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Development of isotopes for theranostics and nuclear medicine in Ukraine

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Relevance:

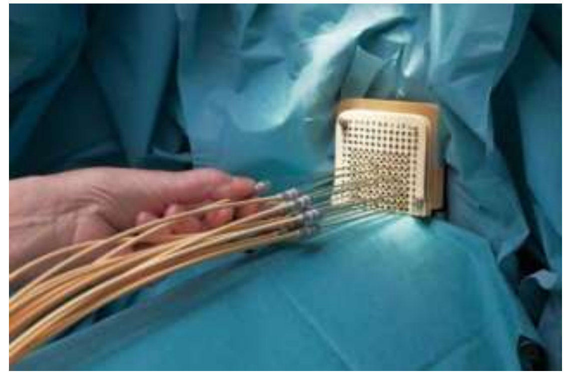
- nuclear medicine is developing rapidly;
- it is critical for the diagnosis and treatment of a number of diseases;
- it is extremely important to have a deep understanding of the existing capabilities and find new ways to produce the necessary radionuclides.

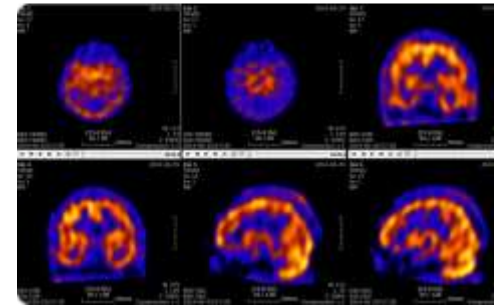
Objective of the work was to find:

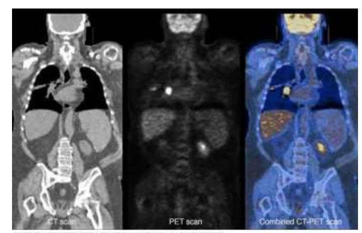
- important radionuclides for nuclear medicine in Ukraine;
- ways to develop them and increase their yield taking into account new channels of nuclear reactions;
- propose such radionuclides with high yield.

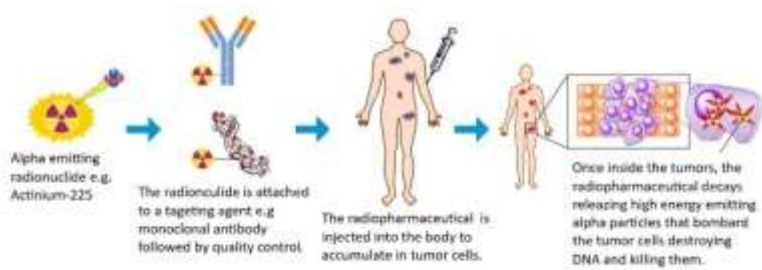
Areas of nuclear medicine in which radionuclides are in demand in the world

- SPECT tomography
- PET tomography
- Targeted alpha therapy
- Radionuclide therapy
- Brachytherapy
- Scintigraphy
- For the diagnosis and treatment of diseases of human organs
- Theranostics





