Symposium on Solving Problems in Research Reactors

Ibaraki University

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STATUS OF MEDICAL RADIOISOTOPE PRODUCTION AND FUTURE PLANS FOR Ac-225

Institute of Nuclear Physics

Sayabek SAKHIYEV, Yelena CHAKROVA, Pavel ORESHKIN, Albina BORISSENKO, Shamil GIZATULIN

e.chakrova@inp.kz

Status of Nuclear Medicine in Kazakhstan

2001 – start of domestic production of radiopharmaceuticals
- 1 operational Nuclear Medicine Centre

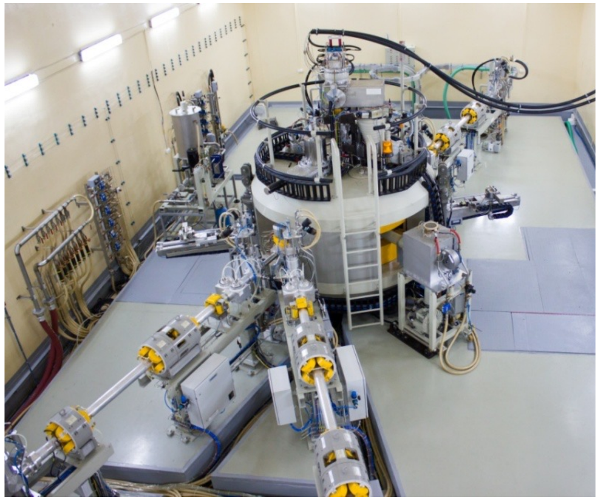
2025
- 11 Nuclear Medicine Centres in operation
- 2 Centres under construction

Radiopharmaceuticals:

- ^{99m}Tc solution from ^{99}Mo/^{99m}Tc gel generators from 2001
- Sodium iodide ^{131}I, oral solution from 2002
- Fluorodeoxyglukose ^{18}F, injection from 2021

INP fully covers local demand in radiopharmaceuticals with ^{99m}Tc and ^{131}I and 70% of local demand in radiopharmaceuticals with ^{18}F

Basic facilities for isotope production



C-30 cyclotron:
Proton: max. 30 MeV,
3 solid target, 2 liquid target

^{18}F, ^{57}Co, ^{109}Cd
^{68}Ge, ^{225}Ac

WWR-K reactor, 6 MW
Max thermal neutron flux: $2.2 \cdot 10^{14}$ $n \cdot cm^{-2}s^{-1}$

$^{99}Mo/^{99m}Tc$, ^{131}I, ^{177}Lu,
^{192}Ir, ^{60}Co, ^{124}Sb, ^{204}Tl, ^{85}Sr, ^{134}Cs

Radiopharmaceutical production facility

Radiochemical building:

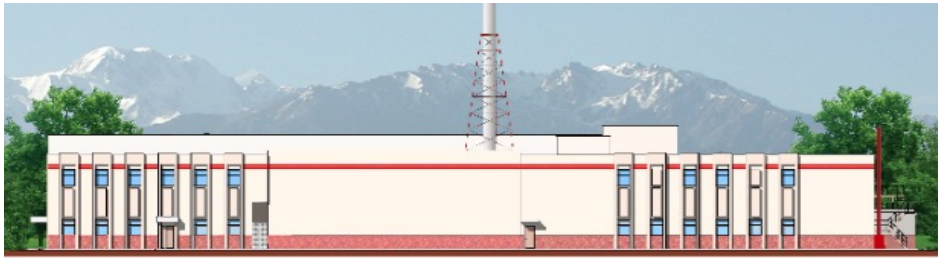
- R&D laboratories
- Hot cells
- Microbiological laboratory, Class A, B, C and D
- Clean rooms, class C and D

~800 m^2

Radiopharmaceutical building:

- Clean rooms, Class C and D
- Hot cells, Class A, B, C and D
- QC laboratory, Class D

~ 730 m^2




ЕВРАЗИЙСКИЙ ЭКОНОМИЧЕСКИЙ СОЮЗ

РГУ «Комитет медицинского и фармацевтического контроля Министерства здравоохранения Республики Казахстан»

СЕРТИФИКАТ
СООТВЕТСТВИЯ ПРОИЗВОДСТВА ЛЕКАРСТВЕННЫХ СРЕДСТВ ТРЕБОВАНИЯМ ПРАВИЛ НАДЛЕЖАЩЕЙ ПРОИЗВОДСТВЕННОЙ ПРАКТИКИ ЕВРАЗИЙСКОГО ЭКОНОМИЧЕСКОГО СОЮЗА

