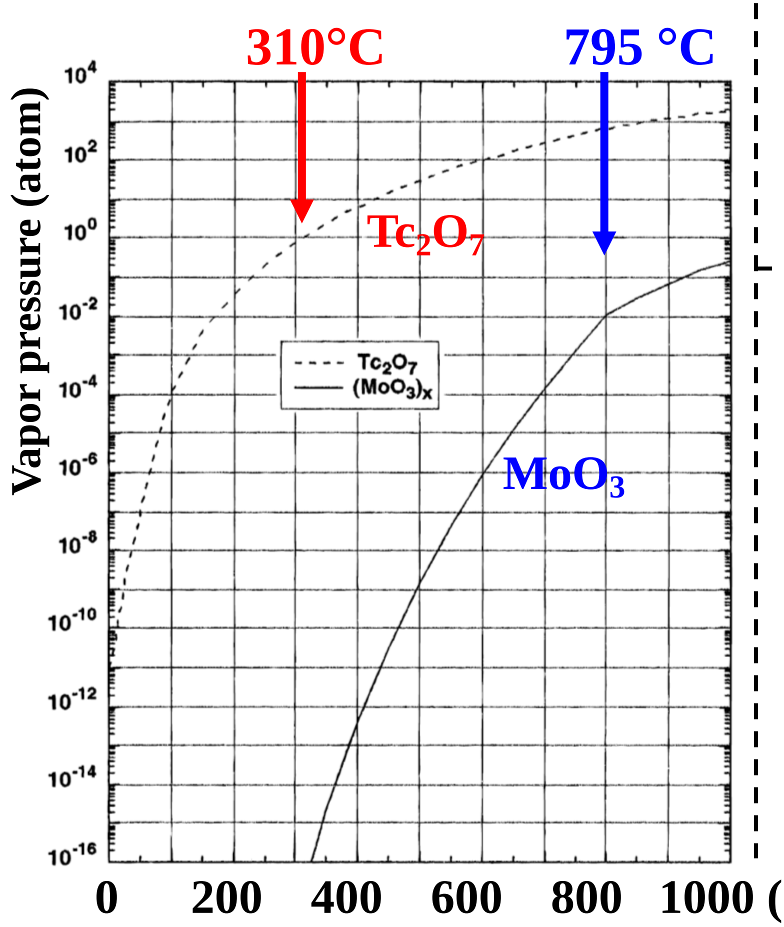
1) ^{99}Mo production: ^{100}Mo(n,2n)^{99}Mo
2) Separation of ^{99m}Tc from ^{100}MoO$_3$: Sublimation
3) Labeling efficiency

Separation of ^{99m}Tc from ^{99}Mo

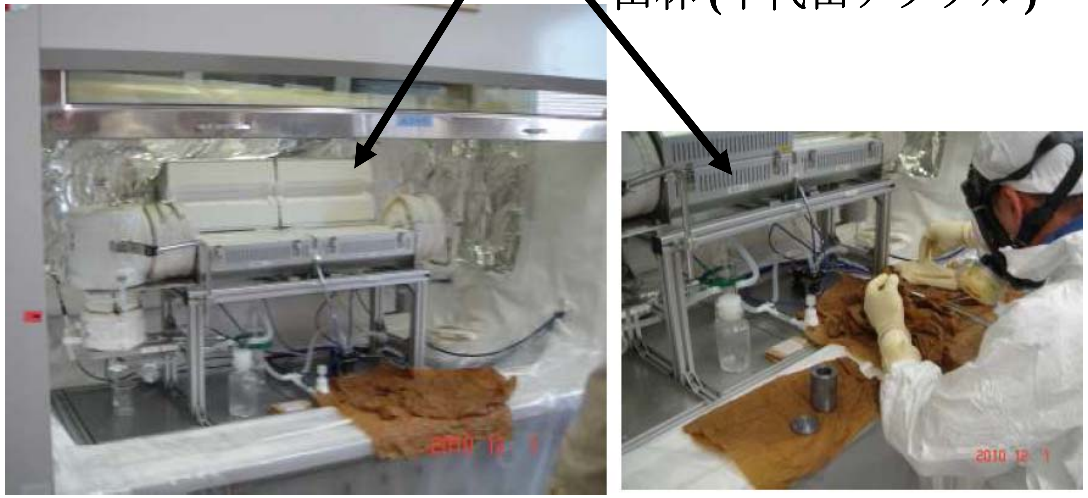
sublimation method:

based on different volatility of Tc_2O_7 and MoO_3; ^{99m}Tc in MoO_3 volatilizes at temperatures lower than that of sublimation of MoO_3, i.e. 790°C