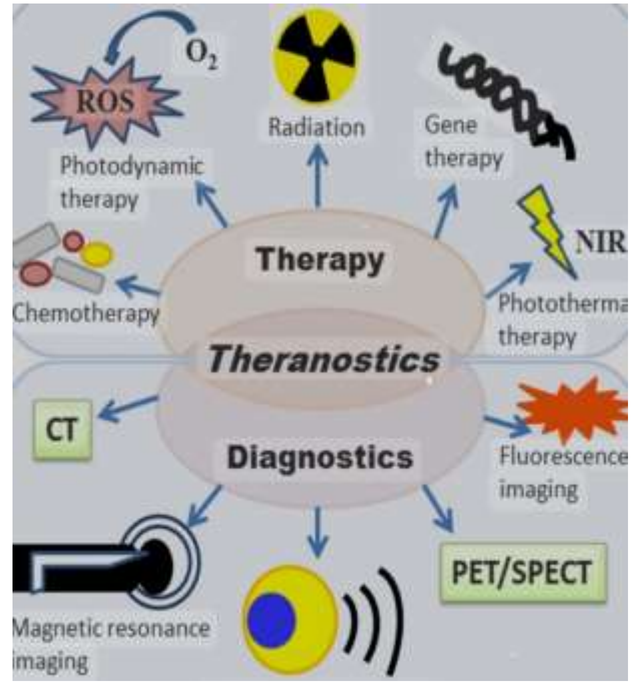


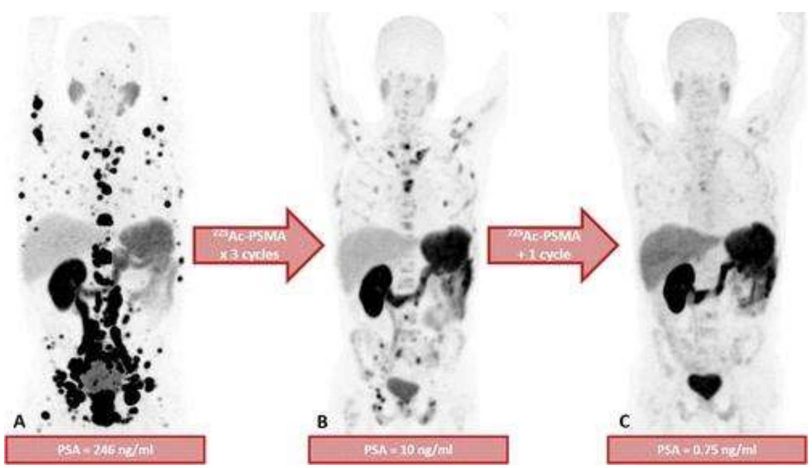


Theranostics

Theranostics is the combination of using two radioactive isotops (radiopharmaceuticals)

Radioisotopes emit radiation which are detected by a gamma camera and PET





Usage:

- pill or injection absorbed over 20- 30 minutes
- monitoring of blood pressure and pulse during infusions

Isotope reactions with dineutron

- **Heavy nucleus is a possible source of** the potential field for detecting the **dineutron**
- **Purpose**: Increase in the yield of reaction products during the generation of dineutron
- We are investigating the possibility of producing a radionuclide by a reaction of the following type $\boldsymbol{A} + \mathbf{n/d/p} = \boldsymbol{B} + \mathbf{2n}$ using $\boldsymbol{B} + \boldsymbol{n} = \boldsymbol{C} + \boldsymbol{\gamma}$ reaction.
- Chose radionuclides with **atomic masses** in the range **of 90-209**
- Present the reactions of the development for these radionuclides

Number	Isotope	Atomic mass (a.u.m	Reactions from the field
1	Iodine-124	123,91	$^{124}Te(d,2n)^{124}I$, $^{125}Te(p,2n)^{124}I$, $^{124}Te(p,n)^{124}I$
2	Thallium-201	200,97	$^{203}Tl(p,3n)^{201}Tl$
3	Iodine-123	122,9	$^{124}Xe(p,2n)^{123}I$, $^{123}Te(p,n)^{123}I$, $^{124}Te(p,2n)^{123}I$
4	Indium-111	110,9	$^{112}Cd(p,2n)^{111}In$, $^{111}Cd(p,n)^{111}In$
5	Xenon-133	132.9	$^{132}Xe(n,\gamma)^{133}Xe$.
6	Xenon-127	126,9	$^{133}Cs(p,2p5n)^{127}Xe$; $^{126}Xe(n,\gamma)^{127}Xe$, $^{127}I(p,n)^{127}mXe$, $^{127}I(d,2n)^{127}mXe$
7	Silver-111	110.9053	$^{110}Pd(n,\gamma)^{111}Pd$
8	Palladium-103	102,9	$natAg(p,xn)^{103}Pd$, $^{103}Rh(p,n)^{103}Pd$, $^{102}Pd(n,\gamma)^{103}Pd$
9	Iodine-131	130.91	$^{130}Te(n,\gamma)^{131}Te$, $^{131}Te \rightarrow ^{131}I + e^- + \nu_e$, $^{131}Te(ec,\beta+)^{131}I$

Isotope production reactions

Number	Radionuclide	Reaction of the work in progress
1	Iodine-124	$^{124}Te(d,2n)^{124}I$, $^{125}Te(p,2n)^{124}I$
2	Molybdenum-99	$^{100}Mo(n,2n)^{99}Mo$,
3	Technetium-99m	$^{100}Mo(p,2n)^{99m}Tc$,
4	Iodine-123	$^{124}Xe(p,2n)^{123}I$, $^{124}Te(p,2n)^{123}I$
5	Indium-111	$^{112}Cd(p,2n)^{111}In$
6	Xenon-127	$^{127}I(d,2n)^{127m}Xe$
7	Reniy-186	$^{186}W(d,2n)^{186}Re$

Reactions with two neutrons in the output channel

Parameters of nuclear reactions

B(n, γ)C reaction is used to calculate the possibility of increasing the yield of reaction products of **A(*,2n)B**

Important parameters for the calculation:

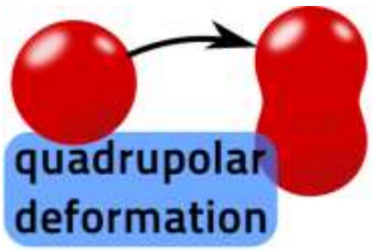
- mass number;
- number of neutrons;
- value of the parameter of the quadrupole deformation of the nucleus-product of the reaction.