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подтверждает следующее:
проведена фармацевтическая инспекция

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ КАЗАХСТАН
КОМИТЕТ МЕДИЦИНСКОГО И ФАРМАЦЕВТИЧЕСКОГО КОНТРОЛЯ

СЕРТИФИКАТ

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ПЛОЩАДКА ПРОИЗВОДСТВА РАДИОФАРМАЦЕВТИЧЕСКОЙ ПРОДУКЦИИ

СТАНДАРТУ НАДЛЕЖАЩЕЙ ПРОИЗВОДСТВЕННОЙ ПРАКТИКИ (GMP)

^{99m}Tc

Sodium pertechnetate ^{99m}Tc, injection from $^{99}Mo/^{99m}Tc$ gel-generator

Irradiation: reactor WWR-K, $1 \cdot 10^{14}$ $n \cdot cm^{-2} \cdot s^{-1}$, MoO_3, 15 g, 120 h

^{99}Mo bulk solution production: alkaline dissolution of irradiated MoO_3

Premises: **class C**

$^{99}Mo/^{99m}Tc$ gel-generator production/ assembling: hot cells **class C**

Production schedule: 2 times/month

Transportation: 24-30 h

Generator activity at delivery 18 GBq

- *Eurasian Patent No. 047185 of 19 June 2024 «Generator for producing sterile radionuclides»*
- *Eurasian Patent No. 048752 of 28 December 2024 «Automatic control system for the process of preparing a matrix with a radioisotope»*

^{18}F

Fluorodeoxyglucouse ^{18}F, injection

Irradiation: cyclotron C-30, 18 MeV protons, 2 ml enriched water, 2- 3 h.

Synthesis modules: Synthera, Neptis, dispensing - Thymotheo LT

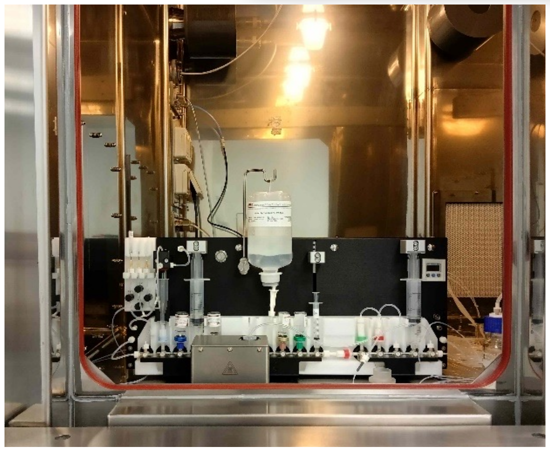
Premises: **class C**

Production: hot cells **class C**

Dispensing/membrane sterilization: hot cells **class A**

Production schedule: 3 times/day

Transportation: 1- 7 h



^{131}I

Sodium iodide ^{131}I for therapy

Irradiation: reactor WWR-K, $1 \cdot 10^{14}$ $n \cdot cm^{-2} \cdot s^{-1}$, TeO_2, 20 g, 72-120 h

^{131}I bulk solution production: dry distillation at 700°C with sorption of ^{131}I in alkaline buffer solution

Premises: **class D**

Production/dispensing/sterilization: hot cells **class C**

Production schedule: 4 times/month,

individual doses,

Transportation 24-30 h to Astana and Semey

EURASIAN PATENT № 050009 of 30 May 2025
"Method for production of a bulk solution of iodine-131 isotope"

^{177}Lu Lutetium chloride ^{177}Lu, solution for labeling

Direct neutron activation of enriched Lu (we use 85% of ^{176}Lu)

$^{176}Lu(n, \gamma)^{177}Lu$, σ = 2100 b

Indirect neutron activation

$^{176}Yb(n, \gamma)^{177}Yb(\beta^-) \rightarrow {}^{177}Lu$, σ = 2.4 b

Irradiation: reactor WWR-K, $1 \cdot 10^{14}$, $n \cdot cm^{-2} \cdot s^{-1}$, 18 days

$^{176}Lu_2O_3$, 20 mg

QC according to Ph.Eur. 11.0, Monograph "Lutetium (^{177}Lu) solution for radiolabeling"

