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Development of new methods for medical radionuclide production for radioisotope complex at NRC "KI"-PNPI

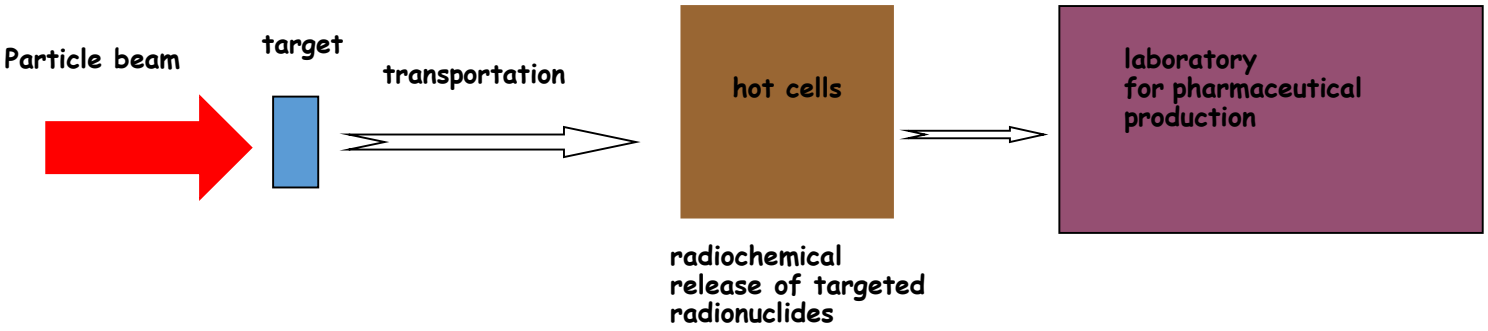
Nuclear (radionuclide) medicine

Diagnostics and treatment can be carried out at the earliest stage of the disease, doing the minimum harm to the patient's helth

Complex molecular compounds with build-in radionuclides are specially constructed for absorbtion by certain malignant tumors for their destruction

Special detection devices make it possible to observe on-line the functioning of investigated organs or their parts

The technology of nuclear medicine used for diagnostics and therapy is based on the use by a special way produced radioactive isotopes with selected properties.



Production of the required radionuclide is determined by the type of nuclear reaction, or by other words by the type of bombarding particle beam (protons, neutrons, heavy ions) and the irradiated target material.

By fission and (n,γ) reactions isotopes are produced with neutron excess utilized mainly for therapy, but the most in the world used for diagnostics

Reactors on thermal neutrons:

Mo-99/Tc-99 produced by U-235 fission.

Proton accelerators (cyclotrons):

By (p,xn) and spallation reactions are produced radionuclides with proton excess utilized for diagnostics and for therapy. Only by cyclotrons isotopes for PET diagnostics can be obtained. Using U-238 targets by fission reaction with protons, it is possible to produce isotopes with neutron excess also as at the reactors.

Present status of new experimental facilities of PNPI

PIK reactor

Max. flux of thermal neutrons 5×10^{15} n/sm^{2}s

Present status:
Power 100 kW - 2019

Planned:
Power 10 MW 2021
Power 100 MW 2023

Cyclotron C-80

Proton beam energy 40-80 Mev, extracted current 100 μA

Present status: beam adjustment at 100 μA

Planned:
radioisotope complex construction
ophthalmologic beam construction

Project of radioisotope complex "ISOTOPE" is being developed at NRC "KI"-PNPI

- The ISOTOPE complex will ensure very wide possibilities for production of pharmaceuticals and radionuclides for diagnostics and therapy

- Three target stations for production of the most widely used radionuclides

- For production of radionuclides of a high purity the mass-separator will be installed at one of the beam lines

Radionuclides planned for production

Cu - 64,
Cu - 67,
Ge-68/Ga-68,
Sr-68/Rb-82,
Tc-99,
In-111,
I-123
I-124,
Tb-149,
Pb-212/Bi-212,
Ra-223,
Ra-224,
Ac-225

Additionally new methods are developed for radionuclide Lu-177 and Re-188 production (reactor)

Development of new methods for medical radionuclide production

High temperature and mass-separation methods for separation of produced radionuclides and target material

Values of enthalpies of adsorption of different elements at the surface of some refractory metals (Nb, Mo, Ta)
R. Kirchner, Nucl. Instr. and Meth. B26(1987) 204 -212