Calculated parameters:

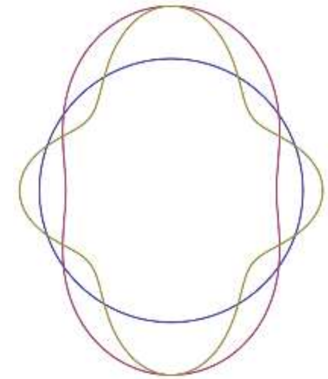
- small radius of the deformed core: R1= $R_0\left(1-\frac{1}{2}\sqrt{\frac{5}{4\pi}}\beta\right)$
- large radius of the deformed core : R2= $R_0\left(1+\sqrt{\frac{5}{4\pi}}\beta\right)$
- value of the radius of the spherical core: R0= $1{,}2 * \sqrt[3]{A}$

Number	Response	A	N	β	R_0	R_1	R_2
1	$^{111}In(n,\gamma)^{112}In$	111	62	0.108	5,77	5,57	6,16
2	$^{127}Xe(n,\gamma)^{128}Xe$	127	73	0.163	6,03	5,72	6,65
3	$^{186}Re(n,\gamma)^{187}Re$	186	111	0.203	6,85	6,41	7,73

Selection criteria



Since heavy nuclei are in most cases deformed, after these calculations, in order to consider all possible combinations between the radius of deformed nuclei and resonance energies of neutrons, we will form four criteria C1-C4 proportional to the deformation radius



$$C_1 = \ln \frac{1}{\boldsymbol{\varepsilon}_1 \cdot R_1^2}$$

$$C_2 = \ln \frac{1}{\boldsymbol{\varepsilon}_2 \cdot R_2^2}$$

$$C_3 = \ln \frac{1}{\boldsymbol{\varepsilon}_1 \cdot R_2^2}$$

$$C_4 = \ln \frac{1}{\boldsymbol{\varepsilon}_2 \cdot R_1^2}$$

Number	Response	ε1	ε2	C1	C2	C3	C4
1	$^{111}In(n,\gamma)^{112}In$	1,1601E-6	7,9153E-6	10,23199	8,110574	10,03087	8,311695
2	$^{127}Xe(n,\gamma)^{128}Xe$	5,595E-7	8,027E-6	10,90768	7,942862	10,60638	8,244153
3	$^{186}Re(n,\gamma)^{187}Re$	2,981E-7	2,197E-6	11,30969	8,938964	10,93638	9,312275

Good criteria to observe dineutron is C1-C4>9

Results

- **all four criteria are greater than 9**, then this radionuclide is the most suitable for observing a dineutron in the output channel. From the above calculations, no radionuclide fell into this category;
- **three criteria are greater than 9**: 186Re(n, γ)187Re;
- two criteria are greater than 9: 111In(n, γ)112In, 127Xe(n, γ)128Xe.

Summary

- Work was carried out to find radionuclides that are important for theranostics and nuclear medicine in Ukraine

- The properties of radionuclides that are important for the treatment and diagnosis of diseases are analyzed

- Isotope production reactions and their cross sections were found

- The reactions that are possible to observe the bound dineutron are determined, specifically from isotopes that are important for medicine, in particular, those in which this phenomenon can occur:
  - $^{112}Cd(p, 2n)^{111}In$
  - $^{127}I\ (d, 2n)\ ^{127m}Xe$
  - $^{186}W(d, 2n)^{186}Re$

Thank you for attention!

A dineutron is a short-lived particle consisting of two neutrons.

