Applied Radiation and Isotopes 84 (2014) 48–56

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

Review

Production of medical radionuclides in Russia: Status and future—a review

B.L. Zhuikov*

Institute for Nuclear Research of the Russian Academy of Sciences, 60th October Anniversary Prospect, 7A, Moscow 117312, Russia

HIGHLIGHTS

- We analyze current and potential production of medical radioisotopes in Russia.
- All main isotope producers in Russia are listed.
- Potential of new isotopes produced at middle energy accelerators are considered.
- Problems arising in with further progress are considered.

ARTICLE INFO

Article history:
Received 29 October 2012
Received in revised form
30 October 2013
Accepted 7 November 2013
Available online 22 November 2013

Keywords:
Radioisotopes
Russia
Molybdenum-99
Strontium-82
Actinium-225
Tin-117m

ABSTRACT

We present a review of reactor and accelerator centers in Russia that produce medical isotopes, the majority of which are exported. In the near future, we anticipate increased isotope production for use in nuclear medicine in Russia. The existing linear accelerator at the Institute for Nuclear Research (Moscow–Troitsk) and several prospective installations are considered to be particularly capable of providing mass production of radionuclides that can substitute, to a certain extent, for the traditional medical isotopes.

Contents

---

* Tel.: +7 903 7977871; fax: +7 495 8511503.
E-mail address: bz@inr.ru

0969-8043 © 2013 Elsevier Ltd. Open access under CC BY-NC-SA license.
http://dx.doi.org/10.1016/j.apradiso.2013.11.025

1. Introduction

The production of radionuclides for medicine and other applications is one of the most important directions of nuclear chemistry and the nuclear industry. Russia traditionally plays an important role in supplying isotopes to the world market; its share is estimated to be 22% (Kirienko, 2011), whereas the fraction of medical isotopes it supplies is somewhat less. At the beginning of the atomic era, powerful facilities were created in Russia, which were, for the most part, oriented toward defense and fundamental research. Now, medical applications are assuming greater importance not only in Russia but throughout the world. The world market for medical diagnostics and therapy is reportedly approximately $12 billion and is expected to increase to $68 billion in 2030. However, the consumption of medical isotopes in Russia is low, and approximately 90% of the isotopes are exported (Kirienko, 2011). The government is anticipated to approve a new program for the development of nuclear medicine in Russia, which would greatly increase the consumption of medical isotopes for domestic needs.

Isotopes for medical diagnostics and therapy are produced in several institutions at large nuclear facilities throughout Russia. The primary producers of medical radioactive isotopes and radiopharmaceuticals in commercial amounts are shown in Table 1. There are also other locations where radionuclides are obtained for research.

The production of short-lived cyclotron radionuclides in medical centers for positron emission tomography (PET) (^{18}F, ^{13}N, ^{13}C, ^{15}O) is not included in the present review. Only 10 PET centers are operational in Russia, and not all of them are used efficiently. However, approximately 40 centers are under construction. Royal Philips Electronics, along with the Russian state corporation ROSATOM, have announced plans for the regular manufacturing of PET scanners in Russia in the immediate future.

Providing enough isotopes for medical diagnostics is, in fact, a global problem, and Russia is determined to resolve this issue. The most important radionuclide in single photon emission computed tomography (SPECT) is ^{99m}Tc ($T_{1/2}=6.0$ h), which is generated from ^{99}Mo ($T_{1/2}=66$ h). The largest proportion of ^{99}Mo is produced in nuclear reactors via fission of highly enriched uranium. The total production and consumption of ^{99}Mo (calculated for a 6-day decay) in the world is approximately 400 TBq/week (about 12,000 Ci/week) (consumption in the USA is 180–260 TBq/week (5000–7000 Ci/week), whereas in Russia, the consumption is less than 4 TBq/week (100 Ci/week)). The primary producers of ^{99}Mo in the world are (Service, 2011): Nordion (irradiation at reactor NRU in Canada), Covidien (reactors HFR in the Netherlands, BR-2 in Belgium and Osiris in France), IRE Belgium (the same reactors HFR, BR2 and Osiris), and NTR (Safari reactor, South Africa). Other producers (in Russia, Australia, Indonesia, Argentina, Chile, Poland, Romania, Pakistan, and Egypt) provide only approximately 5% (Hansell, 2008). Japan (2014), China (2015) and South Korea (2016) have ambitious projects to contribute an important fraction of the world production in the near future. Russia would like to play a more important role in producing ^{99}Mo for export in the facilities in Dimitrovgrad and Obninsk (discussed below) using the traditional approach.

Several methods are being developed to meet the increasing demand for isotopes used for diagnostics. The most promising methods seem to be the following.

Table 1
Primary isotope producers in Russia (see references in the text below).

Institution	Location	Facilities	Radionuclide products
Kurchatov Institute	Moscow	30 MeV cyclotron, liquid fuel reactor, hot cells	^{123}I, ^{201}Tl; Under development: ^{99}Mo, ^{89}Sr
Medical Preparations Plant (Burnazyan Center)	Moscow	hot cells	^{67}Ga-citrate, ^{89}Sr, ^{131}I-radiopharmaceuticals, ^{201}Tl; ^{59}Fe (under development)
Research Institute of Atomic Reactors	Dimitrovgrad, Volga region	nuclear reactors, hot cells	^{99}Mo, ^{125}I, ^{131}I, ^{188}W, ^{89}Sr, ^{117m}Sn, ^{153}Sm, ^{153}Gd, ^{177}Lu, ^{192}Ir, ^{131}Cs, actinides; ^{144}Ce-spring microsources
Institute for Physics and Power Engineering	Obninsk, Central region	hot cells	^{32}P, ^{82}Sr, ^{133}Xe, ^{225}Ac; ^{99}Mo/^{99m}Tc-generator, ^{188}W/^{188}Re-generator, ^{90}Sr-microsources for cardio-vascular therapy; ^{225}Ac/^{213}Bi-generator (under development)
Karpov Institute of Physical Chemistry	Obninsk, Central region	nuclear reactor, hot cells	^{99}Mo, ^{153}Sm; ^{99}Mo/^{99m}Tc-generator, ^{131}I- radiopharmaceuticals, ^{188}W/^{188}Re-generator (under development)
Cyclotron Co.	Obninsk, Central region	23 and 14 MeV cyclotrons	^{67}Ga, ^{68}Ge, ^{85}Sr, ^{103}Pd, ^{111}In, ^{195}Au; ^{68}Ge/^{68}Ga-generator
Production Association MAYAK	Ozersk, Ural region	nuclear reactors, hot cells	^{14}C, ^{32}P, ^{35}S, ^{89}Sr, ^{90}Sr
Institute of Nuclear Materials	Zarechny, Ural region	nuclear reactor, hot cells	^{14}C, ^{32}P, ^{33}P, ^{35}S, ^{90}Y, ^{131}Cs, ^{192}Ir
Khlopin Radio Institute	St-Petersburg	cyclotron, hot cells, nuclear reactor of LAES	^{67}Ga, ^{123}I, ^{124}I, ^{125}I, ^{186}Re; ^{99}Mo/^{99m}Tc-generator
Central Research Institute of Radiology and Roentgenology	St-Petersburg	cyclotron, hot cells	^{123}I-radiopharmaceuticals; ^{82}Sr/^{82}Rb-generator, PET-isotopes
Research Institute of Applied Chemistry	St-Petersburg	hot cells	Compounds labeled with ^{3}H, ^{14}C, ^{33}P, ^{125}I
2nd Central Institute of Ministry of Defense	Tver, Central region	30 MeV cyclotron	^{67}Ga
Institute of Nuclear Physics of Tomsk Polytechnic University	Tomsk, Siberia region	nuclear reactor, cyclotron, hot cells	^{67}Ga, ^{123}I, ^{199}Tl; ^{99}Mo/^{99m}Tc-generator
Institute for Nuclear Research of Russian Academy of Sciences	Moscow–Troitsk	linear accelerator	targets containing ^{68}Ge, ^{82}Sr, ^{103}Pd, ^{117m}Sn; Under development: ^{64,67}Cu, ^{72}Se, ^{223}Ra, ^{225}Ac