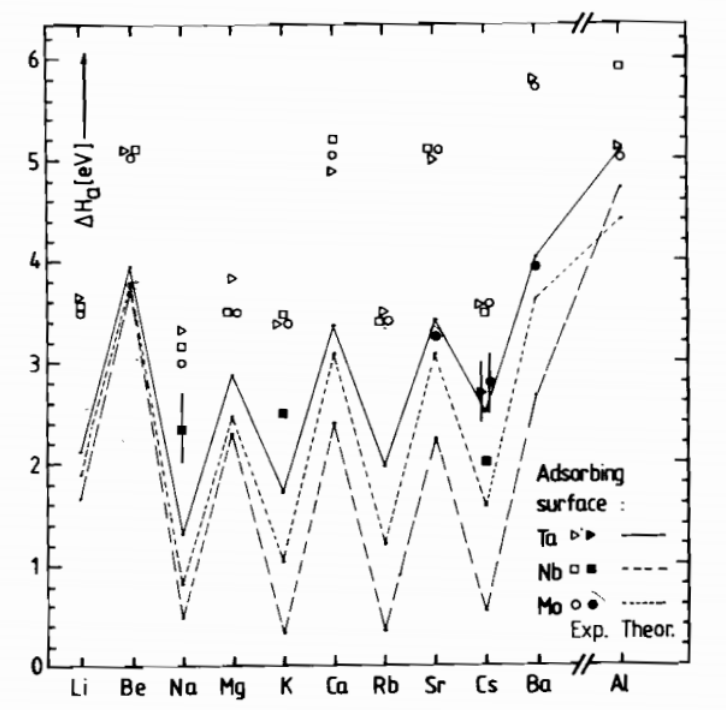


Fig. 5. Semi-empirical [2] and experimental ΔH_a-values of the alkali metals, the alkaline-earths and aluminum. The open symbols are from this work. Closed symbols are from the compilation in ref. [12]; bars show the scatter of different measurements.

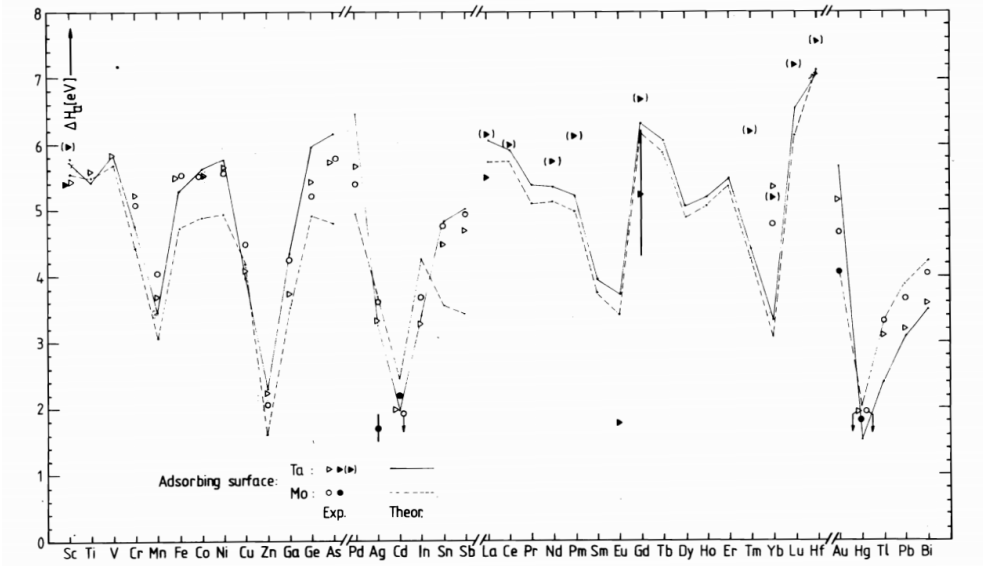


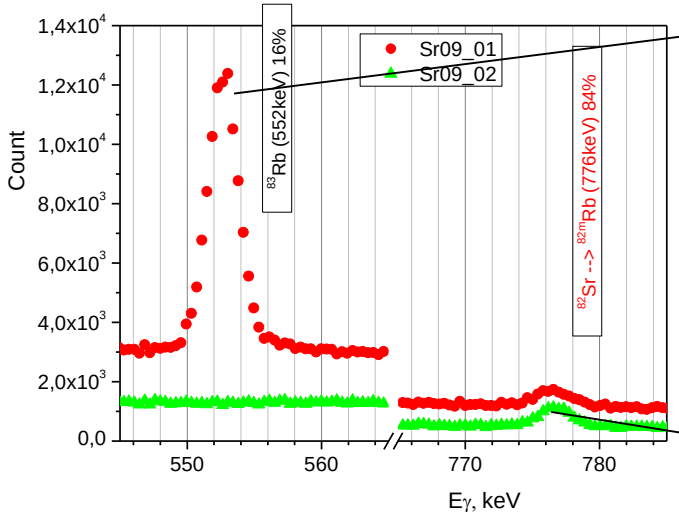
Fig. 6. Semi-empirical [2,3] and experimental ΔH_a-values of the transition elements scandium to nickel, the lanthanides, lanthanum and hafnium. The open symbols are from this work. The data for a niobium surface are not presented, being similar to the data for tantalum and in no case more advantageous. For completeness, the data for copper to arsenic, palladium to antimony and gold to bismuth from ref. [1] are shown, downward pointing arrows indicating upper limits. Note the revised values for germanium, arsenic, palladium and gold. Closed symbols are from the compilation in ref. [12]; bars show the scatter of different measurements. Closed triangles in parentheses are deduced from the t_a-values of ref. [4], using the t_a-versus-ΔH_a dependence in fig. 4.