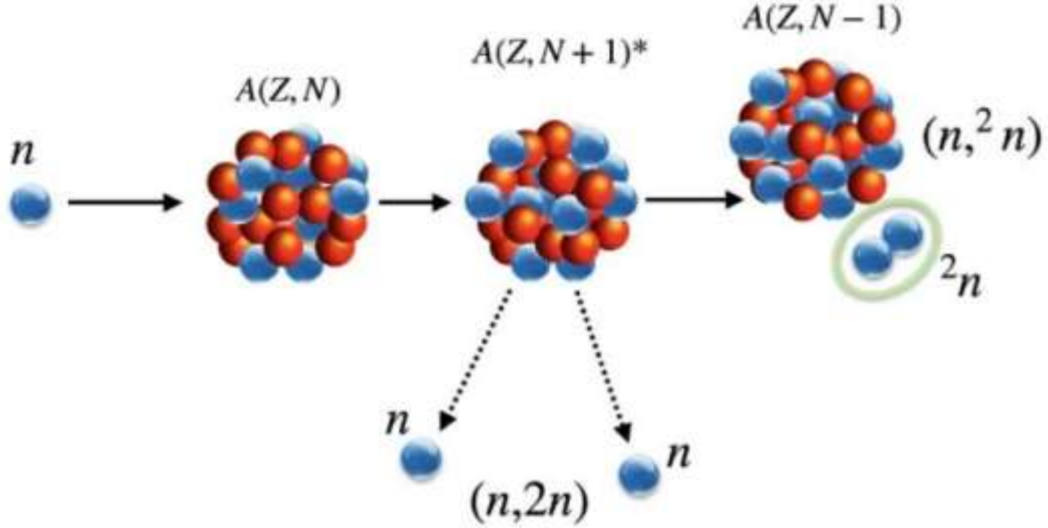
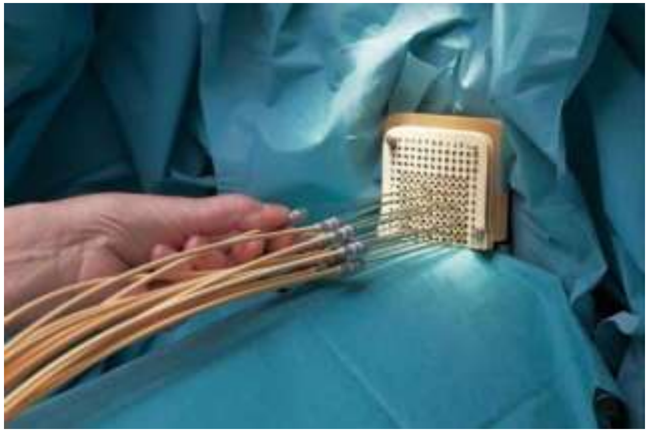


Fig. 1: The scheme of the $(n, 2n)$ and $(n, {}^2n)$ reaction processes

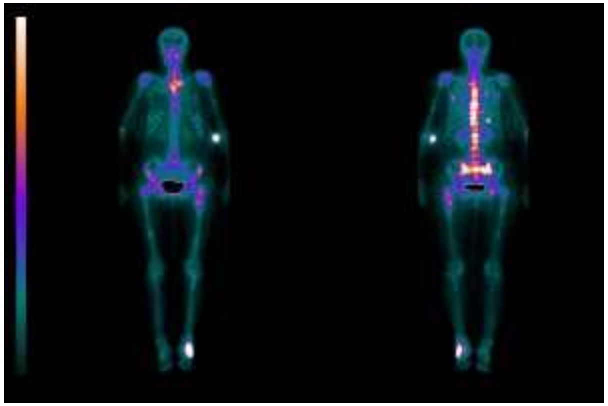
This work was aimed at the concept of the development of nuclear medicine in Ukraine, as well as at the search for new possible ways of producing radionuclides for nuclear medicine, therefore the very possibility of producing an isotope by dineutron generation was investigated

This is because these criteria reflect certain physical parameters, such as binding energy, stability, and other characteristics that determine the possibility of the existence of a dineutron as a stable particle. High values of these criteria indicate that the dineutron may be stable enough to be observed and studied.

Brachytherapy is a type of radiotherapy in which the radiation source is delivered directly to the tumor. A large dose is given to the tumor at one time, cancer cells die, while healthy organs and tissues do not receive radiation exposure.



Scintigraphy is a method of radionuclide diagnostics that makes it possible to detect functional changes in the human body at the initial stages of their development. During the procedure, a substance containing radioactive isotopes is injected into the patient’s vein, which, thanks to the blood flow, quickly reach the desired internal organ or system. After about half an hour, a series of pictures are taken using a gamma camera that detects radioactive radiation



Single-photon emission computed tomography (**SPECT**, or less commonly, **SPET**) is a nuclear medicine tomographic imaging technique using gamma rays. It is very similar to conventional nuclear medicine planar imaging using a gamma camera (that is, scintigraphy), but is able to provide true 3D information. This information is typically presented as cross-sectional slices through the patient, but can be freely reformatted or manipulated as required.

Positron emission tomography (**PET**) is a functional imaging technique that uses radioactive substances known as radiotracers to visualize and measure changes in metabolic processes, and in other physiological activities including blood flow, regional chemical composition, and absorption. Different tracers are used for various imaging purposes, depending on the target process within the body.

