



A. Jalilian 
A. Korde 
V. Starovoitova 
J. Osso Jr. 
A. Koning 
N. Pessoa Barradas 
C. Horak 
M. Denecke 

Radioisotope Products and the Medicine of the Future: an IAEA Perspective

*Department of Nuclear Sciences and Applications,
International Atomic Energy Agency,
Vienna International Centre, Vienna, Austria*









✉ Amirreza Jalilian; a.jalilian@iaea.org

ABSTRACT

The production and application of radioisotopes and radiopharmaceuticals is a major peaceful application of nuclear science and technology and has opened new gateways for nuclear medicine in critical human diseases. Advances in the production of radioisotopes via nuclear reactors, accelerators, fission, etc. has facilitated the access to these products for Member States. ^{99}Mo , ^{131}I , ^{177}Lu are among the most essential radioisotopes for nuclear medicine and human health and their production and availability always has been an important theme for professional societies and the International Atomic Energy Agency (IAEA). In the meantime, a large list of theranostic radioisotopes including but not limited to ^{89}Zr , ^{68}Ga , ^{225}Ac , Cu-series, Sc-series, Tb-series etc. has provided a powerful toolbox for clinicians and the IAEA is taking steps to ensure their safe and appropriate application in radiopharmacy. The Agency promotes the production and application routes, including research reactors, cyclotrons, linear accelerators, and other cutting-edge methods, according to international and national guidelines and regulations. The IAEA also conducts activities such as Coordinated Research Projects (CRPs), Technical Meetings (TMs), national/regional training courses and conferences, to support and join forces with international professional societies in the development of human resources and research and development activities. Development of databases and freely available publications for all Member States are other useful means to support Member States in radiopharmaceutical sciences.

Key words: radiopharmaceuticals; molecular imaging; therapy; diagnosis; cyclotron; research reactors; IAEA

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А. Джалилиан 
А. Корде 
В. Старовойтова 
Ж. Оссу-мл. 
А. Конинг 
Н. Пессоа Баррадаш 
К. Хорак 
М. Денеке 

Радиоизотопные препараты и медицина будущего: взгляд МАГАТЭ

Департамент ядерных наук и применений,
Международное агентство по атомной энергии,
Венский международный центр, Вена, Австрия

✉ Амирреза Джалилиан; a.jalilian@iaea.org

РЕЗЮМЕ

Производство и применение радионуклидов и радиофармацевтических препаратов — яркий пример использования ядерной науки и технологии в мирных целях, для терапии серьезных заболеваний. Достижения в области производства радиоизотопов с помощью ядерных реакторов, ускорителей, деления и т.д. упростили для государств, входящих в Международное агентство по атомной энергии (МАГАТЭ), доступ к радиоизотопным препаратам. ^{99}Mo , ^{131}I , ^{177}Lu являются одними из наиболее важных радиоизотопов для ядерной медицины и здравоохранения, и их производство и доступность всегда были важной темой обсуждений внутри профессиональных сообществ и МАГАТЭ. Тераностические радиоизотопы, в том числе ^{89}Zr , ^{68}Ga , ^{225}Ac , Cu-серию, Sc-серию, Tb-серию и т.д., также имеют большой потенциал использования в клинической практике, и МАГАТЭ предпринимает меры для обеспечения их безопасного и надлежащего применения в радиофармацевтике. МАГАТЭ создает условия для использования передовых методов и технологий, таких как исследовательские реакторы, циклотроны, линейные ускорители и др., в производстве и применении радиоизотопов в соответствии с международными и национальными руководствами и нормами. МАГАТЭ организует и проводит совместные исследования, технические совещания, национальные/региональные учебные курсы и конференции в целях поддержки международных профессиональных сообществ и объединения усилий для развития кадрового потенциала и научно-исследовательской деятельности. Эффективными способами поддержки радиофармацевтической науки также являются разработка баз данных и обеспечение открытого доступа к научным публикациям для всех государств-членов.

Ключевые слова: радиофармацевтические препараты; молекулярная визуализация; терапия; диагностика; циклотрон; исследовательские реакторы; МАГАТЭ

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Introduction

As part of its service to its Member States in nuclear science and technology, the IAEA observes and monitors worldwide developments in the field of medical radioisotope and radiopharmaceutical production, together with professional societies and private companies. The Agency supports and helps its Member States training, technology transfer as well as sustainable establishment of radioisotope and radiopharmaceutical production, quality control, and human application.

Medical radioisotopes and the role of IAEA

Strong national capabilities are necessary to sustain and expand the beneficial applications of radionuclides and radiopharmaceuticals in Member States' health care systems. Over the years, IAEA

support in research and development (R&D) and technical cooperation activities has significantly enhanced capabilities in the field of medical isotope production. Because of the rapid progress of technologies, the majority of Member States still lack trained and qualified personnel, appropriate equipment and medical radioisotopes, and radiopharmaceutical production technology, and need support to develop these locally to effectively improve national health care systems and sustain their economic development. Improving processing methods, developing new products, and enhancing quality assurance is a worldwide effort facilitated through IAEA coordination. Developing Member States increasingly seek agency assistance in harnessing the benefits of such technology. The IAEA, through its Technical Cooperation

Programme, helps Member States achieve self-sufficiency in the production of medical radioisotopes and radiopharmaceuticals, strengthen quality assurance practices and regulatory compliance as well as facilitate human resource development¹. IAEA CRPs support applied research with the aim of enhancing Member States' capabilities of using indigenous resources and support adaptive research for effective technology growth and transfer to developing Member States. Support is also given by making available free of charge relevant publications and implementing technical meetings, workshops, symposia, and conferences dedicated to the field. The Agency Radioisotope Products and Radiation Technology Section is the focal point for disseminating knowledge and experience in this field among Member States.

The world supply of medical radioisotopes is another concern. In particular, the shortage in the supply of fission produced ⁹⁹Mo and ^{99m}Tc generators during 2007–2010 and during transport bottlenecks during the COVID pandemic attracted international attention and directly affected patient care, since more than 30 million diagnosis investigations are carried out annually worldwide using ^{99m}Tc. In this context, the IAEA has been working towards ensuring a sustained supply of ⁹⁹Mo to all Member States. Coordinated efforts with the Organization for Economic Cooperation and Development Nuclear Energy Agency have been undertaken to address the production of ⁹⁹Mo on a large scale. The IAEA is also exploring alternative technologies for ^{99m}Tc production. Specifically, the IAEA promotes CRPs on cyclotron-based, direct production of ^{99m}Tc and the production of ⁹⁹Mo by photo-nuclear reactions, as well as the corresponding new materials to be used in ⁹⁹Mo/^{99m}Tc generators loaded with low specific activity ⁹⁹Mo.

Radioisotopes for radiopharmaceuticals

Radioisotopes, as precursors for the preparation of radiopharmaceuticals, can be prepared by various means, such as research reactors, cyclotrons, generators, and recently linear accelerators. Based on the application, they can be used for preparation of diagnostic and/or therapeutic radiopharmaceuticals.