Isotope	Rb	Sr	Zn	Cu	Yb	Lu	Ga	Ge
Boiling point °C	688	1382	907	2562	1194	3393	2204	2833

^{82}Sr separation from irradiated RbCl target material

(heart and brain diseases diagnostics)

The target material should have a high pressure of saturated vapor at a temperature which ensures fast enough evaporation of the target material without escape of the produced radionuclides



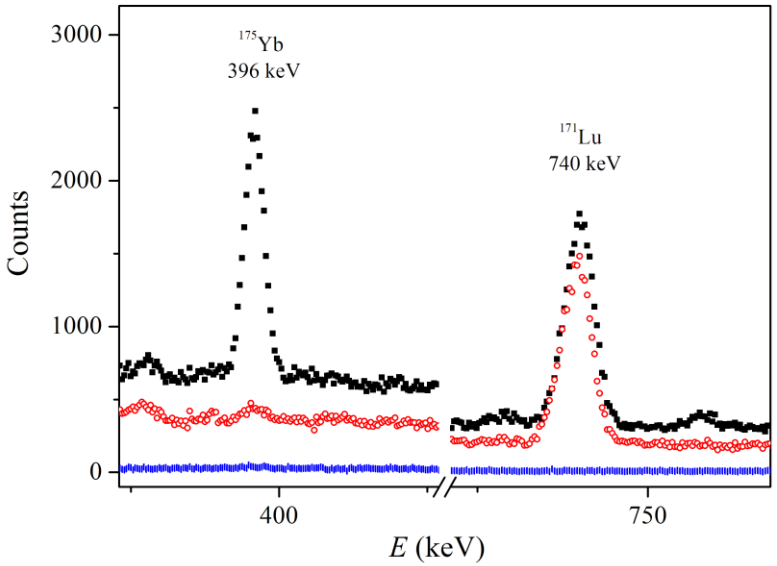
Part of gamma spectra of irradiated RbCl before and after heating in vacuum at a temperature higher 900° C for 1hour

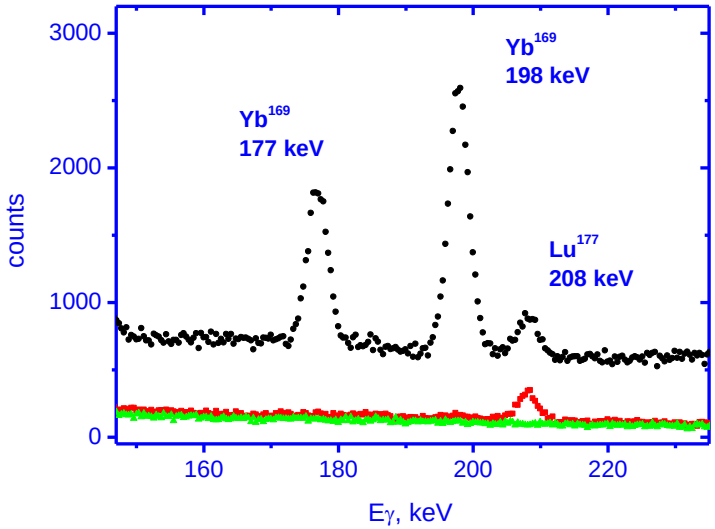
Cavity with RbCl before heating at a temperature lower 800° C

Cavity after heating at a temperature higher 900° C. Target material was completely evaporated

177Lu separation from by proton and neutron irradiated Yb metal target material *(prostate cancer treatment)*