List of radionuclides prioritized for nuclear medicine needs

Fluorine-18, Carbon-11, Nitrogen-13, Oxygen-15, Iodine-124, Strontium-82, Rubidium-82, Molybdenum-99, Technetium-99m, Thallium-201, Iodine-123, Indium-111, Gallium-67, Germanium-68, Chromium-51, Xenon-133, Xenon-127, Iron-59, Phosphorus-32, Scandium-47, Copper-67, Silver-111, Yttrium-90, Palladium-103, Iodine-131, Samarium-153, Holmium-166, Lutetium-177, Rhenium-186, Rhenium-188, Astat-211, Copper-64, Arsenic-72, Arsenic-74, Arsenic-73, Bromine-77, Tin-117m, Cesium-131, Gold-198, Magnesium-28, Lead-203, Cesium-132, Strontium-87m, Strontium-85, Selenium-75, Potassium-43, Oxygen-16, Thulium-170, Iron-52, Rubidium-81, Rubidium-84, Bismuth-212, Bismuth-206, Ytterbium-175

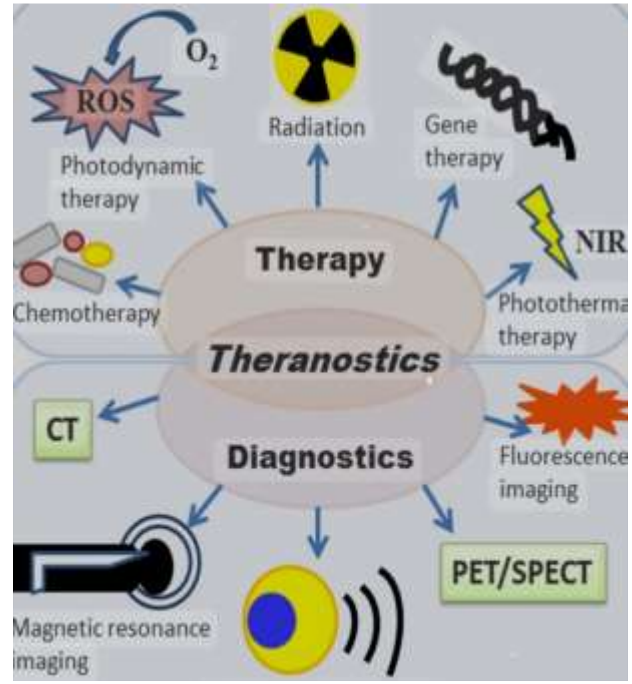
The dineutron bound states correspond to an additional energy branch, which exists in the finite range of single-particle energies and for a typical heavy nuclei concludes at about $\epsilon_{1,2}=\epsilon_c\sim 0.4$ MeV. Therefore, any single particle states are ranged within [0÷0.4] MeV can serve as a source of a dineutron state [3], [16]. For the purposes of the present qualitative study, instead of solving the equations for the anomalous energy branch numerically, we can apply a simple criterion for its existence, which is formulated in [4] as follows: (1) $\ln(1\epsilon_{1,2}\cdot R2)\gg 1$.

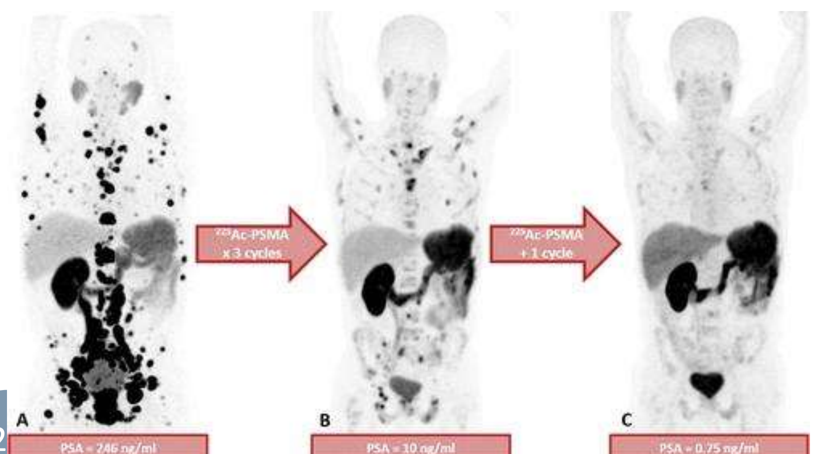
Since the energies ϵ_1 and ϵ_2 correspond to the real levels of the system $X+n$, the values for these energies can be obtained from the excitation functions of the neutron capture (n,γ) reactions with the nuclei of interest. If the energy levels of the nucleus falls into the above criterion, then, upon the reaction of interest $(n,n2)$ is being initiated, two paired up neutrons from compound nucleus might populate that Migdal's level to form a bound dineutron in the potential well of the residual nucleus of the $(n,n2)$ nuclear reaction.