Premises: **class D**

Production/dispensing/sterilization:

hot cells **class C**

Production schedule: as needed for R&D

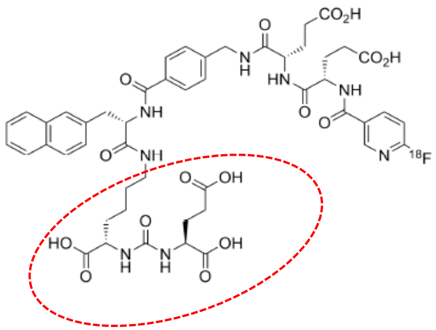
What are we working on today? - Development of a theranostic group of RPhs for the diagnosis and treatment of prostate cancer

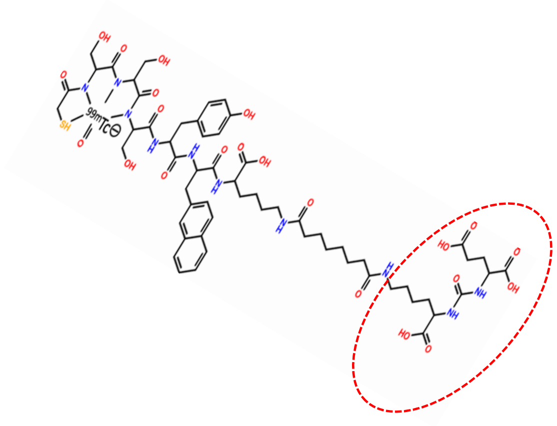
Step 1. Based on the developed technologies for production of ^{18}F, ^{99m}Tc, ^{177}Lu and commercially available PSMA inhibitor molecules, to obtain:

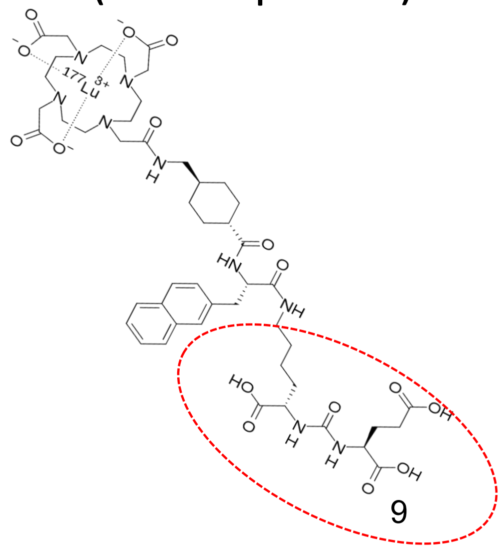
^{18}F-PSMA-1007 – imaging using PET-CT, including for treatment control (implemented into production)

^{99m}Tc-PSMA-I&T – imaging using SPECT-CT, including for treatment control (development)

^{177}Lu/PSMA- I&T – targeted therapy (implemented into production)



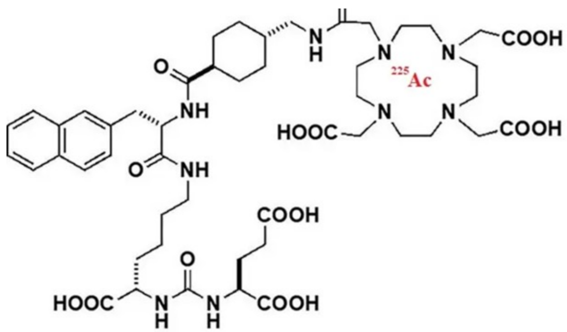




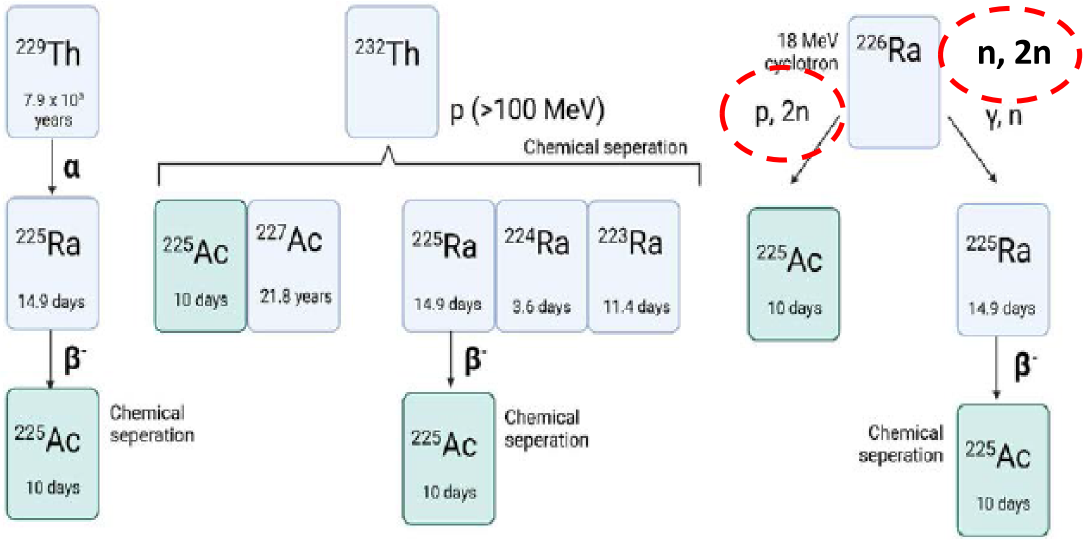
^{225}Ac Future development of the theranostic group of RPhs for the diagnosis and treatment of prostate cancer