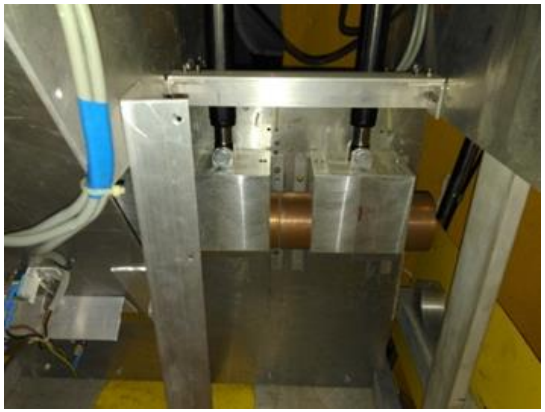
	Lu	Yb
Boiling point, °C	3393	1194





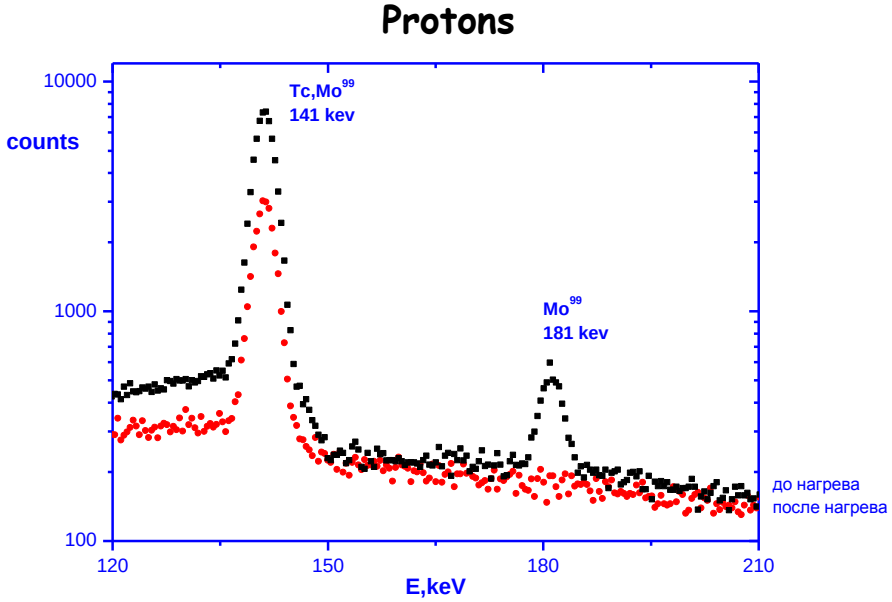
^{177}Lu from ytterbium metal target was produced in the reaction ^{176}Yb(n,γ)^{177}Yb - ^{177}Lu

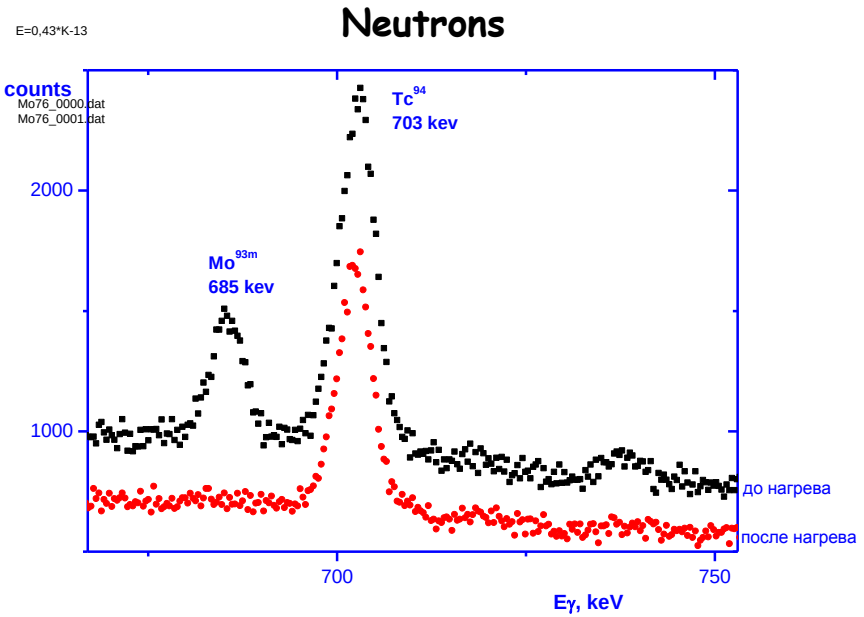
^{171}Lu from ytterbium metal target was produced in the reaction ^{nat}Yb(p,xn)^{171}Lu