Our present study covers a broad mass range of the nuclei starting from A = 91 and ending with A = 209, most of which are deformed. However, the role of core deformation in the dineutron formation effect is not clear so far. In general, we may expect that the dineutron state can be further stabilized in deformed heavy nuclei due to a large spin mismatch between the dineutron state and the ground state of the composite nucleus. To verify such an expectation it is definitely required to collect more experimental evidences within a broader range of heavy nuclei. For the present study, since the majority of nuclei within the mass range of interest are deformed, we can simply formulate four different criteria C1 — C4 to consider all possible combinations between radii of deformed nuclei and the resonance energies of neutrons as they are listed

Theranostics

Theranostics is the term (diagnosis + Therapeutics) used to describe the combination of using one radioactive isotope (radioactive drug) to diagnose the presence of a particular biomarker and a second radioactive isotope (therapeutic) to treat the main tumour and metastatic tumour spread. These radioisotopes are called radiopharmaceuticals. Radioisotopes emit radiation which are detected by a gamma camera and PET, which facilitates diagnosis and treatment.





It is administered intravenously or Intra arterially over 20- 30 minutes, Vital signs like blood pressure and pulse are monitored during infusions. The treatment is tailored for every individual thus resulting in right drug for the right patient at the right time.

Concept for the development of nuclear medicine in Ukraine.

The purpose of this concept is to

- to improve the level of provision of Ukrainian citizens with affordable and up-to-date radioactive medicines;
- creation and re-equipment of nuclear medicine institutions and departments with modern equipment;
- improving the level of qualified personnel in medical institutions,
- Establishment of innovative production of radioactive medicines on the basis of UDVP ISOTOP by installing an industrial cyclotron

Increase in the yield of reaction products during the generation of bound dynetron

From the list of radionuclides that are important for nuclear medicine, those with atomic masses in the range of 90-209 were selected because the heavy nucleus was considered as a source of the potential field for detecting the bound dineutron. We also present the reactions of the development for these radionuclides

Number	Isotope	Atomic mass (a.u.m	Reactions from the field
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4	Indium-111	110,9	$^{112}Cd(p,2n)^{111}In$ $^{111}Cd(p,n)^{111}In$
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6	Xenon-127	126,9	$^{133}Cs(p,2p5n)^{127}Xe$; $^{126}Xe(n,\gamma)^{127}Xe$ $^{127}I(p,n)^{127}mXe$ $^{127}I(d,2n)^{127}mXe$
7	Silver-111	110.9053	$^{110}Pd(n,\gamma)^{111}Pd$
8	Palladium-103	102,9	natAg $(p,xn)^{103}Pd$ $^{103}Rh(p,n)^{103}Pd$ $^{102}Pd(n,\gamma)^{103}Pd$
9	Iodine-131	130.91	$^{130}Te(n,\gamma)^{131}Te$ $^{131}Te \rightarrow ^{131}I + e^- + \nu_e$ $^{131}Te(ec,\beta+)^{131}I$

Number	Isotope	Atomic mass (a.u.m	Reactions from the field
			$^{130}Te(d,x)^{131}I$
10	Samarium-153	152.92	$^{152}Sm(n,\gamma)^{153}Sm$
11	Holmium-166	165.93	$^{165}Ho(n,\gamma)^{166}Ho$ $^{165}Ho(n,\gamma)^{166m}Ho$
12	Lutetium-177	176.94	$^{176}Lu(n,\gamma)^{177}Lu$, $^{176}Yb(n,\gamma)^{177}Yb$, $^{177}Yb \rightarrow ^{177}Lu + e^- + \nu e$
13	Rhenium-186	186,207	$^{185}Re(n,\gamma)^{186g}Re$ $^{186}W(p,n)^{186}Re$ $^{186}W(d,2n)^{186}Re$, $^{189}Os(p,\alpha)^{186}Re$ $^{192}Os(p,\alpha 3n)^{186}Re$.
14	Rhenium-188	187.9594	$^{186}W(n,\gamma)^{187}W$, $^{187}W(n,\gamma)^{188}W$, $^{188}W \rightarrow ^{188}Re + e^- + \nu$
15	Molybdenum-99	98.9077	$^{98}Mo(n,\gamma)^{99}Mo$, $^{100}Mo(n,2n)^{99}Mo$, $^{99}Tc(\beta-)^{99}Mo$ $^{100}Mo(n,2n)^{99}Mo$ $^{100}Mo(d,x)^{99}Mo$ $^{100}Mo(p,x)^{99}Mo$ $^{100}Mo(g,n)^{99}Mo$
16	Tin-117m	118,71	nat Sb $(p,x)^{117m}Sn$. $^{116}Cd(\alpha,3n)^{117m}Sn$ $^{114}Cd(\alpha,n)^{117m}Sn$