山林 (千代田テクノル)



Separate ^{99m}Tc from ^{99}Mo (JAEA)

Quality of ^{99m}Tc

◆ **before separation**

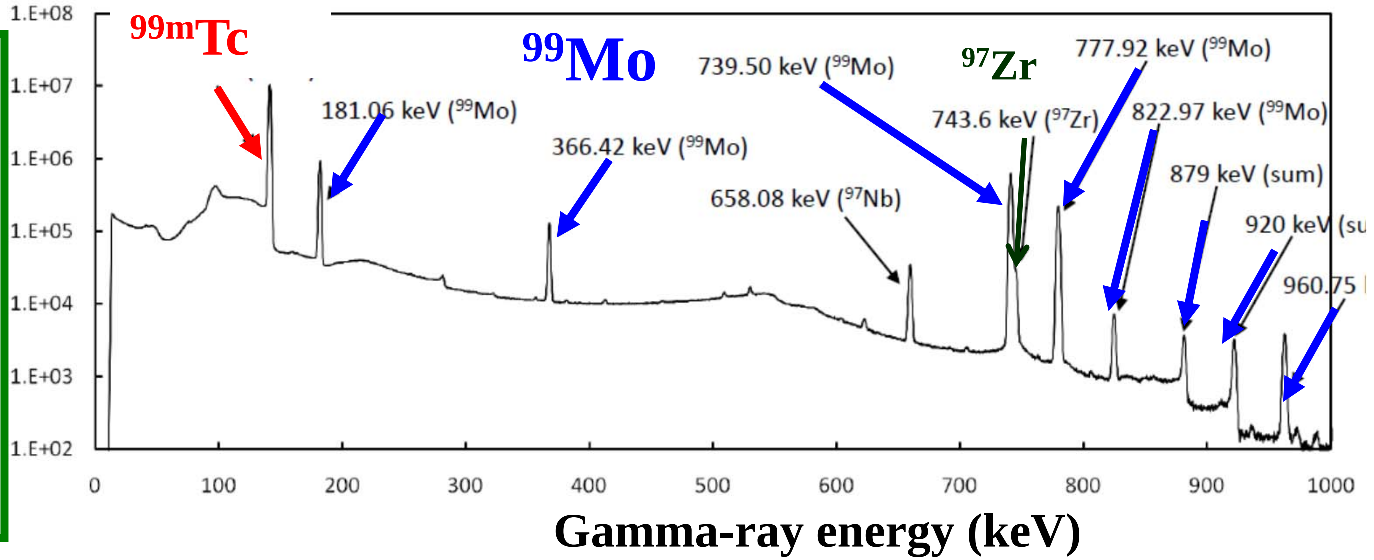
^{99}Mo

^{97}Zr ($T_{1/2}$=17 h)

^{97}Nb ($T_{1/2}$=1.2 h)