1.1. *Use of targets comprised of low enriched uranium (LEU) – 19.9% of ^{235}U or lower*

Highly enriched uranium (HEU) is used regularly as a target for ^{99}Mo production. LEU targets minimize the risk of nuclear weapon proliferation and provide a wider availability of irradiation and processing facilities; such successful LEU developments are located in South Africa, Argentina, South Korea, Australia, and Belgium. It is not very critical to install facilities with LEU in Russia because Russia possesses a large amount of HEU. Nevertheless, a new technology with LEU is scheduled to be developed in Russian nuclear centers in the Kurchatov Institute, Obninsk and Dimitrovgrad for subsequent exportation to other countries.

1.2. *Homogeneous aqueous solution low power reactors*

In this case, reactor fuel consisting of a water solution of uranyl sulfate or nitrate is used. All of the fuel may be utilized as a target for ^{99}Mo production in the low power reactor (20–200 kW). Many difficult technical and chemical problems must be solved to establish high-level production. Important HEU-based developments are being made in the USA (Babcock and Wilcox – Covidien), Taiwan and Russia. A prospective challenge is to modify the technology using LEU.

1.3. *Neutron capture: ^{98}Mo (n, γ) ^{99}Mo*

^{99}Mo produced by this method contains a carrier and requires large stationary ^{99m}Tc generators, which are less convenient than those where "fission" ^{99}Mo is used. The neutron capture method is less productive and is used in a number of places with a comparably low level of radionuclide production. This approach is being successfully developed in Russia.

1.4. *Accelerator production of ^{99}Mo and ^{99m}Tc*

Electron accelerators generated bremsstrahlung and obtaining "fission" ^{99}Mo with a uranium target are considered to be the best candidates for this purpose. Proton accelerators used for generating gammas and neutrons on heavy targets also hold much promise. In particular, an IRE/IBA project (Belgium) has been announced for the development of a facility that will provide neutrons and gammas via the nuclear reaction Ta + p (350 MeV, 1000 μA) and use uranium target to produce fission ^{99}Mo. The direct production of ^{99m}Tc from the ^{100}Mo-enriched targets in low-energy proton accelerators (nuclear reaction (p, 2n)) also has good prospects for local needs (Zyuzin et al., 2011).

1.5. *Substitution of ^{99}Mo/^{99m}Tc generator by different radionuclides for diagnostics*

^{99}Mo/^{99m}Tc can be substituted, to some extent, for other accelerator-produced radionuclides: ^{201}Tl (in cardiodiagnostics), ^{123}I, ^{67}Ga and ^{111}In. Use of radionuclides with PET diagnostics is the most advanced approach. Positron Emission Tomography with X ray computed tomography (PET/CT) can provide high-quality imaging and, in many cases, evaluation of organ function. The number of PET scanners is increasing around the world. One very promising approach is to use ^{68}Ga or ^{82}Rb obtained from ^{68}Ge/^{68}Ga and ^{82}Sr/^{82}Rb generators. The ^{44}Ti/^{44}Sc generator for PET was found to be promising in the future, although ^{44}Ti is expensive. The short-lived ^{44}Sc that is obtained commonly from the generator may also be produced directly. Important similar developments are underway in Russia. New radionuclides used for PET-diagnostics, such as ^{64}Cu and ^{89}Zr, cannot be obtained from generators and should be produced near hospitals (WIPR, 2011). All of them are more expensive than ^{99}Mo but are more efficient in many cases.

Only part of the production cost is considered; the majority of the produced isotopes are not sold at their actual price since production costs are subsidized by the governments.

Despite the small consumption of isotopes in national nuclear medicine, Russian centers intend to play a more significant role in solving the "^{99}Mo- problem" and producing the alternative generator radionuclides ^{82}Sr and ^{68}Ge for PET.

In the present review, we describe the production of medical isotopes in the most important facilities in Russia, their role in the current world market and in the near future, following the trends in nuclear medicine. We consider new approaches based on isotope production on middle energy protons. This information may be useful for developing collaboration between Russian institutions and foreign partners. We do not focus on the medical application of the produced radionuclides in Russia. This information is presented in (Korsunsky et al., 2007; Analytical report, 2008).

2. National research center "Kurchatov institute" (RNC KI)

RNC KI is the oldest Russian nuclear center, where the first nuclear reactor in Europe was installed in the 1940s. The majority of the reactors in RNC KI have been closed. However, the solution reactor ARGUS, which was constructed in 1981, is still operational (Pavshuk, 2007) and can be used for isotope production (Pavshuk and Chuvilin, 2005). UO_2SO_4 (90% HEU) dissolved in water is utilized as fuel. The reactor is compact and the power is only 20 kW, but the whole nuclear fuel serves as target material and is used for isotope production. After a few days of operation, the reactor is stopped and the uranyl solution is pumped through the sorbent material to extract ^{99}Mo (RNC KI, 2010). A successful development supported by the GIPP program (Global Initiatives for Proliferation Prevention) provided a technology for selective Mo recovery with the help of a special THERMOXID inorganic sorbent developed in Russia (Betenekov et al., 2002). The first samples of ^{99}Mo have been produced and delivered for validation; however, there is no regular mass production yet. One of the most important isotopes for medical therapy ^{89}Sr ($T_{1/2}$=50.5 d) may be produced as a by-product by collecting gaseous ^{89}Kr ($T_{1/2}$=3.2 min), which is volatilized from the solution and which decays into ^{89}Sr (Chuvilin et al., 2005).