^{99}Tc separation from irradiated MoO_3 target material by protons and neutrons

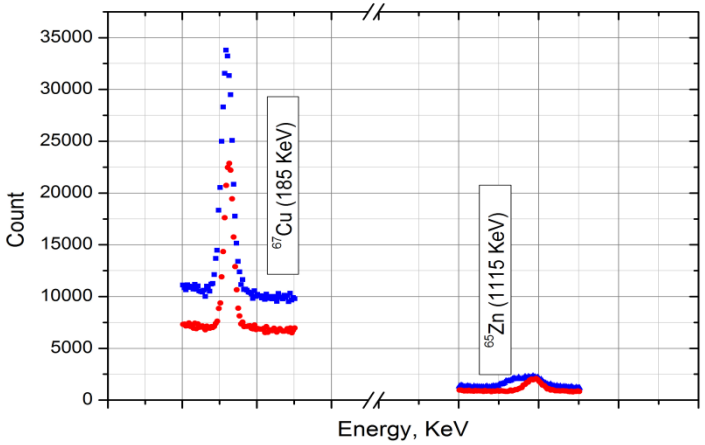
	Tc	MoO_3
Boiling point, °C	4265	1155

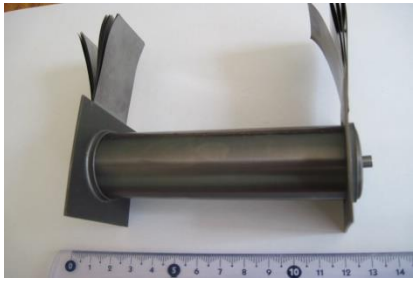


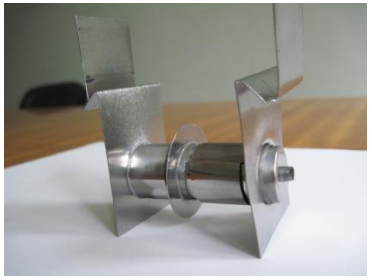


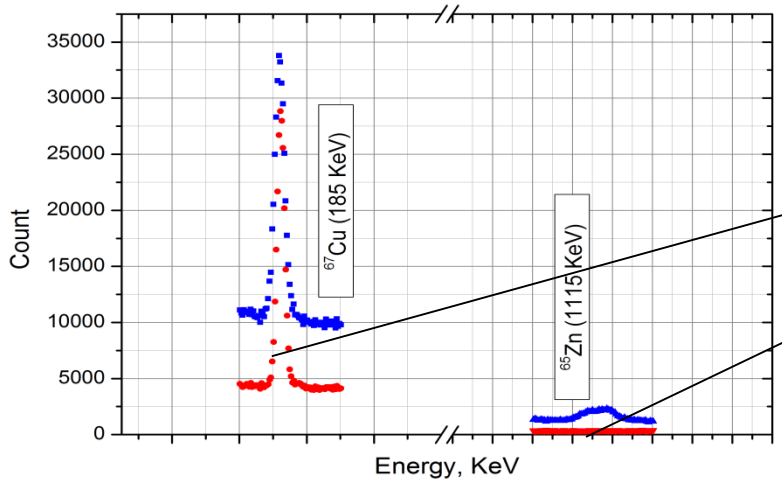
Gamma spectrum of irradiated MoO_3 before (black points) and after (rad points) heating at 800 °C

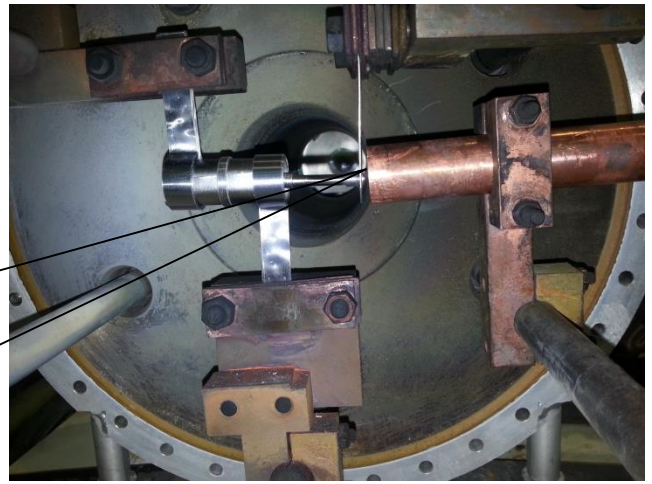
^{67}Cu separation from proton irradiated Zn metal targrt