Diagnostic radioisotopes. Diagnostic radioisotopes usually emit photons that are used in the imaging of human diseases, usually using Single Photon Computed Emission Tomography (SPECT) systems or Positron Emission Tomography (PET) Positron. Most of these radionuclides are prepared by a medical cyclotron. Some of the most regularly used radioisotopes of this group are summarized in Table 1 and 2.

Therapeutic radioisotopes. Several radioisotopes emit energetic particles during their radioactive decay process. The most well-known particles are beta and alpha particles. A beta particle is literally an electron expelled from radionuclide nucleolus that has specific energy that is a “finger-print” of any nuclide. While alpha particles are usually emitted from specific fission products radionuclides; they have the size of a He atom but with a 2+ charge. Both particles can be useful in bombardment of unwanted cells in humans, if successfully transferred near or inside the target cells. Usually two cells types are targets to this kind of irradiation, mostly cancerous cells and sometimes inflammatory cells in some human chronic diseases, such as arthrorheumatoid diseases. In any case, the choice of a suitable “carrier molecule” capable of being attached to the radionuclide and also being able to “seek and find” the targeted malicious cell is crucial. Fig. 1 depicts schematically a targeted drug including the radionuclide, also called “targeting radiopharmaceutical”.

Table 1. Some example radioisotopes used in Single Photon Computed Emission Tomography systems

Таблица 1. Примеры радиоизотопов, используемых в системах однофотонной эмиссионной компьютерной томографии

Radioisotope <i>Радиоизотоп</i>	Half-life <i>Период полураспада</i>	γ Energy (keV) & Abundance (%) <i>Энергия (кэВ) и интенсивность (%) γ-квантов</i>	Production route <i>Метод получения</i>
^{99m} Tc	6 h / ч	140 (89%)	⁹⁹ Mo/ ^{99m} Tc generator / <i>генератор</i>
¹²³ I	13.2 h / ч	159 (83.3%)	¹²⁴ Xe (p, pn) ¹²³ I
¹¹¹ In	2.8 d / <i>сут</i>	171.3 (91%)	¹¹² Cd (p, 2n) ¹¹¹ In
²⁰¹ Tl	3 d / <i>сут</i>	135 (2.5%), 167 (10%)	²⁰³ Tl(p,3n) ²⁰¹ Pb → ²⁰¹ Tl
⁶⁷ Ga	3.26 d / <i>сут</i>	93 (38%), 185 (21.4%)	⁶⁸ Zn (p,2n) ⁶⁷ Ga

¹ Quality control in the production of radiopharmaceuticals. IAEA TECDOC. No. 1856. 2018. <https://www.iaea.org/publications/13422/quality-control-in-the-production-of-radiopharmaceuticals>

Table 2. Short-lived radiopharmaceuticals produced in cyclotrons for Positron Emission Tomography applications²

Таблица 2. Короткоживущие радиофармацевтические препараты для позитронно-эмиссионной томографии, полученные на циклотронах²

Radiopharmaceutical Радиофармацевтический препарат	Identical (similar) molecule Идентичная (сходная) молекула	Application Применение
¹⁸ FDG	Glucose Глюкоза	Lung, breast, melanoma tumor and brain imaging Визуализация легких, молочной железы, меланомы и головного мозга
¹³ NH ₃	NH ₃	Heart, brain or tumor; blood flow imaging Сердце, мозг или опухоль; визуализация кровотока
¹⁵ O-H ₂ O	H ₂ O	Tumor and other tissues perfusion Перфузия опухолей и других тканей
¹¹ C-Acetate	Acetate Ацетат	Cell metabolism Клеточный метаболизм
¹¹ C-Choline	Choline Холин	Cell energy consumption Потребление энергии клетками
⁶⁸ Ga-DOTATATE/ DOTATOC	Somatostatin Соматостатин	Gastrointestinal tumor imaging Визуализация опухолей желудочно-кишечного тракта
⁶⁸ Ga-PSMA	Prostate specific membrane antigen Простатспецифический мембранный антиген	Prostate tumor imaging Визуализация опухолей предстательной железы

Most of therapeutic radiopharmaceuticals are used in the form of injections for the treatment of various cancers and malignancies. Successful agents based on alpha and beta emitters have been developed based on clinical targets, such as somatostatins (SSTR), prostate specific membrane antigen (PSMA), fibroblast activated protein inhibitors (FAPI). In rare cases, radiosynovectomy has been applied for the treatment of arthrorheumatoid diseases. Though this is a niche section in radiopharmaceuticals sciences, IAEA has recently published a detailed publication on the production, quality control and clinical application of radiosynovectomy agents³.

Beta emitters. Most therapeutic radiopharmaceuticals used today are labeled with beta-emitting isotopes due to reasonable tissue penetration of these particles (less than a mm to few mm depending on energy of the radioisotope). The advantage of beta emitters compared to gamma emitters is their short range, so they do not damage the surrounding healthy tissue and are thus

safer. Commonly used beta emitters in routine nuclear oncology include ¹⁷⁷Lu (tissue penetration: 0.5–2 mm) and ⁹⁰Y (tissue penetration: 2.5–11 mm) [1].

Alpha emitters. Due to higher alpha particle mass and double positive charge, they have a limited range in materials (including cells and tissues) and they disseminate their kinetic energy faster to the surrounding cell environment with higher damage to the target cells at the sub-cellular scale. Despite these limitations and present limited production, various alpha emitters and related radiopharmaceuticals have been used in medicine. A recent review article describes the production of the important alpha emitters [1]. Table 3 summarises the properties of the most important alpha emitters for use in medicine.

Theranostic radioisotopes. Therapeutic isotopes provide either curative or palliative radiation therapy to treat disease by killing cancerous cells. Radioisotopes are often used to treat the prostate,

² Cyclotron produced radionuclides: guidance on facility design and production of fluorodeoxyglucose (FDG). IAEA Radioisotopes and Radiopharmaceuticals Series No. 3. 2012. <https://www.iaea.org/publications/8529/cyclotron-produced-radionuclides-guidance-on-facility-design-and-production-of-fluorodeoxyglucose-fdg>

Production and quality control of Fluorine-18 labelled radiopharmaceuticals. IAEA TECDOC No. 1968. 2021. <https://www.iaea.org/publications/14925/production-and-quality-control-of-fluorine-18-labelled-radiopharmaceuticals>
Atlas of non-FDG PET-CT in diagnostic oncology. IAEA Human Health Series No. 38. 2021. <https://www.iaea.org/publications/13581/atlas-of-non-fdg-pet-ct-in-diagnostic-oncology>

³ Production, quality control and clinical applications of radiosynovectomy agents. IAEA Radioisotopes and Radiopharmaceuticals Reports No. 3. 2021. <https://www.iaea.org/publications/13500/production-quality-control-and-clinical-applications-of-radiosynovectomy-agents>