Future reactors of the same type with 50–200 kW power will be able to provide production of up to approximately 1000 Ci of ^{99}Mo per week, and the technology can be transferred to LEU fuel use. Similar developments have been made in the USA by the Babcock and Wilcox company with $UO_2(NO_3)_2$-solution fuel (Adelfang et al., 2008).

Another prospective development in the Kurchatov Institute is ^{99}Mo and ^{89}Sr production from the molten fluoride fuel at reactor IR-8 (Gnedoj et al., 2011; RNC KI, 2010).

Additionally, an old 35 MeV proton cyclotron in the Institute (Marchenkov, 2000; Isochronic cyclotron of NRC, 2012) produces ^{201}Tl from the targets of enriched thallium in the nuclear reaction ^{203}Tl (p, 3n) ^{201}Pb → ^{201}Tl (Kozlova et al., 1987) and ^{123}I is produced from the gaseous targets of enriched xenon in nuclear reaction ^{124}Xe (p, 2n) ^{123}Cs → ^{123}Xe → ^{123}I (Malinin and Marchenkov, 1985). The radiopharmaceuticals from these radionuclides are prepared at the **Medical Preparations Plant** located at the site of the **A.I. Burnazyan Federal Medico-Biological Center** near the Kurchatov Institute. These radionuclides can substitute for ^{99m}Tc in many diagnostic applications. The amount of medical radionuclides produced is small and its production is not commercially profitable because the beam current at the cyclotron is only approximately 25 μA (RNC KI, 2010).

Mass production of medical isotopes is hardly possible at the Kurchatov Institute for safety reasons because it is located not far from the center of Moscow; however, there are several prospective developments discussed above.

3. Production association “MAYAK”

Located in the Ural region (Ozersk), MAYAK is the oldest and the largest Russian nuclear weapon facility (Fetisov et al., 2000). It has a heavy water nuclear reactor “Ludmila”, which is now primarily used for isotope production. MAYAK is one of the most powerful producers of isotopes in the country, although few of them can be used for medical purposes: ^{89}Sr, ^{90}Sr, ^{35}S, ^{32}P, ^{14}C (Pavshuk and Chuvilin, 2005). MAYAK was declared in the 1990s to be oriented toward peaceful nuclear goals; thus, it is now intended to produce medical isotopes, in particular, a large amount of ^{99}Mo. Because it is a closed defense institution, it is difficult to organize up-to-date transportation logistics and manage efficient technology. Additionally, there are serious ecological problems in the city of Ozersk and its environs, including those connected with radioactive storage facilities and contaminated lakes. These problems absorb much effort on the part of personnel and restrict future developments.

Another nuclear facility in the Ural region is **the Institute of Nuclear Materials** located in Zarechny with a powerful reactor, IVV-2M, provides both thermal and fast neutrons. The institute produces ^{14}C, ^{32}P, ^{33}P, ^{35}S, ^{90}Sr/^{90}Y, ^{131}Cs, and ^{192}Ir for medical implants (Zlokazov et al., 2011).

4. Research institute of atomic reactors (RIAR)

There are promising perspectives in another large Russian reactor center, the RIAR located in Dimitrovgrad, Volga region. Several nuclear reactors are operating in this center, including a high-flux reactor SM-3 ($3 \cdot 10^{15}$ n/cm$^2 \cdot$ s), a fast-neutron reactor BOR-60, and reactors RBT-10/1, RBT-10/2 and RBT-6, all of which may be used for isotope production. The center produces various isotopes for medicine, such as ^{89}Sr, ^{117m}Sn (the development was supported by GIPP), ^{125}I, ^{131}I, ^{131}Cs, ^{144}Ce, ^{153}Sm, ^{153}Gd, ^{177}Lu, ^{188}W, as well as a number of actinides (Kuznetsov and Toporov, 2009).

A new, ambitious project for ^{99}Mo mass production is being realized at RIAR, in which reactors RBT-10/2 and RBT-6 are used to irradiate HEU targets. The other reactors may also be involved in providing continuous supplies. A new radiochemical technology is used in the old existed hot cells which were upgraded according to the modern safety requirements. Approximately 800–1000 Ci per week will be produced at the first stage of the project, and up to 2200–2500 Ci per week at the second stage (Bychkov, 2011; Kuznetsov, 2010). Thus, 10–30% of the world market's share of ^{99}Mo can be provided by RIAR in the near future. Collaboration with western partners plays an important role in this project: the radiochemical technology was supplied by the German company Isotope Technologies Dresden GmbH, the certification and distribution of the produced ^{99}Mo were provided by the Canadian company Nordion. The project was supported by the Russian government through Joint Stock Company (JSC) “Isotope,” which is under the supervision of the Russian state corporation ROSATOM. However, RIAR must overcome many hurdles to improve technology and transportation logistics in order to achieve the desired high-production volumes.

A center of nuclear medicine, which is to be opened in Dimitrovgrad in 2014, is expected to widely use medical isotopes produced at RIAR.

5. Karpov institute of physical chemistry – Obninsk branch

Several facilities around Moscow produce isotopes for research and medical use (Fig. 1).Presently, the regular production of “fission” ^{99}Mo, ^{99m}Tc generators and other medical isotopes is conducted at the Karpov Institute in Obninsk (Kaluga Region), which is located approximately 100 km from Moscow. The nuclear reactor WWR-C operates with HEU provides approximately 100–150 Ci of ^{99}Mo per week for domestic needs and export (Kochnov and Pozdeev, 2011; Bokshits, 2011). The existing reactor channels and hot cells are capable of absorbing an increase in ^{99}Mo production volume up to several hundreds of Ci per week after optimizing the target design. The Karpov Institute developed

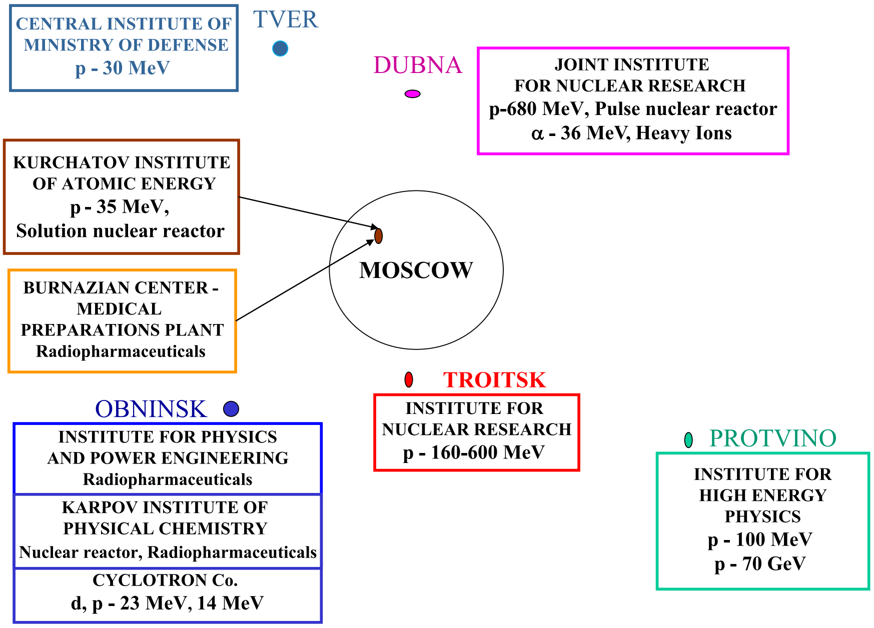

Fig. 1. Nuclear facilities around Moscow producing isotopes for medical application and research.

a ^{99m}Tc generator based on the original design, which now constitutes the primary portion of the Russian demand.