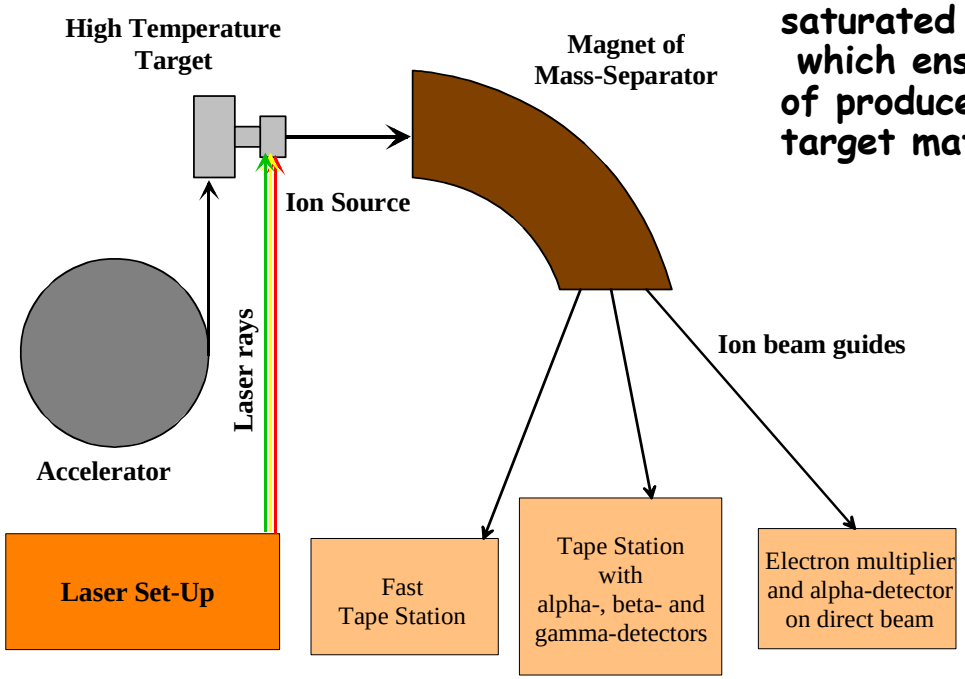


The target unit for evaporation and collection of irradiated target materials

In lower part of the spectra evaporated cooper atoms collected at the cold finger cooled by floating water after the vessel heating at a temperature 1460°C in two hours (circles) is presented. For comparison by squares the spectrum of the vessel with the irradiated Zn before the heating is shown (upper part of the spectra).

Mass-separation method for radionuclide production

Traditional mass-separator method



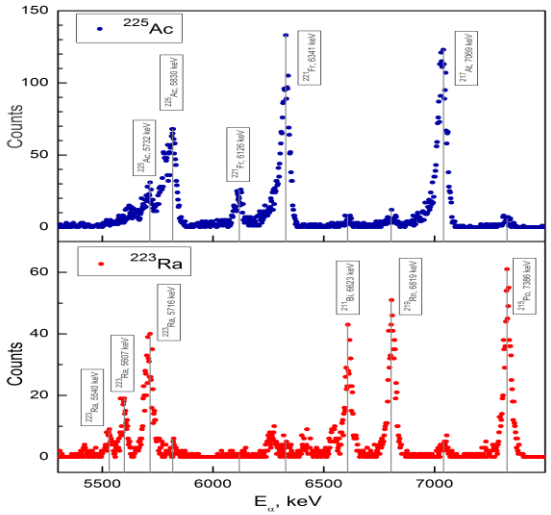
If the target material has a low pressure of saturated vapor at a temperature which ensures fast enough diffusion and effusion of produced radionuclides, it can be used as a target material for a mass-separator method.

The isotopes of one element can be separated with the selectivity better 0.1%

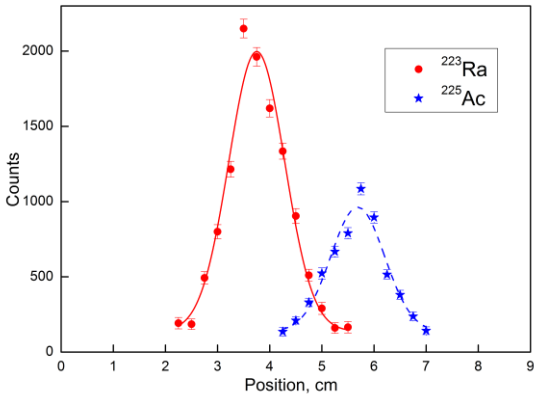
Schematic view of IRIS mass-separator at synchrocyclotron Sc-1000 at NRC KI-PNPI

Mass-separator method for production of alpha emitters Ra-223 и Ac-225 from uranium carbide target of a high density *(cancer tumor treatment at an early stage)*