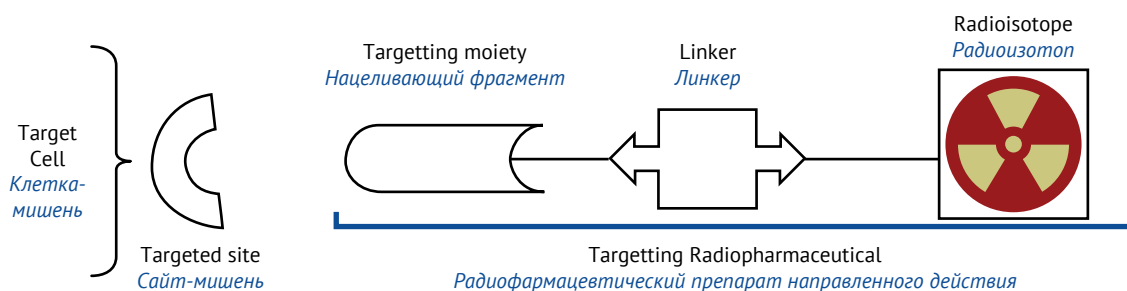


Fig. 1. An overview of targeting radiopharmaceutical

Рис. 1. Схема таргетного радиофармацевтического препарата

the breast, the head, the neck, the thyroid, and the skeletal system. These isotopes can be attached to a molecule that targets diseased tissue, a so-called radiopharmaceutical (see above), fabricated into a device that implanted directly into a tumor as part of brachytherapy, or incorporated into microspheres that become lodged in tumorous tissue when introduced into a patient's blood stream. The theranostic approach, which couples diagnostic imaging and therapy using the same molecule or at least very similar molecules, is also possible. Radioisotopes used for this are called theranostic. For example, a combination of ^{123}I (gamma emitter) and ^{131}I (gamma and beta emitters) can be used for theranostic purposes – to image the cancerous cells and to destroy them at the same time.

Radioisotopes for radiotherapy and brachytherapy. One of the most common applications of radioactive sources is radiotherapy – a widely used form of cancer treatment [2]. Radiation, used alone or in combination with surgery or chemotherapy, effectively destroys cancerous cells. External radiotherapy, also known as teletherapy, is provided

by an external radiation source, usually cobalt-60, which emits 1.1 MeV and 1.3 MeV gamma rays. Brachytherapy, or internal radiotherapy, places encapsulated radioactive sources inside the patient. This technique has the advantage of using a highly localized dose of radiation and significantly decreases the risk of radiation-induced second malignancies. Radioactive implants, in the form of wires or seeds, are inserted for hours, days, or, in some cases, even permanently. Currently, brachytherapy is predominantly used for localized tumors, such as cancers of the prostate, cervix, and endometrium. Mostly alpha- or beta-emitting radionuclides are used for brachytherapy due to their short penetration into biological tissues and high linear energy transfer. Among them are ^{131}I , ^{125}I , ^{192}Ir , ^{103}Pd , ^{106}Ru .

Radioisotope production

Radioisotopes are prepared via select nuclear reactions. Several approaches to isotope production are available, including those using research reactors, cyclotrons, and decay of other radioisotopes (i.e. generators). Although these are the most important routes, other methods such as application

Table 3. Physical properties of important alpha emitters for use or potential use in medicine

Таблица 3. Физические свойства некоторых альфа-излучателей, использующихся в медицине

Radioisotope Радиоизотоп	Half life Период полураспада	Production routes Методы получения	Decay products Продукты распада
^{213}Bi	46 min / мин	^{227}Ac decay chain Цепочка распада ^{227}Ac	^{209}Tl
^{149}Tb	4.12 h / ч	^{152}Gd (p, 4n) ^{149}Tb	^{145}Eu , ^{149}Gd
^{211}At	7.2 d / сут	$^{209}\text{Bi}(\alpha, 2n) ^{211}\text{At}$	^{207}Bi , ^{211}Po
^{224}Ra	3.63 d / сут	$^{228}\text{Th}/^{224}\text{Ra}$ generator $^{228}\text{Th}/^{224}\text{Ra}$ генератор	^{220}Rn
^{225}Ac	10 d / сут	^{227}Ac decay chain Цепочка распада ^{227}Ac	^{221}Fr
^{223}Ra	11.4 d / сут	^{227}Ac decay chain Цепочка распада ^{227}Ac	^{219}Rn
^{227}Th	18.68 d / сут	^{227}Ac decay chain Цепочка распада ^{227}Ac	^{223}Ra

of linacs and neutron generators are also gaining attention in recent years.

Research reactors. Research reactors are facilities capable of initiating a nuclear reaction to prepare radioisotopes. Some production routes generate radioisotopes of the same target element via a neutron capture reaction (n, γ) or a new element in case the neutron has enough energy to kick-out a proton from the nucleus (n, p). The most interesting example of such reactions are production of the well-known beta emitter ^{177}Lu by irradiation of ^{176}Lu in a research reactor with thermal neutrons, $^{176}\text{Lu} (n, \gamma) ^{177}\text{Lu}$. Another nuclear reaction used in specific research reactors for radioisotope production is initiated by high energy/fast neutrons; the best example is $^{32}\text{S}(n,p)^{32}\text{P}$. Probably the most important reaction is fission using neutrons of fissionable targets such as U to produce various important radionuclides for use in humans such as ^{99}Mo , ^{131}I and ^{90}Y . A detailed IAEA publication in the production of reactor-based radionuclides is available⁴.

Generators. Radionuclide generator systems are a safe and user-friendly option for producing short-lived radionuclides for busy hospital radiopharmacies. Generator systems consist of parent radionuclide, which decays to daughter radionuclide of shorter half-life.

The differences in chemical properties of decay daughter and isotope parent allows the separation of daughter from time to time. This principle is used in the most used medical generator system of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$. Most of the current $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators use the parent radionuclide ^{99}Mo ($T_{1/2}$ 67h), produced from the fission reaction of ^{235}U , where high specific activity ^{99}Mo in anionic molybdate form is adsorbed on a positively charged acidic aluminum oxide column and the $^{99\text{m}}\text{Tc}$ daughter can be conveniently eluted off.

Use of ^{68}Ga radiopharmaceuticals is increasing and the $^{68}\text{Ge}/^{68}\text{Ga}$ generator is the convenient method to obtain $^{68}\text{GaCl}_3$ suitable for radiopharmaceutical preparations. The parent ^{68}Ge is produced in a cyclotron. Absorbent materials such as titanium dioxide are used for retaining ^{68}Ge on the generator column. ^{68}Ge decays by electron capture with a 275 days half-life to ^{68}Ga . Based on secular equilibrium, this generator system has relatively long shelf life of around 6 to 9 months and ^{68}Ga

can be eluted every 4 h for radiopharmaceutical synthesis.

$^{82}\text{Sr}/^{82}\text{Rb}$ generators are another example based on secular equilibrium, with the ^{82}Sr parent (half-life: 5.5 days) and its ^{82}Rb the daughter radionuclide half-life 76 seconds, decaying by positron emission. The monocationic $^{82}\text{RbCl}_2$ useful for cardiac PET imaging can be eluted every 10 min from the generator for almost one month.