Step 2

1. Assessment of the ^{225}Ac production:
   - at the research reactor WWR-K
   - at the cyclotron Cyclone-30
2. Design and construction of research and production facilities for working with alpha-emitting isotopes
3. Development and implementation of the ^{225}Ac solution production technology
4. Development and implementation of the technology for production of ^{225}Ac-PSMA- I&T for targeted therapy



^{225}Ac Approaches to Actinium-225 Production



Production and quality control of actinium-225 radiopharmaceuticals / Vienna: International Atomic Energy Agency, 2024 / Series: IAEA TECDOC no. 2057;
Schematic overview on the different production methods of 225Ac (courtesy of V. Radchenko, TRIUMF, and of J. Kleynhans, KU Leuven)

The current primary supply of ^{225}Ac comes from thorium-229 decay. Process involves "milking" of the generator and separation of ^{225}Ac from other thorium decay products.
3 main sources: Oak Ridge National Laboratory (ORNL, USA), the Institute for Transuranium Elements (ITU, Karlsruhe, Germany), and the A.I. Leipunsky Institute of Physics and Power Engineering (Russia). Additional smaller sources of ^{229}Th are available in Canadian Nuclear Laboratories and Belgian Nuclear Research Centre.

n, 2n Year 2008
Research Reactor WWR-K

p, 2n Year 2025
Cyclotron Cyclone-30

^{225}Ac Assessment of ^{225}Ac production at the WWR-K research reactor

Assessment of ^{225}Ac production feasibility at the WWR-K reactor was carried out in 2008 in collaboration with NNC RK.

A series of neutron-physics calculations using the MCU-REA* code was done by Dr. Gizatulin Reactor's team for irradiation of ^{226}Ra under three scenarios: **no shielding**, **cadmium shielding**, and **boron-carbide shielding** to suppress thermal neutrons.

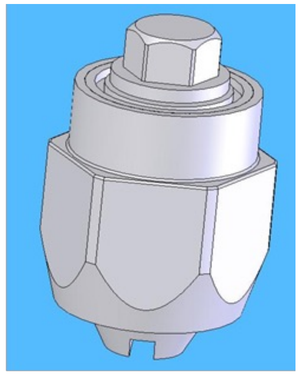
**1. E. A. Gomin, M. I. Gurevich, L. B. Maiorov, C. B. Marin "The MCU-3 code for Monte Carlo calculation neutronics parameters of nuclear reactors",Vol.1, Description of an application and manual for users", Preprint IAE-5772/5, M., 1994*

Results:

- A 1-mm Cd screen effectively suppresses thermal neutrons but leaves a significant fraction of epithermal neutrons.
- Boron-carbide shielding provides the most efficient reduction of low-energy neutrons parasitic for ^{225}Ra production.
- The calculated **production rate of ^{225}Ra is ~0.3 MBq/h** per 1 g ^{226}Ra for in-core irradiation with 1-mm B_4C shielding

Experiment:

- Target – 10 ug ^{226}Ra
- In-core irradiation in special container with 1mm boron carbide shielding during 50 h
- Calculated equilibrium ^{225}Ac activity after irradiation and 18 days decay - 7±2 kBq
- Measured ^{225}Ac activity after chemical separation - 5±1 kBq




^{225}Ac

Assessment of ^{225}Ac production at cyclotron Cyclone-30

In 2025, the review of nuclear reactions of accelerated protons with ^{226}Ra was carried out.