Target chamber of IRIS facility at the beam of synchrocyclotron Sc-1000



Alpha spectra of mass-separated Ra-223 и Ac-225

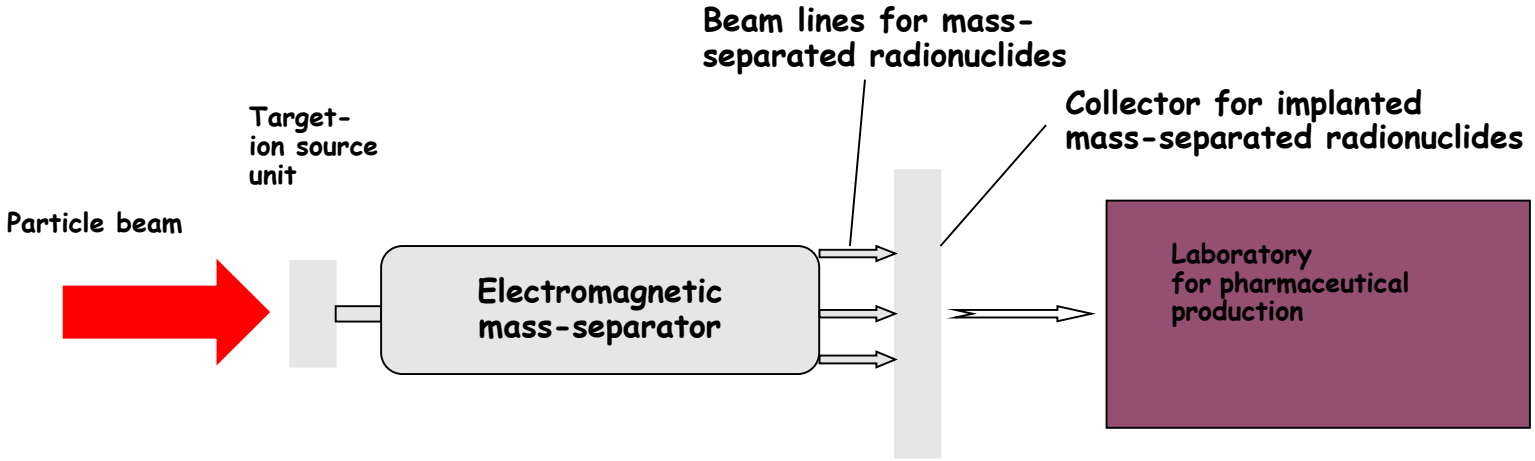


Mass-separated isotopes of radium-223, and actiniu-225

Element	Ionization potential (eV)	Efficiency (%)
Cs	3.9	51(15)
Rb	4.2	47(10)
Ra	5.3	38(10)
In	5.8	33(8)
Tl	6.1	21(8)

Mass-separation method efficiency for some radionuclides

Mass-separator method for medical radionuclide production



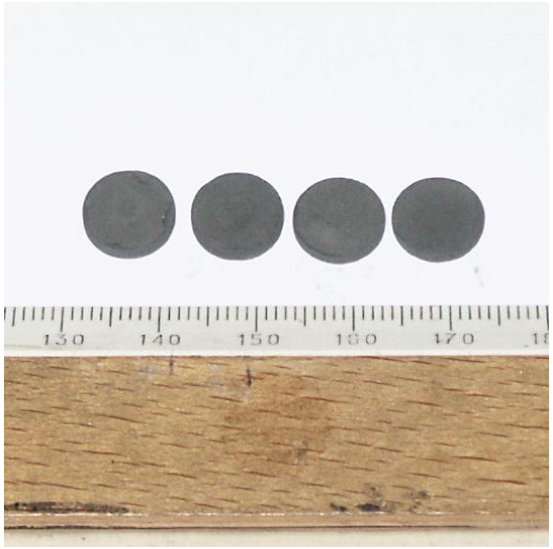
Processed radioactivity is sevral tens of times less than the irradiated target activity
The use of mass-separated method ensures production of targeted radionuclides of a high isotopic purity
The group of radionuclides with close mass numbers can be accumulated simultaneously
Produced samples allow a very fast process of pharmacetical production

*Radionuclides planned by mass-separator method production

Cu-64,67, Ge-68, *Sr-82, Tc-99, *In-111, *I-123I,124, *Tb-149, Pb-212/Bi-212, *Ra-223,224, *Ac-225

Pb-212 and Ra-224 production and extraction from thorium carbide target

The radionuclides ^{224}Ra and ^{212}Pb can be produced in the ^{232}ThC target irradiated by high-energy protons in general as a result of a chain of α-decays: ^{228}Th(T1/2= 1.9 y) → ^{224}Ra(T1/2 = 3.66 days) → ^{220}Rn(T1/2 = 56 s)→ ^{216}Po(T1/2 = 145 ms) → ^{212}Pb(T1/2 = 10.6 h) → ^{212}Bi (T1/2 = 25 min) → ^{208}Tl(T1/2 = 3 min) → ^{208}Pb(stable).