Additionally, the Institute produces ^{131}I and various radiopharmaceuticals for commercial distribution, such as sodium iodide, sodium hippurate, “rose bengal”, and human serum albumin. The obtained ^{153}Sm is used effectively in the nearby Medical Radiological Research Centre of the Russian Academy of Medical Sciences for bone cancer therapy.

There are also new developments for a ^{188}W/^{188}Re generator, a facility for ^{125}I production at the reactor and recovery of ^{103}Pd from silver targets, as well as ^{225}Ac from thorium targets irradiated with middle energy protons in the linear accelerator of the Institute for Nuclear Research (INR, Troitsk).

A portion of the ^{99}Mo and other isotopes produced at the reactor is delivered to another large Obninsk facility – the Institute for Physics and Power Engineering (IPPE, described below).

6. Institute for physics and power engineering (SSC RF-IPPE)

The IPPE in Obninsk, which is one of the oldest and largest Russian nuclear facilities, was founded in 1946. The first nuclear power station in the world was constructed here in 1954. There were several nuclear reactors at this site in the past. Some of them were used for isotope production (Nerozin and Smetanin, 2005); they are now shut down. Several projects aim to construct up-to-date reactors, including a solution reactor for ^{99}Mo and ^{89}Sr production.

Meanwhile, the existing hot cells are used for preparing radioisotope products (IPPE, 2012; Nerozin, 2012). ^{99}Mo/^{99m}Tc generators, ^{125}I microsources for prostate cancer therapy, ^{90}Sr microsources for cardiovascular therapy, ^{188}W/^{188}Re generators, ^{133}Xe, and ^{32}P are obtained from radioactive materials provided by the reactors of the Karpov Institute and RIAR. The α-radioactive isotope ^{225}Ac ($T_{1/2}$=10 d), which is being investigated for radioimmunotherapy, is obtained from the long-lived ^{229}Th ($T_{1/2}$=7880 yr) recovered from ^{233}U. Development of an ^{225}Ac/^{213}Bi generator is also under way. The parent nuclide of the ^{82}Sr/^{82}Rb generator, ^{82}Sr, is recovered from rubidium targets and ^{117m}Sn is recovered from Sb-containing targets irradiated at the INR-linac in Troitsk. These effective developments were supported by GIPP.

7. “CYCLOTRON” Co.

“CYCLOTRON” Co. is a private company at the IPPE site in Obninsk. This rare example of private commercial enterprise produces an important component of the radioactive isotope supply in Russia and is one of the most successful companies in the country. The old but efficient cyclotron is capable of operating with high-intensity beams of 23-MeV protons (approximately 1000 μA, limited by targetry), as well as deuterons and α-particles. Subsequently, another 14-MeV cyclotron was constructed and is now operational. “CYCLOTRON” Co. possesses hot cells for processing irradiated targets but with radioactivity level limited by the cell shielding.

The company is the primary supplier of cyclotron isotopes in Russia. The produced medical radionuclides (^{68}Ge, ^{103}Pd, ^{85}Sr) are exported abroad in large quantities, whereas ^{67}Ga and ^{111}In are supplied for Russian nuclear medicine (Krasnov et al., 2011; Cyclotron Co., 2012).

A ^{68}Ge/^{68}Ga generator has been developed by Cyclotron Co. in collaboration with Burnazyan Center (Bruskin et al., 2009) using THERMOXID inorganic sorbents (Sharyghin et al., 2002). Presently, this generator is successfully undergoing trials in Russia and abroad. It is considered to be an alternative to the short-lived PET radionuclides obtained in small cyclotrons that are installed in hospitals, along with the ^{82}Sr/^{82}Rb (Chudakov et al., 2005) and ^{44}Ti/^{44}Sc generators (Ksenofontov et al., 2009), which were both manufactured in Russia. The most prospective application of ^{68}Ga pharmaceuticals is cancer diagnostics, although they were also reported to be used in cardiology. There are several worldwide developments of ^{68}Ge/^{68}Ga generators (Rosch, 2013 and references herein).

The 2nd Central Institute of Ministry of Defense (in the city of Tver, not far from Moscow) has a 30-MeV cyclotron RIC-30 (Vorogushin et al., 2002; Marchenkov, 2000) with an internal beam current up to 250 μA. This cyclotron produces the medical radionuclide ^{67}Ga and proposes to produce ^{201}Tl in the future (Analytical report, 2008). It is difficult to organize efficient commercial activity in this institute because of its affiliation with the Defense Ministry. This is the most serious problem relevant to the fact that foreign companies are involved in the export of isotopes and data flow and communication from the facility are strongly restricted.

8. Institute of nuclear physics of Tomsk polytechnic university

This is an old university and nuclear center in Tomsk, Siberia. The reactor ITT-T of the Institute of Nuclear Physics provides a flux of 10^{14} n/cm^2·s and ^{98}Mo-enriched targets are irradiated to produce ^{99}Mo with a comparably high-specific activity (Ryabchikov et al., 2004). The production of “fission” ^{99}Mo is also discussed; however, this method is more complicated and must meet safety requirements for operating with a higher radioactivity level and processing targets containing alpha emitters and requiring difficult waste management. The amount of ^{99m}Tc generators (of both the extraction and adsorption types) produced is sufficient to cover the current demand of this large region. However, the transportation infrastructure is insufficient to provide a wider distribution of ^{99}Mo and generators outside of the immediate region.

A 27-MeV α-particle cyclotron in Tomsk with a beam current of a few tens of μA produces for cardiodiagnostics, namely the short-lived ^{199}Tl ($T_{1/2}$=7.4 h) via the nuclear reaction ^{197}Au (α, 2n) ^{199}Tl, as well as ^{123}I produced with enriched tellurium targets irradiated with 8-14 MeV deuterons with the ^{122}Te (d, n) ^{123}I reaction (Zelichenko and Larionov, 2009).