Cyclotrons. These particle accelerating systems equipped with one or more solid, liquid, or gas target(s) are rapidly evolving and available machines to produce artificial radioisotopes starting from natural, enriched or radioactive target materials⁵. Historically, conventional short-lived PET radioisotopes (^{15}O , ^{13}N , ^{11}C and ^{18}F) were the first used to generate radiopharmaceuticals. ^{11}C , ^{15}O and ^{13}N radioisotopes had identical natural isotope pairs in biological systems and were considered the best surrogates to study and evaluate the metabolism and fate of various natural substances comprised of these atoms, such as H_2O , NH_3 and all organic biological molecules containing carbon atoms. Table 2 shows the most important short half-lived PET radiopharmaceuticals and their applications. Although ^{18}F has almost no identical natural pair in any biological system, its near identical size to hydrogen atom, high polarity and longer half-life (110 min) have made it evolve to be a major role player in PET radiopharmacy.

In addition to the above-mentioned PET radiopharmaceuticals prepared and used for several decades, the need for imaging longer biological processes, requiring detection periods greater than several hours and possibly days, have led to many other interesting PET radioisotopes being prepared and employed in radiopharmaceutical production. For instance, in order to visualise and follow antibody fate and tumor detection using them, radionuclides with half-lives in the range of days should be used, since the biological half-life of these biomolecules are between 1–3 days. A recent IAEA publication covers the production of alternative and emerging radioisotopes using medical cyclotrons⁶. Table 4 represent a list of radioisotopes and radiopharmaceuticals that are emerging future PET.

Linacs. Linear accelerators can be used to produce many radionuclides, many of which cannot be

⁴ Manual for reactor produced radioisotopes. IAEA. 2003. https://www-pub.iaea.org/MTCD/publications/PDF/te_1340_web.pdf

⁵ Cyclotron produced radionuclides: operation and maintenance of gas and liquid targets. IAEA Radioisotopes and Radiopharmaceuticals Series No. 4. 2012. <https://www.iaea.org/publications/8783/cyclotron-produced-radionuclides-operation-and-maintenance-of-gas-and-liquid-targets>

⁶ Alternative radionuclide production with a cyclotron. IAEA Radioisotopes and Radiopharmaceuticals Reports No. 4. 2021. <https://www.iaea.org/publications/13649/alternative-radionuclide-production-with-a-cyclotron>