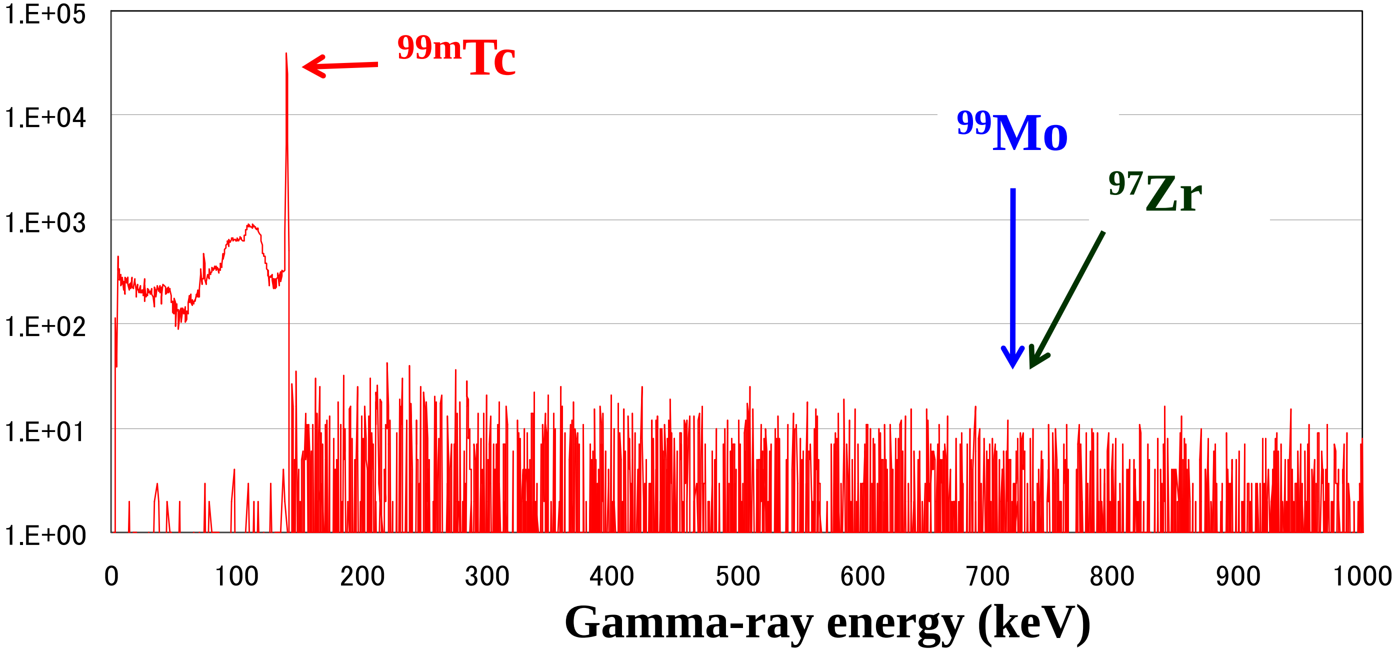
⇒separation easy

⇒Waste very small



◆ **after separation**

impurity < 0.01%



Labeling efficiency of ^{99m}Tc

Labeling efficiency (an important factor in the compounding and dispensing of radiopharmaceuticals), was shown to be > 99% by formulating a radiopharmaceutical with the use of commercially available methylene diphosphonate (^{99m}Tc-MDP). The efficiency is above the USP requirement (>90%). {^{99m}Tc-MDP: for a bone scan in routine ^{99m}Tc scans}.

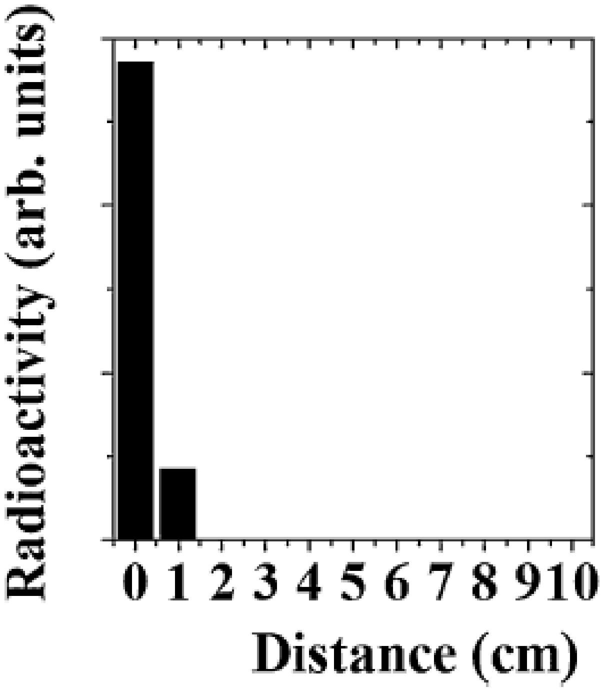
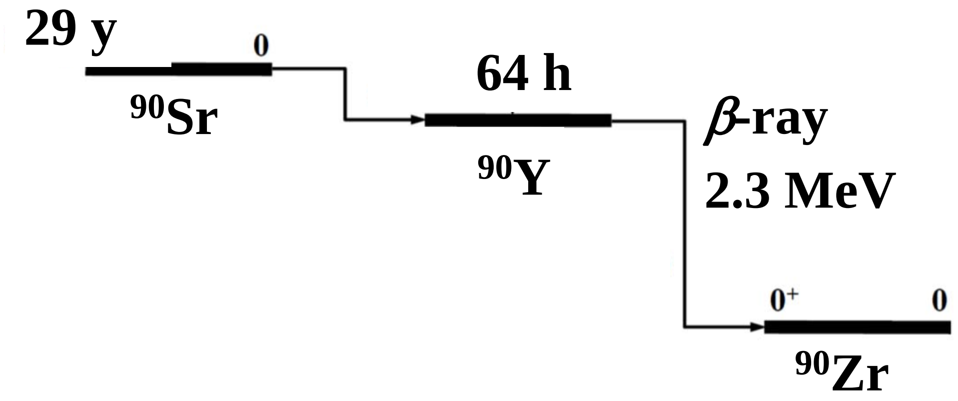