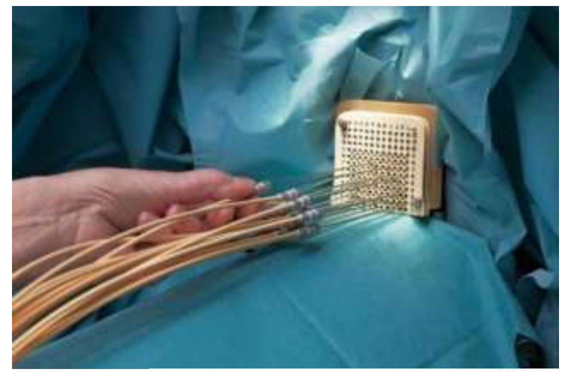
17	Cesium-131	130.91	$^{133}Cs(p,3n)^{131}Cs$. $^{130}Ba(n,\gamma)^{131}Ba\beta \rightarrow ^{131}Cs$. $^{131}Xe(p,n)^{131}Cs$.
19	Lead-203	202.97	$^{205}Tl(p,3n)^{203}Pb$ $^{203}Tl(p,n)^{203}Pb$ $^{nat}Tl(d,x)^{203}Pb$ $^{nat}Tl(p,x)^{203}Pb$
20	Thulium-170	169.9358	$^{169}Tm(n,\gamma)^{170}Tm$
21	Ytterbium-175	173.04	$^{174}Yb(n,\gamma)^{175}Yb$
22	Technetium-99m	98.9063	$^{100}Mo(p,2n)^{99m}Tc$, $^{100}Mo(d,3n)^{99m}Tc$

Relevance: Nuclear medicine is developing rapidly and is critical for the diagnosis and treatment of a number of diseases, so it is extremely important to have a deep understanding of the existing capabilities and find new ways to produce the necessary radionuclides.

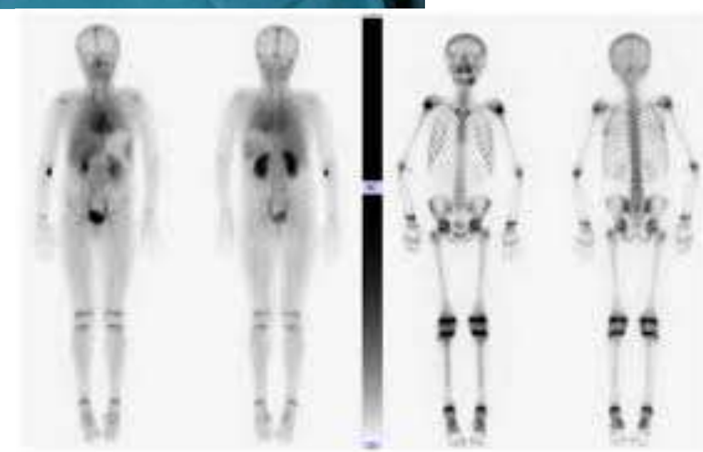
Objective of the work was to determine the list of important radionuclides for the development of nuclear medicine in Ukraine, ways to develop them and propose those radionuclides for which it is possible to increase the yield taking into account new channels of nuclear reactions.

- **Radionuclide therapy:** Actinium-225, Radium-223, Arsenic-77, Astat-211, Terbium-149, Bismuth-212 and Bismuth-213, Strontium-89, Samarium-153, Phosphorus-32, Palladium-103, Silver-111, Cadmium-115, Iodine-131…

- **Brachytherapy:** Паладій-103, Радій-223, Ірідій-192 Цезій-131, Радій-223, Йод-125, Ітрій-90, Цезій-137



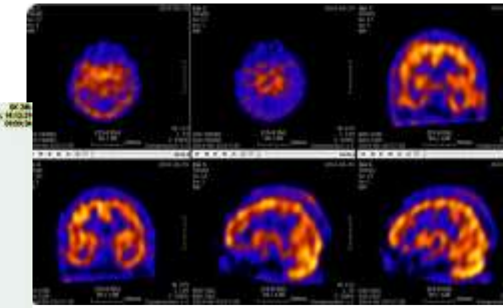
- **Scintigraphy:** Thallium-207, Arsenic-73 and Arsenic-74, Mercury-197 and Mercury-203, Krypton-81m.