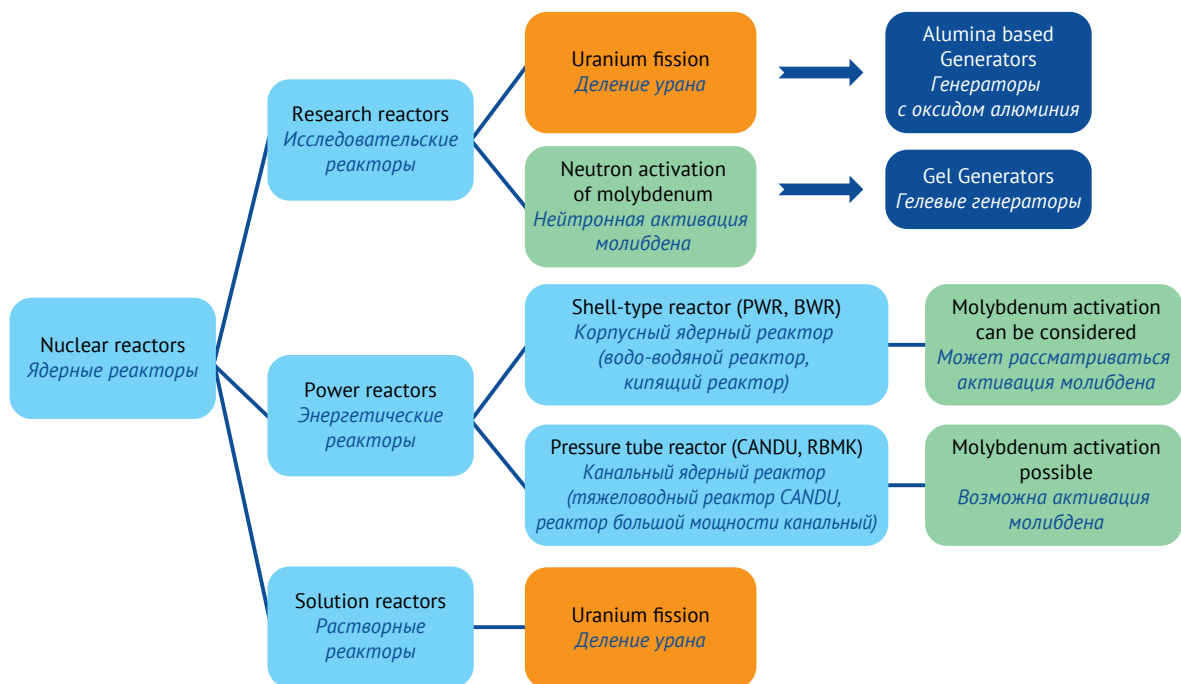


Fig. 2. Production of ^{99}Mo using nuclear reactors

Рис. 2. Производство ^{99}Mo с использованием ядерных реакторов

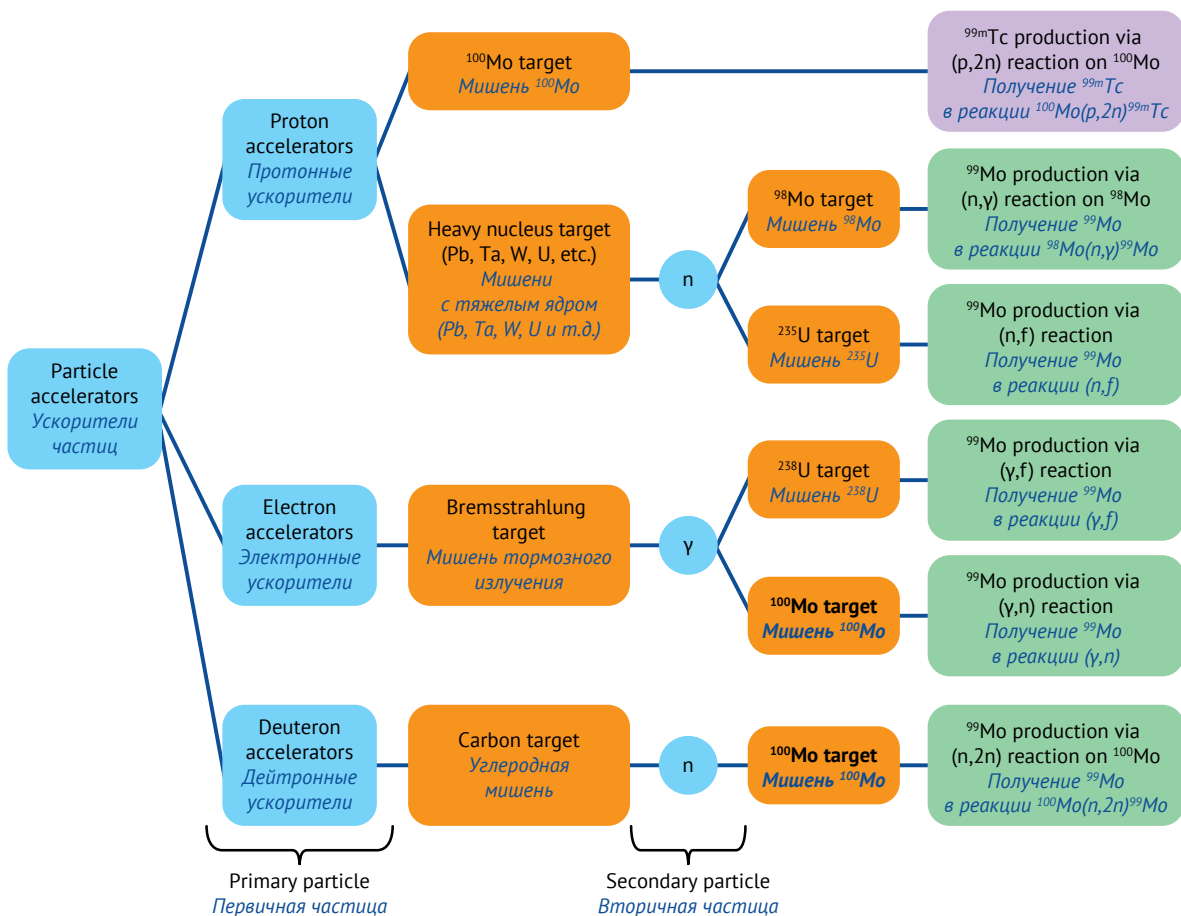


Fig. 3. Production of ^{99}Mo and $^{99\text{m}}\text{Tc}$ using particle accelerators

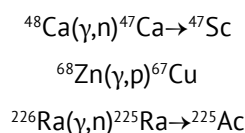
Рис. 3. Производство ^{99}Mo и $^{99\text{m}}\text{Tc}$ с использованием ускорителей частиц

Table 4. Selected emerging PET radioisotopes and potential radiopharmaceuticals

Таблица 4. Некоторые новые радиоизотопы и потенциальные радиофармацевтические препараты для ПЭТ

Radioisotope <i>Радиоизотоп</i>	Radiopharmaceuticals <i>Радиофармпрепараты</i>	Half life <i>Период полураспада</i>	Application <i>Применение</i>	Reference <i>Источник</i>
⁶⁴ Cu	⁶⁴ Cu SARTATE, ⁶⁴ Cu ATSM, ⁶⁴ Cu chloride / <i>хлорид</i>	12.7 h / ч	Neuroendocrine tumors, hypoxia, prostate and brain tumors <i>Нейроэндокринные опухоли, гипоксия, опухоли предстательной железы и головного мозга</i>	7
⁸⁹ Zr	⁸⁹ Zr trastuzumab <i>⁸⁹Zr трасстузаб</i>	78 h / ч	Breast cancer <i>Рак молочной железы</i>	[3]
⁸⁶ Y	⁸⁶ Y peptides, ⁸⁶ Y-mAbs <i>⁸⁶Y пептиды, ⁸⁶Y -МАТ</i>	14.7 h / ч	Various cancers <i>Различные виды рака</i>	8
¹²⁴ I	¹²⁴ I NaI, ¹²⁴ I MIBG	4.2 d / <i>сут</i>	Thyroid imaging, Neuroendocrine tumors <i>Визуализация щитовидной железы, нейроэндокринные опухоли</i>	9

harvested with cyclotrons. For example, electron accelerators equipped with a bremsstrahlung converter can be used to generate intense photon flux causing photonuclear reactions in the target material. Such machines are used in several facilities for photonuclear production of ⁴⁷Sc, ⁶⁷Cu, and other isotopes:



Proton linacs can also be used for isotope production. Unlike relatively inexpensive and compact cyclotrons, high energy (>100 MeV) proton linacs are rather complex and expensive machines and are typically housed in national laboratories. While their number is limited they open an opportunity to produce some radioisotopes which are impossible or extremely difficult to produce otherwise. Examples of radioisotopes produced by these high energy accelerators include ⁶⁸Ge, ⁸²Sr, ¹⁰³Pd, ²²⁵Ac, and others.

Important radioisotopes in nuclear medicine

^{99m}Tc. The most used ^{99m}Tc radiopharmaceuticals are prepared at hospital radiopharmacies using pharmaceutical grade ^{99m}Tc eluted from ⁹⁹Mo/^{99m}Tc generators and approved cold kits. ⁹⁹Mo is an essential radioisotope used in at least 80% of annual nuclear medicine procedures worldwide. Various activities are supported and strengthened by IAEA in the production and meeting the global

demand of both ⁹⁹Mo and ^{99m}Tc. Using nuclear reactors various routes are possible for ⁹⁹Mo production with various specific activities (Fig. 2).

Production of accelerator based (cyclotron or linacs) ^{99m}Tc is another route when research reactors are not in place or when transport or production is diminished or paralyzed worldwide due to technical, commercial, political, or supply problems. Figure 3 depicts the possible routes of ⁹⁹Mo or ^{99m}Tc production using accelerators.

A recent, important IAEA action focused on the production of ^{99m}Tc using cyclotrons under an IAEA CRP (2011–2015) with 18 participants from 16 Member States. In this CRP a technology was successfully developed to produce >30 Ci ^{99m}Tc per run in medical cyclotrons of energies (<24 MeV proven). Successful clinical trials in Canada led to regulatory approvals and a monograph approved in Europe. Another recently concluded IAEA project focused on the use of low specific activity ⁹⁹Mo for generator preparation via accelerator production of ⁹⁹Mo (¹⁰⁰Mo (γ, n) reaction). Sixteen Member States participants worked together to formulate guidelines to enhance and strengthen the expertise in this new method based on photodynamic reaction.

¹³¹I. Historically the first therapeutic radiopharmaceutical/radioisotope used in medicine was ¹³¹I and ¹³¹I can be a diagnostic radioiodine as well when used in low doses (185 MBq). It is produced locally by countries having research reactor facilities via

⁷ Cyclotron produced radionuclides: emerging positron emitters for medical applications: ⁶⁴Cu and ¹²⁴I. IAEA Radioisotopes and Radiopharmaceuticals Reports No. 1. 2016. <https://www.iaea.org/publications/10791/cyclotron-produced-radionuclides-emerging-positron-emitters-for-medical-applications-64cu-and-124i>

⁸ Production of emerging radionuclides towards theranostic applications: Copper-61, Scandium-43 and -44, and Yttrium-86. IAEA TECDOC No. 1955. 2021. <https://www.iaea.org/publications/14857/production-of-emerging-radionuclides-towards-theranostic-applications-copper-61-scandium-43-and-44-and-yttrium-86>

⁹ Manual for reactor produced radioisotopes. IAEA. 2003. https://www-pub.iaea.org/MTCD/publications/PDF/te_1340_web.pdf

neutron capture on ^{130}Te targets. ^{131}I is also generated by ^{99}Mo producers by isolation from their target fission products. Due to huge interests worldwide and also importance in both diagnosis and therapy of human thyroid diseases and some other cancers. The supply chain is quite important for all Member States and therefore the IAEA, together with the other international organisations, continually scrutinizes its production and supply.