Based on the existing experience, creation of a new center of nuclear medicine including PET in the Tomsk region is proposed in 2016.

9. V.G. Khlopin radium institute

Khlopin Radium Institute in St. Petersburg is one of the oldest institutions in Russia. The production of reactor isotopes is organized on the basis of a large reactor at the Leningrad Nuclear Power Station (LAES) in the town of Sosnovyi Bor, located 80 km from the city. This is a channel type reactor, which is similar to that in Chernobyl.

The primary medical isotopes produced at this reactor are ^{99}Mo (from ^{98}Mo) and ^{125}I (see also radionuclides in Table 1) (Solin et al., 2003). A stationary ^{99m}Tc extraction type generator covers the demand of the St. Petersburg region. The reactor has the potential to produce more medical isotopes; however, continuous operation of this type of reactor is problematic, as reactors of this design type are to be decommissioned.

The cyclotron MGC-20 operating at the institute provides 18-MeV protons with a current up to 50 μA at the external beam (Solin, 2011). ^{123}I from the enriched ^{123}Te targets and ^{67}Ga from the enriched ^{67}Zn targets are regularly produced, and radiopharmaceuticals based on these radionuclides are distributed in the St. Petersburg region.

The Russian Research Center of Radiology and Surgical Technologies (RRCRST, previously Central Research Institute for Roentgenology and Radiology, CRIRR) in St. Petersburg is a medical institution where radioisotopes and radiopharmaceuticals are produced. Founded in 1918, RRCRST is the oldest radiological center in the world and the first institute in Russia in which a full-body PET scanner was installed in 1996 (RRCRST, 2012). The center has two 18-MeV Russian cyclotrons that provide regular short-lived PET radionuclides and ^{123}I. Other radionuclides, such as ^{67}Ga, ^{124}I and ^{111}In, are anticipated to be produced in the near future. The ^{82}Sr/^{82}Rb generator developed at the Institute for Nuclear Research is loaded and utilized for PET diagnostics; the ^{68}Ge/^{68}Ga generator produced by “CYCLOTRON” Co. and the Burnazyan Center is undergoing laboratory and clinical trials.

Several institutions in Russia also produce medical radionuclides for scientific research purposes, among which is the **Joint Institute for Nuclear Research**, located in Dubna in the Moscow region. It has a pulse nuclear reactor, a 680-MeV synchrocyclotron with a proton beam current of a few μA, a cyclotron U-200 accelerating alpha-particle and ^{12}C with a beam current of a few tens of μA, and a microtron electron accelerator, which provides a low flux of neutrons and γ-quanta (Dmitriev and Zaitseva, 1996). Methods of producing a number of medical radionuclides, in particular, ^{26}Al, ^{123}I, ^{201}Tl, ^{149}Tb, ^{211}At, and ^{237}Pu have been developed in this Institute, but there is no regular commercial production yet since the beam currents are low.

10. Institute for nuclear research of Russian academy of sciences (INR RAS) and a new potential for isotope production on middle energy protons

INR is another large institute where accelerator radionuclides are produced. Established in 1970, INR is the youngest nuclear institution in Russia. The primary facilities, including a linear accelerator, are located in the town of Troitsk (Fig. 1), which is situated approximately 15 km to the south of Moscow and recently became part of the city. The LINAC has been operating since the beginning of the 1990s and was designed to accelerate protons and H^{-} ions up to 600 MeV with a beam current up to 500 μA. Presently, a 160-MeV intensive proton beam with a current up to 140 μA is available for isotope production. It was the first facility with high-intensity beams of middle energy protons that regularly operates for this purpose in Europe and Asia. Another facility in Europe (ARRONAX, Nantes, France) just started to produce isotopes in 2012, and INR collaborates with this facility to transfer technologies. Similar facilities with comparable parameters throughout the world are listed in Table 2.

A number of radionuclides (Table 3) are produced at INR; however, the primary radionuclide is strontium-82, which cannot be obtained at nuclear reactors or low-energy proton accelerators. ^{82}Sr ($T_{1/2}=25.5$ d) is used for preparing the generator of the short-lived daughter ^{82}Rb ($T_{1/2}=1.3$ min). This generator is regularly produced and distributed in North America by Bracco Diagnostics for cardiodiagnostics with PET.

To produce metallic ^{82}Sr at INR, Rb targets are irradiated with protons in the energy range of between 40 MeV and 100 MeV. The irradiated targets are then processed in Los Alamos National Laboratory (USA) (Phillips et al., 2000) and also in IPPE (Obninsk, Russia), where they use a new method of recovering Sr directly from liquid rubidium (Zhuikov et al., 2008). Pure ^{82}Sr is transported to RRCRST (St. Petersburg) for loading the ^{82}Rb-generator (Chudakov et al., 2005). This generator has passed pre-clinical and clinical trials in Russia (Granov et al., 2011). The experience of ^{82}Rb application in cardiology has demonstrated that it is, in many cases, more efficient and definitely more convenient than ^{13}N ($T_{1/2}=10$ min) synthesized in a cyclotron at the hospital. The first successful results of the application of ^{82}Rb for oncology have also been reported (Arcila et al., 2010; Granov et al., 2011), which may be an important complement to diagnostics with ^{18}F (FDG). In the near future, more than 40 PET centers in Russia are expected to use this type of generator.

Collaboration between INR and North American and European laboratories and companies played a significant role in isotope development. INR headed several GIPP projects funded by the United States Department of Energy (USDOE) with the participation of the following Russian centers: Institute for Physics and Power Engineering (Obninsk), Karpov Institute of Physical Chemistry (Obninsk), Production Association MAYAK (Ozersk), Research Institute of Atomic Reactors and other institutions. From the USA, Los Alamos National Laboratory (LANL) and Brookhaven National Laboratory (BNL), as well as several US private companies, were also involved in these projects. Cardiodiagnostic studies for approximately 200,000 patients in the USA were provided using

Table 3
Radionuclides produced at the INR accelerator and possibilities for production in one bombardment.

Radio-nuclide	$T_{1/2}$	Target	Energy range (MeV)	Bombardment period (h)	Produced activity at EOB, Ci
Sr-82[a]	25.5 d	Rb	100–40	250	10
Na-22[b]	2.6 yr	Mg, Al	150–35	250	2
Cd-109[b]	453 d	In	150–80	250	2
Pd-103[b]	17 d	Ag	150–50	250	50
Ge-68[b]	288 d	Ga, GaNi	50–15	250	0.5
Sn-117 m[b]	14 d	Sb, TiSb	150–40	250	3
Se-72[c]	8.5 d	GaAs	60–45	250	3
Cu-67[c]	62 h	Zn-68	150–70	100	10
Cu-64[c]	12.7 h	Zn	150–40	15	15
Ac-225[c]	10 d	Th	150–40	250	4
Ra-223[c]	11.4 d	Th	150–40	250	13

[a] Regularly produced.
[b] Technology is developed, samples are delivered to customers.
[c] Production method is developed, technology is under development.