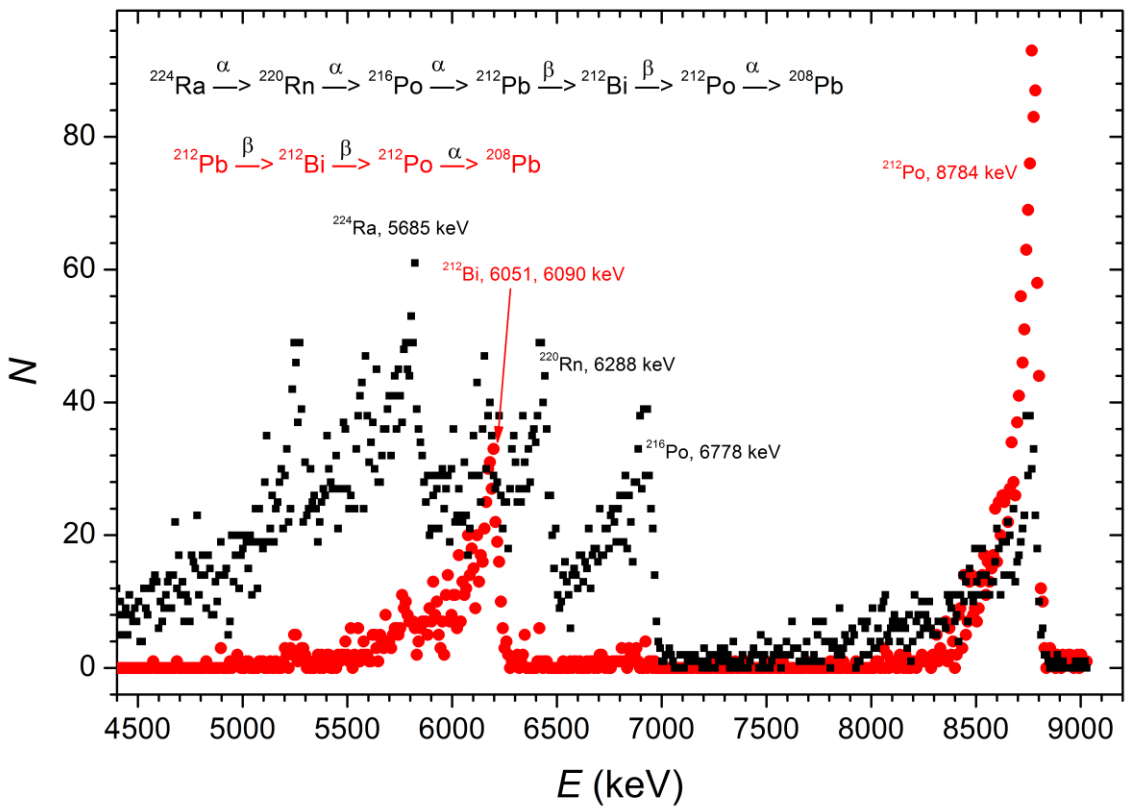


^{232}ThC target material

High density ThC target material

Density	~6g/cm^3
Melting point	~2500 °C
Boiling point	~3500 °C

Pb-212 and Ra-224 production and extraction from thorium carbide target



For ^{212}Pb separation from the target material it was kept at a temperature of 1230 °C for one hour in a high vacuum.

In order to evaporate and collect ^{224}Ra after the process of 212Pb extraction, the target was kept at a temperature 1500 °C for the period of one hour in a high vacuum.

Alpha spectrum of the daughter isotopes of ^{212}Pb (^{212}Bi and ^{212}Po, red circles) and alpha spectrum of ^{224}Ra with α-lines of its daughter isotopes (black squares) measured on the copper collector.

Conclusion

The results of experiments confirmed the idea that the target material can be selectively evaporated without loss of produced radionuclides, if there is considerable difference in the values of saturated vapours pressure of the target substance and radionuclides of interest.

Method works regardless of in which reactions target radionuclides are produced.

The next step in the method development will be construction and tests of the real target prototype of some tens of gramms.

The use of thorium carbide target material which allows extraction of produced nuclides without the target destruction similar to targets from carbides of other metals can give good possibilities for production of radionuclides alpha-emitters Ra-223,224, Ac-225.