^{177}Lu . Currently the beta emitter ^{177}Lu is the highest potential therapeutic radionuclide for use in theranostic radiopharmacy in the forms of ^{177}Lu -DOTATATE and ^{177}Lu -PSMA. ^{177}Lu is produced via two routes:

- $^{176}\text{Lu}(n, \gamma)^{177}\text{Lu}$: ^{176}Lu can be natural or enriched (limitation of specific activity)
- $^{176}\text{Yb}(n, \gamma)^{177}\text{Yb} \rightarrow ^{177}\text{Lu}$ (high specific activity, no carrier added)

IAEA supports the local production and distribution as well as commercial manufacturers supply of pharmaceutical grade $^{177}\text{LuCl}_3$ suitable active product ingredient or radiopharmaceutical preparation. Two IAEA CRPs with the focus on the production and quality control of ^{177}Lu biomolecules and simple radiopharmaceuticals have concluded and the results published¹⁰.

^{68}Ga . ^{68}Ga decays with a half-life of 67.71 min. It has played a remarkable role in the worldwide growth of clinical research and routine clinical studies with PET over the last 20 years. ^{68}Ga is very well suited as a diagnostic isotope for pairing with therapeutic radiometal isotopes, particularly when targeting molecules can utilize the same chelator for both ^{68}Ga and the therapy isotope (e.g. ^{177}Lu , ^{225}Ac). The most common method of obtaining ^{68}Ga is currently via a $^{68}\text{Ge}/^{68}\text{Ga}$ generator. Generators are convenient for many applications because the long half-life of the parent nuclide ^{68}Ge (270.93 days) guarantees an ongoing supply of Ga-68 for up to nine months. A former IAEA CRP about generator-based Ga-68 radiopharmaceuticals has already been completed¹¹. The usable ^{68}Ga activity from current generators is nevertheless limited by the amount of loaded activity, the minimum interval between two elutions, the maximum number of elutions, the

elution efficiency, and the possibility of parent radionuclide breakthrough. Direct production of ^{68}Ga radionuclide using medical cyclotrons and ^{68}Zn targets¹² is possible and a new IAEA project is promoting this route as well suited for centers with multiple patients and high expertise in cyclotron operations¹³.

^{89}Zr . Due to its attractive physicochemical properties, ^{89}Zr (half-life 78.41 h) has attracted greater attention, especially in the pharmacokinetics studies and clinical evaluation of monoclonal antibodies (mAbs) and large proteins. The additional gamma emission from ^{89}Zr does not negatively impact image quality obtained with in modern whole-body PET/CT or PET/MR scanners. In terms of committed dose per administered activity, ^{89}Zr is probably one of the best choices for a late-stage PET imaging agent. The production of ^{89}Zr radioisotope using medical cyclotrons through the $^{89}\text{Y}(p,n)^{89}\text{Zr}$ reaction is rather straightforward and various radiopharmaceuticals have already been prepared. An IAEA CRP started in 2019 for the development of standardized production and quality control of ^{89}Zr radioisotope as well as ^{89}Zr radiopharmaceuticals covering all preclinical stages for ultimate use in diagnostic nuclear medicine.

^{225}Ac . ^{225}Ac (half-life 10 d) can be prepared with various methods such as radiochemical extraction from ^{229}Th , irradiation of ^{226}Ra with medium energy protons (16 MeV), irradiation of ^{232}Th with high energy protons, research reactor irradiation of ^{226}Ra as well as photonuclear transmutation of ^{226}Ra . The IAEA is continuously supporting and following the production and application of ^{225}Ac ¹⁴. Due to the advances in the preparation and clinical application of alpha-emitter radiopharmaceuticals, especially ^{225}Ac , an IAEA project started in 2022 to assist the member States with the development, production, and quality control of ^{225}Ac therapeutic radiopharmaceuticals¹⁵ (Fig. 4).

Tb-radioisotopes. Terbium is unique in that it has four medically interesting radioisotopes, ^{149}Tb , ^{152}Tb , ^{155}Tb and ^{161}Tb . ^{155}Tb (half-life 5.32 d) and ^{152}Tb (half-life 17.5 h) can be used for SPECT and PET, respectively. Both radioisotopes have been produced and tested preclinically. ^{152}Tb

¹⁰ Comparative evaluation of therapeutic radiopharmaceuticals. Technical Reports Series No. 458. IAEA. 2007. <https://www.iaea.org/publications/7654/comparative-evaluation-of-therapeutic-radiopharmaceuticals>

¹¹ Development of Ga-68 based PET-radiopharmaceuticals for management of cancer and other chronic diseases.

¹² Gallium-68 cyclotron production. <https://www.iaea.org/publications/13484/gallium-68-cyclotron-production>

¹³ Jalilian A. New CRP: production of cyclotron-based gallium-68 radioisotope and related radiopharmaceuticals (F22073). <https://www.iaea.org/newscenter/news/new-crp-production-of-cyclotron-based-gallium-68-radioisotope-and-related-radiopharmaceuticals-f22073>

¹⁴ Report on joint IAEA-JRC workshop "Supply of Actinium-225". IAEA. 2018. http://www.naweb.iaea.org/napc/iachem/working_materials/Report_Workshop%20on%20Supply%20of%20Ac-225_IAEA_JRC_October2018.pdf

¹⁵ Production and quality control of Ac-225 radiopharmaceuticals. <https://www.iaea.org/projects/crp/f22075>

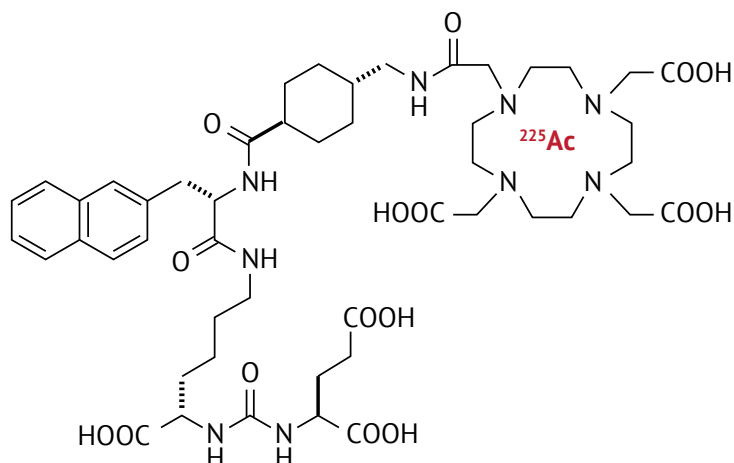


Fig. 4. Chemical structure of an ^{225}Ac therapeutic radiopharmaceutical

Рис. 4. Химическая структура терапевтического радиофармацевтического препарата ^{225}Ac

was the first Tb isotope that was tested (as ^{152}Tb -DOTATOC) in a patient. Both these radionuclides may be of interest for dosimetry purposes, due to photon and positron emission, suitable for accumulation studies, prior to the application of radiolanthanide therapy. The decay properties of ^{161}Tb (half-life 6.89 d) are like ^{177}Lu , but with the co-emission of Auger electrons, which make it attractive for a combined β -/Auger electron therapy that has been demonstrated to be effective in preclinical experiments. ^{149}Tb (half-life 4.1 h) has been proposed for targeted α -therapy with the possibility of PET imaging. In terms of production, ^{161}Tb and ^{155}Tb are most promising to be made available at the large quantities suitable for future clinical translation. Due to interesting and diverse application of the Tb radioisotopes for the development of theranostic agents, IAEA intends to hold various activities in this regard in 2022 onwards.