Table 2
Existing world isotope production facilities with middle energy protons.

Institution	Location	Proton energy used for isotope production, MeV	Beam current at typical targets, μA
Institute for Nuclear Research	Troitsk, Moscow, Russia	160	120
Los Alamos National Laboratory	New Mexico, USA	100	200
Brookhaven National Laboratory	Upton, New York, USA	200	90
TRIUMF	Vancouver, Canada	110	60
		500	100
iThemba Laboratory	Faure, South Africa	66	150
ARRONAX	Nantes, France,	70	2 beams of 100 μA each

the ^{82}Sr product produced at INR, and many important results on ^{82}Sr-production, were achieved using the technology transferred from INR to LANL. A fruitful collaboration for ^{82}Sr/^{82}Rb-generator production in Europe is being developed by INR, together with ARRONAX and the French commercial company LEMER PAX.

The collaboration also participated in developing new production methods of other medical isotopes, in addition to ^{82}Sr. In particular, these were ^{117m}Sn, ^{68}Ge, and ^{103}Pd. ^{82}Sr/^{82}Rb and ^{68}Ge/^{68}Ga generators can substitute, to some extent, ^{99}Mo/^{99}Tc generator using PET imaging, whereas ^{117m}Sn may be effective for bone cancer diagnostics and therapy, as well as for atherosclerosis therapy (Srivastava, 2011). Having a 159-keV γ-line, ^{117m}Sn may be used with widely available SPECT scanners, which are routinely used with ^{99m}Tc radiopharmaceuticals. The technology for no-carrier-added ^{117m}Sn production is a mutual development of INR, BNL and IPPE (Zhuikov et al., 2006; Ermolaev et al., 2009).

INR can also produce a large amount of ^{225}Ac and ^{223}Ra (Zhuikov et al., 2011, Ermolaev et al., 2012) (Table 3). These α emitters (along with ^{225}Ac/^{213}Bi- and ^{223}Ra/^{211}Pb generators) can provide effective therapy for various oncological diseases (Mulford et al., 2005).

The potential for accelerators to produce enough ^{82}Sr and other radionuclides is the most critical problem. Today, none of the existing accelerators with middle energy protons (Table 2) is capable of providing isotopes in the course of a year in the required amount. Thus, collaboration between different producers is necessary. There are several new projects, all with different completion schedules, that have been announced in Russia and abroad for the production of ^{82}Sr and other isotopes using middle energy protons (Table 4). To support a steady supply of ^{82}Sr at present and in the future, INR collaborates with ARRONAX (France), INR NAN (Ukraine) and Positron Co. (USA), as well as with the traditional American partners LANL and BNL.

In Russia, additional potential for isotope production on middle energy protons is limited now. There is a LINAC U-100 (proton energy up to 100 MeV) operating as an injector with a large 70-GeV accelerator in the **Institute for High Energy Physics** at Protvino (Moscow region). Its beam current does not exceed 10 μA and it was used in the first experiments in Russia for ^{82}Sr production performed in collaboration with INR (Zhuikov et al., 1994). Serious efforts are necessary to upgrade the accelerator and construct a target facility capable of providing a beam current of at least several tens of μA to produce a considerable amount of medical isotopes. A new project has been announced recently in the **Petersburg Nuclear Physics Institute** (currently under the supervision of the Kurchatov Institute) to construct an 80-MeV H^- cyclotron for producing ^{82}Sr from Y targets with a mass separator (Panteleev et al., 2011). The approach seems doubtful because of low cross-sections and expected low production yields. Additionally, positive experience and tremendous efforts are required to create such installations and move them toward an actual production scale, which may take a long time.

New facilities, including a new H^- cyclotron and hot cells, are scheduled to be constructed at INR in Troitsk. This is, in fact, the most realistic project because it is based on currently operable facilities with experienced staff, existing buildings and areas with the appropriate infrastructure. The most promising approach would be to construct a target with cycling liquid Rb metal for ^{82}Sr production (Zhuikov et al., 2008) operating with a very high-intensity beam. If proton energy of approximately 120 MeV is provided, the production of large amounts of ^{225}Ac, ^{223}Ra and ^{117m}Sn and other medical isotopes will be possible. These new installations will generate medical radionuclides for diagnostics and therapy for a large number of patients (Table 5).

11. Conclusion: problems to be solved

There is a large potential to produce medical isotopes in Russia. The first opportunity to realize this potential is to update the existing facilities for the technology oriented to medical isotopes. These facilities, for the most part, belong to the Russian governmental agency ROSATOM. The production of the most important medical

Table 4
Proposed accelerator facilities for medical radioisotope production at high intensity proton beam of middle energy.

Institution	Location	Accelerator facility	Beam current	Production goals
Institute for Nuclear Research of National Academy of Sciences of Ukraine	Kiev, Ukraine	H^+ Cyclotron 70 MeV	100 μA	^{82}Sr production from RbCl-target
Petersburg Nuclear Physics Institute	St. Petersburg, Russia	H^- Cyclotron 80 MeV	100-200 μA	Isotope separator: ^{82}Sr from Y-target
Legnaro National Laboratory, INFN	Padova, Italy	H^- Cyclotron 70 MeV	2 beams of 400 μA each	Isotopes for heavy ion physics and medicine
Positron Corporation	Illinois, USA	H^- Cyclotron, 70 MeV	2 beams of 375 μA each	^{82}Sr
Proton Engineering Frontier Project	Gyoungju, South Korea	LINAC 100 MeV	>300 μA	Isotopes for physics and medicine
National Institute for Radioelements and IBA	Belgium	H^- Cyclotron 350 MeV	1000 μA	^{99}Mo produced on secondary neutrons obtained with Ta-target
Institute for Nuclear Research RAS	Troitsk, Russia	H^- Cyclotron, 70-120 MeV	2 beams of 500 μA each	^{82}Sr, ^{225}Ac, ^{223}Ra,^{117m}Sn,

Table 5
Future production of medical isotopes at INR.

Radio-nuclide	Application	Annual production, Ci		Number of patients (per year)
		Linear accelerator	New cyclotron	
^{82}Sr	PET- diagnostics (cardiology)	30	400	500,000
^{117m}Sn	Therapy, γ-diagnostics (bone cancer, cardio vascular disease)	10	30	1000
^{67}Cu	Therapy (oncology)	20	100	1000
^{64}Cu	Therapy, PET- diagnostics (oncology)	150	700	1000
^{72}Se	PET- diagnostics (oncology)	15	60	80,000
^{103}Pd	Therapy cancer (prostate, liver, mammary gland, rheumatoid arthritis)	200	800	10,000
^{225}Ac	Therapy (oncology)	8	100	100,000
^{223}Ra	Therapy (bone cancer)	20	500	300,000

radionuclide ^{99}Mo may be increased up to a few thousands of Ci per week in the years ahead.