Assumed target - metallic radium; Proton energy – up to 30 MeV

The reaction cross sections were taken from the TENDL* nuclear data library

** A.J. Koning, D. Rochman, J. Sublet, N. Dzysiuk, M. Fleming and S. van der Marck, "TENDL: Complete Nuclear Data Library for Innovative Nuclear Science and Technology", Nuclear Data Sheets 155 (2019) 1*

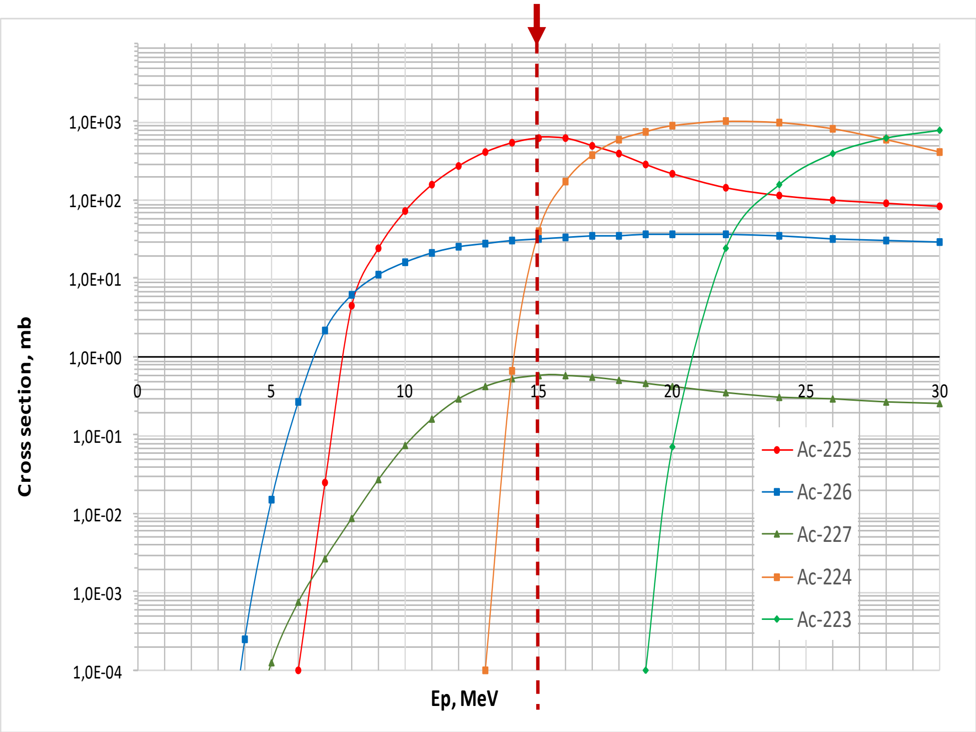
List of isotopes produced in reactions of protons with ^{226}Ra are given in the table:

Isotope	Half-life	Energy of threshold, MeV	Maximum cross section (up to 30 MeV), mb	Isotope	Half-life	Energy of threshold, MeV	Maximum cross section (up to 30 MeV), mb
^{223}Ac	2,2 m	19,2	796	^{224}Ra	3,6 d	2,83	58,35
^{224}Ac	2,9 h	13,55	1035	^{225}Ra	14,8 d	4,19	104,6
^{225}Ac	10 d	6,85	636	^{220}Fr	27,4 s	7,2	0,81
^{226}Ac	29,4 h	1,43	36,7	^{221}Fr	4,9 m	0,89	8
^{227}Ac	21,8 y	0,0	0,59	^{222}Fr	14,4 m	0,0	23,56
^{221}Ra	29 s	21,3	10^{-4}	^{223}Fr	21,8 m	0,0	20,0
^{222}Ra	38 s	14,5	0,86	^{224}Fr	3,3 m	5,75	0,12
^{223}Ra	11,4 d	9,34	7,13				

^{225}Ac Assessment of ^{225}Ac production at the cyclotron Cyclone-30

Results of the review of nuclear reactions :

- The main impurity isotopes are $^{226,\,227}Ac$
- The threshold energy for nuclear reactions producing isotopes ^{225}Ac and $^{226,\,227}Ac$ have similar values
- The maximum cross sections for reactions producing isotopes ^{225}Ac and $^{226,\,227}Ac$ also correspond to similar proton energy values (~15 MeV), so it is not possible to specify the optimal proton energy range for a "purer" production of the target isotope;
- Technological process must include a time period for decay of impurities



Design and construction of research and production facilities for work with alpha-emitting isotopes

Development of ^{225}Ac production is limited by lack of suitable facilities for handling α- and high-γ-emitting ^{226}Ra, as well as limited availability of ^{226}Ra

Steps we are taking to overcome these difficulties:

- funding request for designing and equipping dedicated α-/high-γ laboratories compliant with radiological safety requirements for ^{226}Ra handling
- looking for a reliable source of ^{226}Ra

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kiite kurete arigatou

Thank you for attention