IAEA support to member states in radiopharmaceutical science

Coordinated Research Projects (CRPs). The IAEA supports and assists research on and development and practical use of nuclear applications for peaceful purposes throughout the world. It brings together research institutions from its developing and developed Member States to collaborate on research projects of common interest in IAEA CRPs. Radioisotopes and radiopharmaceutical sciences are a major component of atoms for peace approach for all Member States and IAEA has supported them via this mechanism since the 1980's. These activities have resulted in sustainable and

successful production and application of radiopharmaceuticals in many Member States in all regions. Table 5 shows IAEA CRPs on the production and quality control of radioisotopes and radiopharmaceuticals since 2010.

Information support

IAEA Medical Cyclotron and Research Reactor Databases. Advances in access and application of web-based information sheets and worldwide application of modules and live webpages supports the accumulation, dissemination, and updating of data. The IAEA database for "Cyclotrons used for Radionuclide Production" was created as a follow-up action to the older hard-copy "Directory of Cyclotrons" developed in 1983 and updated in 1998 and 2006 by the IAEA and international experts. The database was established and is constantly under revision in response to the request of Member States and world-wide interest in the installation and application of cyclotrons for medical radioisotope production. At present, information of over 1300 cyclotrons from 89 MSs is uploaded into the database. The database has an online data query system as well as a mapping function of the accumulated data¹⁶.

The IAEA Research Reactor Database (RRDB) is the most authoritative source of technical, statistical, and historical information on research reactors ever built, currently being constructed or planned worldwide. Developed in 1984, some of its information was made available online in 2000. Since 2009, it is a fully web-based resource and was upgraded in 2021. RRDB contains technical and administrative information on

¹⁶ Cyclotrons used for Radionuclide Production. <https://nucleus.iaea.org/sites/accelerators/Pages/Cyclotron.aspx>

Table 5. An overview of IAEA CRPs on the production and application of radioisotopes and radiopharmaceuticals since 2010

Таблица 5. Обзор проектов совместных исследований МАГАТЭ по производству и применению радиоизотопов и радиофармацевтических препаратов с 2010 г.

CRP title Название проекта	Code Код	Timeline Период, гг.	Status Статус	Outcome Результат	Member States Государства-члены	Reference Источник
Development of therapeutic radiopharmaceuticals based on ^{177}Lu for radionuclide therapy Разработка терапевтических радиофармацевтических препаратов на основе ^{177}Lu для радионуклидной терапии	F22042	2006–2010	Closed Завершен	Final report Итоговый отчет	Argentina, Austria, Brazil, Chile, China, Cuba, Czech Republic, Hungary, India, Italy, Pakistan, Peru, Poland, Russian Federation, United States of America, Uruguay Австрия, Аргентина, Бразилия, Венгрия, Индия, Италия, Китай, Куба, Пакистан, Перу, Польша, Российская Федерация, Соединенные Штаты Америки, Уругвай, Чешская Республика, Чили	¹⁷
Development of ^{68}Ga based PET-radiopharmaceuticals for management of cancer and other chronic diseases Разработка радиофармацевтических препаратов для ПЭТ на основе ^{68}Ga для лечения рака и других хронических заболеваний	F22050	2010–2017	Closed Завершен	Final report Итоговый отчет	Australia, Austria, Brazil, Chile, China, Cuba, Germany, India, Italy, Mexico, Poland, Romania, Saudi Arabia, Singapore, South Africa, Thailand, Uruguay Австралия, Австрия, Бразилия, Германия, Индия, Италия, Китай, Куба, Мексика, Польша, Румыния, Саудовская Аравия, Сингапур, Таиланд, Уругвай, Чили, Южная Африка	¹⁸
Production and utilization of emerging positron emitters for medical applications with an emphasis on ^{64}Cu and ^{124}I Производство и использование новых позитронных излучателей для медицинского применения на примере ^{64}Cu and ^{124}I	F22049	2010–2014	Closed Завершен	IAEA publication Публикация МАГАТЭ	Argentina, Brazil, Canada, China, Denmark, Finland, France, Italy, Japan, Republic of Korea, Saudi Arabia, Syrian Arab Republic, Turkey, United States of America Аргентина, Бразилия, Дания, Италия, Канада, Китай, Республика Корея, Саудовская Аравия, Сирийская Арабская Республика, Соединенные Штаты Америки, Турция, Финляндия, Франция, Япония	¹⁹
Accelerator-based Alternatives to Non-HEU production of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Использование ускорителей в качестве альтернативных методов производства $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ без применения ВОУ	F22062	2011–2015	Closed Завершен	IAEA publication ²⁰ Публикация МАГАТЭ ²⁰	Armenia, Brazil, Canada, Germany, Hungary, India, Italy, Japan, Malaysia, Poland, Republic of Korea, Saudi Arabia, Syrian Arab Republic, Turkey, United States of America Армения, Бразилия, Венгрия, Германия, Индия, Италия, Канада, Малайзия, Польша, Республика Корея, Саудовская Аравия, Сирийская Арабская Республика, Соединенные Штаты Америки, Турция, Япония	²¹

¹⁷ Development of therapeutic radiopharmaceuticals based on ^{177}Lu for radionuclide therapy. <https://www.iaea.org/projects/crp/f22042>

¹⁸ Development of Ga-68 based PET-radiopharmaceuticals for management of cancer and other chronic diseases. <https://www.iaea.org/projects/crp/f22050>

¹⁹ Production and utilisation of emerging positron emitters for medical applications with an emphasis on Cu-64 and I-124. <https://www.iaea.org/projects/crp/f22049>

²⁰ Cyclotron based production of Technetium-99m. IAEA Radioisotopes and Radiopharmaceuticals Reports No. 2. 2017. <https://www.iaea.org/publications/10990/cyclotron-based-production-of-technetium-99m>

²¹ Jalilian A. CRP success story: F22062 accelerator-based alternatives to non-HEU production of Mo-99/Tc-99m (2011–2015). <https://www.iaea.org/newscenter/news/crp-success-story-f22062-accelerator-based-alternatives-to-non-heu-production-of-mo-99/tc-99m-2011-2015>

Table 5 (continued)