INR under the supervision of the Russian Academy of Sciences and the private company CYCLOTRON have demonstrated a high efficiency, but unfortunately they are not sufficiently supported by the government.

The second opportunity is to create modern facilities based on new concepts and approaches, especially focused on isotope production on middle energy protons. We must resolve several important technical issues. To organize a new efficient radioisotope production in Russia, the government must address the following problems

1. To overcome agency barriers in the disposition of funds for R&D;
2. To provide sufficient governmental funding to establish new facilities or to upgrade the existing facilities;
3. To form a qualified and independent international committee for the distribution of funds to create and realize isotope projects;
4. To improve the transportation logistics system;
5. To reduce bureaucratic regulations (without prejudice to safety and security);
6. To limit the rapidly growing rates for electricity power, heat, leasing, and waste treatment;
7. To prepare highly qualified specialists; and
8. To organize efficient international collaboration.

The development of medical isotope production in Russia is certain to succeed if national and international scientific and medical communities support this concept and work together to persuade the government and businesses that this effort is significant and can be realized through effective corroboration.

References

Adelfang, P., et al., 2008. Homogeneous aqueous solution nuclear reactors for the production of Mo-99 and other short lived radioistotopes. IAEA-TECDOC-160. IAEA, Vienne.

Analytical report, 2008. Status and Perspectives of Development of Nuclear Medicine and Ray Therapy in Russia in the Light of World Tendencies. Moscow, pp. 1–100 (⟨www.oprf.ru/files/yad_medicine.doc⟩) (in Russian).

Arcila, G., Savant, R., GildeMontes, A., 2010. Unexpected exracardiac findings during Rubidium-82 (Rb-82) myocardial positron emission tomography (PET) perfusion imaging: three years of experience. J. Nucl. Med. 51, 1735.

Betenekov, N.D. et al., 2002. Inorganic sorbent for molybdenum-99 extraction from irradiated uranium solution and its method of use. U.S. patent 6337055.

Bokshits, V., 2011. Program of Development of Nuclear Medicine and Radiopharmacy Ensures Isotope Demand. Energy expert center (⟨http://www.energy-experts.ru/comments3655.html⟩) (in Russian).

Bruskin, F.B., Kodina, G.E., Razbash, A.A., 2009. Gallium-68 in nuclear medicine: "state-of-the-art". In: Proceedings of the 6th Russian Conference on Radiochemistry. October 12–16, Moscow. Abstracts, p. 361 (in Russian).

Bychkov, A., 2011. Establishing Mo-99 production facility at Research institute of Atomic Reactors, Dimitrovgrad, Russia. IAEA, Vienna, pp. 1–11 (⟨http://www.iaea.org/OurWork/ST/NE/NEFW/Technical_Areas/RRS/documents/mo99/RUSSIAmo99CM.pdf⟩); Handling the acceleration. Nuclear. Ru (⟨http://www.nuclear.ru/eng/comments/2123305/⟩); Panel of Fissile Materials (⟨http://www.fissilematerials.org/blog/2010/08/niiar_at_dimitrovgrad_pre.html⟩).

Chudakov,V. et al., 2005. Russian Sr/Rb-82 generator for PET investigations, In: Proceedings of the 5th International Conference on isotopes. 25–29 April, Brussels, Belgium, Abstract Book, p. 9.

Chuvilin, D.Yu. et al., 2005. Experimental demonstration of the new technology of medical Sr-89 production in solution reactor, In: Proceedings of the 5th Conference on Isotopes. Brussels, April 25–29, 2005. International proceedings, pp. 77–82.

Cyclotron Co., 2012. Radioisotope production. Official Internet site. Obninsk (⟨http://www.cyclotronzao.ru/?page=cyclotron-zao&lng=eng&design=home⟩).

Dmitriev, S.N., Zaitseva, N.G., 1996. Radionuclides for biomedical investigation. Phys. Elem. Particl. Atom. Nucl. 27 (4), 977–1024.

Ermolaev, S.V., et al., 2009. Production of no-carrier-added ^{117m}Sn from proton irradiated antimony. J. Radioanalyt. Nucl. Chem 280 (2), 319–324.

Ermolaev, S.V., et al., 2012. Production of actinium, thorium and radium isotopes from thorium-232 irradiated with protons up to 141 MeV. Radiochim. Acta 100 (4), 223–229.

Fetisov, V.I. et al., 2000. MAYAK Production Association. US-Russian Joint Coordinating Committee for Environmental Restoration and Waste Management (⟨http://www.jccem.fsu.edu/Partners/MAYAK.cfm⟩).

Gnedoj, I. et al., 2011. Demonstration installation for substantiation of heavy way ^{99}Mo production in molten salt fluoride fuel. in: 7th International Conference on Isotopes, Moscow, 4-8 Sept., 2011. Collection of abstracts, p. 25.

Granov, A., et al., 2011. Domestic radiopharmaceutical for PET. Modern Medical Technologies (Sovremennye meditsinskie technologii) 8, 17–19. (in Russian).

Hansell, C., 2008. Nuclear medicine double hazard. Nonproliferation Rev. 15 (2), 185–208.

IPPE, 2012. State scientific center of Russian Federation A.I. Leipunsky Institute for Physics and Power Engineering. Official Internet site (⟨http://www.ippe.ru/prod/isotop/isot-1en.php⟩).

Isochronic cyclotron of NRC "Kurchatov Institute" U-150, 2012. Department of foreground for science and technology of Ministry of Education and Science. Mordern infrastructure of Russian Federation (⟨http://www.ckp-rf.ru/unique_displays_and_installations/?ELEMENT_ID=73601⟩) (in Russian).

Kirienko, S., 2011. Role of Russian Federation in providing constant delivery of isotope production to the world market, In: Proceedings of the 7th International Conference on Isotopes. September 4–8, 2011, Moscow, Rosatom (⟨http://www.strf.ru/material.aspx?CatalogId=222&d_no=42107⟩) (in Russian).

Kochnov, O.Yu., Pozdeev, V.V., 2011. Prospects for the development of Mo-99 production consistent with WWR-c reactor modernization at the branch of FSUE Karpov Institute of Physical Chemistry, In: Proceedings of the International Conference on Research Reactors. Morocco-2011, IAEA, pp. 60–61.

Korsunsky, V.N., Kodina, G.E., Bruskin, A.B., 2007. Nuclear medicine: modern status and perspectives of development. Atomic Strategy (Atomnaya Strategiya) 5 (31), 4–6. (in Russian).

Kozlova, M.D., et al., 1987. New method of ^{201}Tl production from ^{203}Tl-targets. Radiat. Appl. Isot. 38, 1090–1091.