Fig. 3. Analysis of MDP labeled with ^{99m}Tc separated from ^{99}Mo produced by ^{100}Mo(n, $2n$)^{99}Mo. Thin layer chromatograms on silica gel strips developed with acetone.

Y. Nagai et al., J. Phys. Soc. Japan, 80(2011)

^{90}**Y** radiopharmaceuticals for cancer therapy

Zevalin:^{90}Y-labelled radiopharmaceutical (for non-Hodgkin's lymphoma)



Problems:

♦ **import:**

⇒ **decrease quality (freshness)**

due to the decay

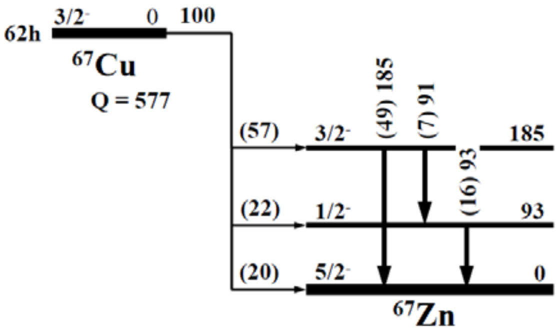
⇒ **difficult to label**

Accelerator neutrons

1) $^{90}Zr + n \Rightarrow {}^{90}Y + p$

Y.Nagai, O.Iwamoto, N.Iwamoto. T.Kin, M.Segawa, Y.Hatsukawa, and H.Harada: J. Phys. Soc. Japan, (2009)

^{64}Cu and ^{67}Cu productions using accelerator neutrons



Kim et al.: submitted (2012)

	Yield
^{68}Zn + p → ^{67}Cu + 2p	1
→ ^{64}Cu + ^{4}He + n	13
^{68}Zn + n → ^{67}Cu + pn (d)	1
→ ^{64}Cu + x	$5\text{x}10^{-3}$

^{64}Zn + n → ^{64}Cu + p

(^{64}Zn: 19% abundance

^{64}Ni: 1% abundance)

Proposal (Available Facilities)

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Determine the neutron induced reaction cross sections of emerging diagnostic and therapeutic radionuclides as well as the well established and commonly used diagnostic and therapeutic radionuclides

^{100}Mo(n,2n)^{99}Mo, ^{90}Zr(n,p)^{90}Y, ^{64}Zn(n,p)^{64}Cu, ^{67}Zn(n,p)^{67}Cu, ^{68}Zn(n,x)^{67}Cu

$\Rightarrow$

1) Fusion Neutronics Source (JAEA):

14 MeV neutrons from ^{3}H(d,n)

2) Takasaki Ion Accelerators for Advanced Radiation Application (JAEA) and Cyclotron Radioisotope Center (Tohoku University)

14 MeV neutrons from C(d,n)