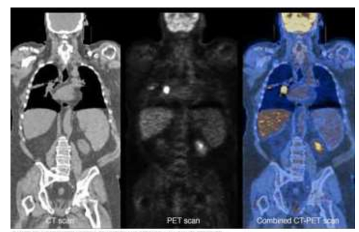


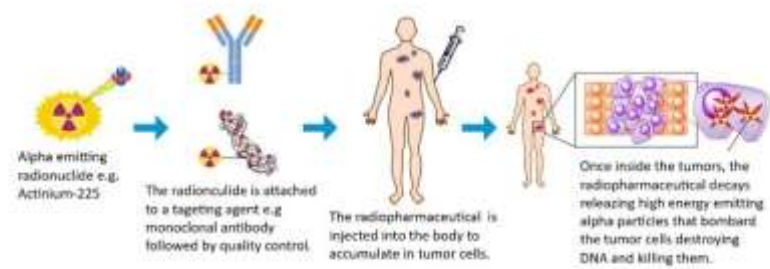
- For the diagnosis and treatment of diseases of human organs

Areas of nuclear medicine in which radionuclides are in demand in the world

- **SPECT tomography**: Tc-99m, Tb-155, Tb-149, Tl-201, Ga-67, In-111.
- **PET tomography:** F-18, C-11, O-14,15, N-13, Rb-82, Sr-82, As-72, Al-13
- **Targeted alpha therapy:** Bi-212, Ac-225, At-211, Th-227, Tb-149…
- **Radionuclide therapy:** Ac-225, Ra-223, As-77, At-211, Tb-149, Bi-212… **Brachytherapy:** Pd-103, Ra-223, Ir-192, Cs-131, Ra-223, I-125, Cs-137
- **Scintigraphy:** Tl-207, As-73 and As-74, Hg-197 and Hg-203, Kr-81m.
- **For the diagnosis and treatment of diseases of human organs**







List of operating reactions with two neutrons in the output channel

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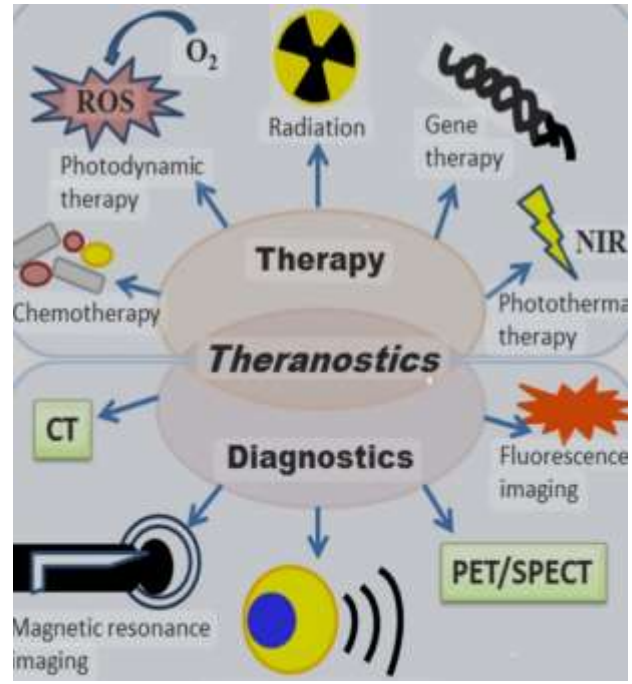

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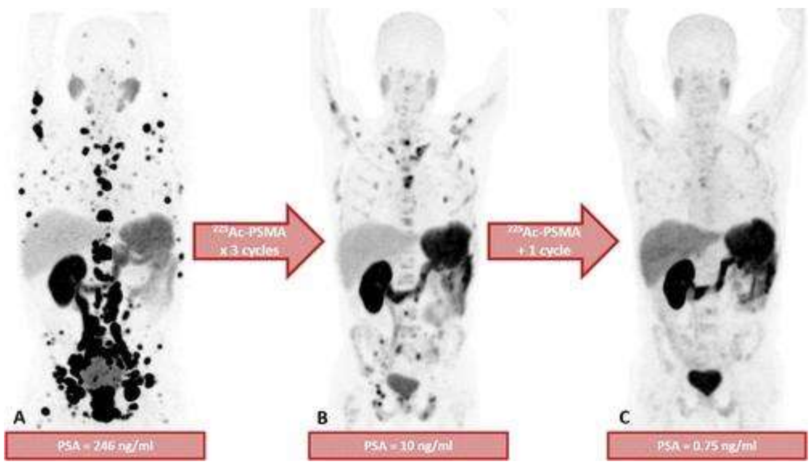

Usage:

- pill or injection absorbed over 20- 30 minutes
- monitoring of blood pressure and pulse during infusions

Treatment made for every individual thus resulting in right drug for the right patient at the right time.