Krasnov, N. et al., 2011. Status of radionuclide production at Cyclotron Co, In: Proceedings of the 7th International Conference on Isotopes, Moscow, 4–8 September, 2011. Collection of abstracts, Rosatom, p. 29.

Ksenofontov, E.G. et al., 2009. Generator of scandium-44, In: Proceedings of the 6th Russian Conference on Radiochemistry, October 12–16, Moscow. Abstracts, p. 373 (in Russian).

Kuznetsov, R., 2010. Molybdenum for health. Rossiiskaya gazeta, November 16 (⟨http://www.rg.ru/2010/11/16/reg-svolga/molibden.html⟩) (in Russian).

Kuznetsov, R.A., Toporov, Yu.G., 2009. Development of radionuclide production using research reactors of RIAR, In: Proceedings of the 6th Russian Conference on Radiochemistry. October 12–16, Moscow. Abstracts, p. 352.

Malinin, A.B., Marchenkov, N.S., 1985. Iodine-123 and its application in nuclear medicine, Report of IPHE. Institute for High Energy Physics, Protvino (Russia).

Marchenkov, N.S., 2000. Production of radionuclides at accelerators of charged particles. In: Baranov, V.Yu. (Ed.), Isotopes: properties, production, application. IzdAT, Moscow, pp. 418–419. (in Russian).

Mulford, D.A., Scheinberg, D.A., Jurcic, J.G., 2005. The promise of targeted α-particle therapy. J. Nucl.Med. 46, 199S–204S.

Nerozin, N.A., 2012. Radiochemical technologies at IPPE. Report. MEPhI, Moscow. (in Russian).

Nerozin, N.A., Smetanin, E.Ya., 2005. Production of radionuclides as fission fragments of nuclear fuel. In: Baranov, V.Yu. (Ed.), Isotopes: Properties, Production, Application, Vol. 1. Fizmatlit, Moscow, pp. 548–561. (in Russian).

Panteleev, V. et al., 2011. Project of RIC-80 facility at PNPI RAS for medical isotope production, in: Proceedings of the 7th International Conference on Isotopes. Moscow, 4–8 September, 2011. Collection of abstracts. p. 35.

Pavshuk, V.A., 2007. Effective method of ^{99}Mo and ^{89}Sr production using liquid fuel reactor. IAEA`s Consultancy (⟨http://www.iaea.org/OurWork/ST/NE/NEFW/Technical_Areas/RRS/documents/crp_1548/A1-_2007_Consultancy_Meeting_on_AHRs_%28CD%29/3Presentations/Russia_-_Kurchatov_Institute_-_Pavshuk_-_IAEA2007_-_ppt.pdf⟩).

Pavshuk, V.A., Chuvilin, D.Yu., 2005. Production of radionuclides as fission fragments of nuclear fuel. In: Baranov, V.Yu. (Ed.), Isotopes: properties, production, application, vol. 1. Fizmatlit, Moscow, pp. 513–530. (in Russian).

Phillips, D.R., et al., 2000. Production of strontium-82 for the Cardiogen PET generator: a project of the department of energy virtual isotope center. Radiochim. Acta 88, 149–155.

RNC KI, 2010. Developments and Technologies at RNC Kurchatov Institute. Moscow, pp.111–114.

Rosch, F., 2013. ^{68}Ge/^{68}Ga generators and ^{68}Ga radiopharmaceutical chemistry on their way into a new century. J. Postgrad. Med. Educ. Res. 47, 18–25.

RRCRST, 2012. Russian Research Center of Radiology and Surgical Technologies. Ministry of Public Health of Russian Federation. Official Internet site. St. Petersburg, Pesochny-2. (⟨http://rrcrst.ru⟩) (in Russian).

Ryabchikov, A.I., et al., 2004. Obtaining molybdenum-99 in research reactor IR-T with using resonance neutrons. Nucl. Instr. Methods B 213, 364–368.

Service, R.F., 2011. Scrambling to close the isotope gap. Science 331, 277–279.

Sharyghin, L.M., et al., 2002. Selective and thermostable inorganic sorbents THERMOXID. Beloyarskaya NPP, Zarechny, pp. 1–21. (in Russian).

Solin, L.M. et al., 2003. Development of medical isotope production methods at the V.G. Khlopin Radioinstitute, In: Proceedings of Khlopin Radioinstitute. Trudy Radievogo Instituta im. V.G. Khlopina, vol. 10, pp. 17–21 (in Russian).

Solin, L.M., 2011. Radioinstitute cyclotron MGC-20 for production of medical isotopes (Review), In: Proceedings of Khlopin Radioinstitute. Trudy Radievogo Instituta im. V.G. Khlopina, vol. 15, pp. 62–92 (in Russian).

Srivastava, S.C., 2011. Paving the way to personalized medicine: production of some theragnostic radionuclides at Brookhaven National Laboratory. Radiochim. Acta 99, 635–640.

Vorogushin, M.F., et al., 2002. Beam and ion plasma technologies. Voprosy atomnoi nauki i techniki 3, 101–109. (in Russian).

WIPR, 2011. Workshop: Is there a future for Innovative PET Radionuclides ^{64}Cu, ^{68}Ga, ^{89}Zr and …. ^{44}Sc? Radiochim. Acta 99 (10), 607–678.

Zelichenko, V.M., Larionov, V.V., 2009. The active-educational environment of school and university: role of physics in social sphere and ecology. Vestnik TGPU 6, 102–106. (in Russian).

Zhuikov, B.L., et al., 1994. Preparation of strontium-82 from metallic rubidium target at 100 MeV proton beam. Radiochemistry 36, 548–553.

Zhuikov, B.L. et al., 2006. Process and Targets for Production of No-Carrier-Added Tin. Russian Patent #2313838. U.S. Patent Application, 2007, 20110216867.

Zhuikov, B.L., et al., 2011. Production of ^{225}Ac and ^{223}Ra by irradiation of Th with accelerated protons. Radiochemistry 53 (1), 73–80.

Zhuikov, B.L., Ermolaev, S.V., Kokhanyuk,V.M., 2008. Method for Producing Radiostrontium. Russian Patent 2356113. PCT Application, 2009, PCT/RU2009/000124. U.S. Patent Application 2010, 12/919527, 2010, Publ. No.: 2011/0051873 A1.

Zlokazov, S. et al., 2011. Production of radioisotopes in the IVV-2M reactor, In: Proceedings of the 7th International Conference on Isotopes, 4–8 September, Moscow Collection of abstracts, p. 21.

Zyuzin, A. et al., 2011. Cyclotron production of ^{99m}Tc in Canada. In: Proceedings of the 7th International Conference on Isotopes. 4–8 September, 2011, Moscow. Collection of abstracts, p. 31.