Продолжение таблицы 5

CRP title Название проекта	Code Код	Timeline Период, гг.	Status Статус	Outcome Результат	Member States Государства-члены	Reference Источник
Development and preclinical evaluations of therapeutic radio-pharmaceuticals based on ^{177}Lu and ^{90}Y labeled monoclonal antibodies and peptides <i>Разработка и доклиническая оценка терапевтических радиофармацевтических препаратов на основе моноклональных антител и пептидов, меченных ^{177}Lu и ^{90}Y</i>	F22052	2011–2015	Closed <i>Завершен</i>	Final report <i>Итоговый отчет</i>	Argentina, Austria, Brazil, China, Cuba, Czech Republic, Hungary, India, Iran, Italy, North Macedonia, Poland, Saudi Arabia, Syrian Arab Republic, Turkey, United States of America <i>Австрия, Аргентина, Бразилия, Венгрия, Индия, Иран, Италия, Китай, Куба, Польша, Саудовская Аравия, Северная Македония, Сирийская Арабская Республика, Соединенные Штаты Америки, Турция, Чешская Республика</i>	²²
Sharing and developing protocols to further minimize radioactive gaseous releases to the environment in the manufacture of medical radioisotopes, as good manufacturing practice <i>Совместное использование и разработка протоколов для дальнейшей минимизации выбросов радиоактивных газов в окружающую среду при производстве медицинских радиоизотопов – в качестве надлежащей производственной практики</i>	F23031	2015–2019	Closed <i>Завершен</i>	Final report <i>Итоговый отчет</i>	Belgium, Canada, Germany, Indonesia, Pakistan, Poland, Republic of Korea, United States of America <i>Бельгия, Германия, Индонезия, Канада, Пакистан, Польша, Республика Корея, Соединенные Штаты Америки</i>	²³
Therapeutic radiopharmaceuticals labelled with new emerging radionuclides (^{67}Cu , ^{186}Re , ^{47}Sc) <i>Терапевтические радиофармацевтические препараты, меченные новыми радионуклидами (^{67}Cu, ^{186}Re, ^{47}Sc)</i>	F22053	2016–2020	Closed <i>Завершен</i>	IAEA publication <i>Публикация МАГАТЭ</i>	Egypt, France, Hungary, India, Iran, Italy, Japan, Malaysia, Poland, Republic of Korea, Saudi Arabia, Syrian Arab Republic, United States of America <i>Венгрия, Египет, Индия, Иран, Италия, Малайзия, Польша, Республика Корея, Саудовская Аравия, Сирийская Арабская Республика, Соединенные Штаты Америки, Франция, Япония</i>	²⁴ , [4]
New ways of producing $^{99\text{m}}\text{Tc}$ and $^{99\text{m}}\text{Tc}$ generators <i>Новые способы производства $^{99\text{m}}\text{Tc}$ и генераторов $^{99\text{m}}\text{Tc}$</i>	F22068	2017–2021	Closed <i>Завершен</i>	IAEA publication (in press) <i>Публикация МАГАТЭ (в печати)</i>	Brazil, Canada, China, Egypt, India, Indonesia, Iran, Japan, Morocco, Pakistan, Peru, Poland, Romania, South Africa, Ukraine, United States of America <i>Бразилия, Египет, Индия, Индонезия, Иран, Канада, Китай, Марокко, Пакистан, Перу, Польша, Румыния, Соединенные Штаты Америки, Украина, Южная Африка, Япония</i>	²⁵

²² Development and preclinical evaluations of therapeutic radiopharmaceuticals based on Lu-177 and Y-90 labeled monoclonal antibodies and peptides. <https://www.iaea.org/projects/crp/f22052>

²³ Sharing and developing protocols to further minimize radioactive gaseous releases to the environment in the manufacture of medical radioisotopes, as Good Manufacturing Practice. <https://www.iaea.org/projects/crp/f23031>

²⁴ Jalilian A. Concluded CRP – Coordinated Research Project (CRP F22053) on therapeutic radiopharmaceuticals labelled with new emerging radionuclides (^{67}Cu , ^{186}Re , ^{47}Sc). <https://www.iaea.org/newscenter/news/concluded-crp-coordinated-research-project-crp-f22053-on-therapeutic-radiopharmaceuticals-labelled-with-new-emerging-radionuclides-67cu186re-47sc>

²⁵ Osso Junior JA, Jalilian A. NEW CRP: New ways of producing Tc-99m and Tc-99m generators (F22068). <https://www.iaea.org/newscenter/news/new-crp-new-ways-of-producing-tc-99m-and-tc-99m-generators-f22068>

Table 5 (continued)

Продолжение таблицы 5

CRP title Название проекта	Code Код	Timeline Период, гг.	Status Статус	Outcome Результат	Member States Государства-члены	Reference Источник
⁶⁴Cu radiopharmaceuticals for theranostic applications Радиофармацевтические препараты ⁶⁴ Cu для тераностического применения	F22067	2016–2020	Closed Завершен	IAEA publication Публикация МАГАТЭ	Australia, Brazil, Canada, China, Denmark, India, Iran, Mexico, Netherlands, Pakistan, Saudi Arabia, Syrian Arab Republic, United States of America Австралия, Бразилия, Дания, Индия, Иран, Канада, Китай, Мексика, Нидерланды, Пакистан, Саудовская Аравия, Сирийская Арабская Республика, Соединенные Штаты Америки	²⁶ , [5]
Nanosized delivery systems for radiopharmaceuticals Наноразмерные системы доставки радиофармацевтических препаратов	F22064	2014–2019	Closed Завершен	IAEA publication Публикация МАГАТЭ	Argentina, Brazil, Egypt, Iran, Italy, Malaysia, Mexico, Pakistan, Poland, Singapore, Thailand, United States of America Аргентина, Бразилия, Египет, Иран, Италия, Малайзия, Мексика, Пакистан, Польша, Сингапур, Таиланд, Соединенные Штаты Америки	²⁷
Production of ⁸⁹Zr and development of ⁸⁹Zr radiopharmaceuticals Получение ⁸⁹ Zr и разработка радиофармацевтических препаратов ⁸⁹ Zr	F22071	2019–2023	Ongoing В процессе	n.a. Не применимо	Canada, China, France, Germany, India, Iran, Italy, Japan, Mexico, Poland, Portugal, Republic of Korea, Romania, Saudi Arabia, South Africa, United States of America Германия, Индия, Иран, Италия, Канада, Китай, Мексика, Польша, Португалия, Республика Корея, Румыния, Саудовская Аравия, Соединенные Штаты Америки, Франция, Южная Африка, Япония	²⁸
Production of cyclotron-based ⁶⁸Ga radioisotope and related radiopharmaceuticals Производство радиоизотопов и радиофармацевтических препаратов ⁶⁸ Ga на циклотроне	F22073	2020–2024	Ongoing В процессе	n.a. Не применимо	Armenia, Brazil, Canada, Hungary, India, Iran, Mexico, Portugal, Slovakia, Saudi Arabia, United States of America Армения, Бразилия, Венгрия, Индия, Иран, Канада, Мексика, Португалия, Саудовская Аравия, Словакия, Соединенные Штаты Америки	²⁹
Production and quality control of ²²⁵Ac radiopharmaceuticals Производство и контроль качества радиофармацевтических препаратов ²²⁵ Ac	F22075	2022–2026	Initiated Начат	n.a. Не применимо	Open for proposals Принимаются предложения	³⁰

841 research reactors in 70 countries, including critical and subcritical assemblies and planned reactors. The information is provided and updated by Facility Data Providers designated by IAEA Member States and reviewed by the IAEA. Besides general information, such as facility location, status, and contact data, the RRDB also provides technical data such as reactor power and flux, experimental facilities available, and utilization of each research reactor. Utilization for radioisotope production includes information

for instance on the radioisotopes and respective activity produced in a given research reactor. Custom searches of the database can also easily retrieve the research reactors involved in radioisotope production in each country or region.

Medical Isotope Browser App. In 2019, the IAEA released the Medical Isotope Browser, a web-based tool that makes it possible to directly predict the production yield of a medical isotope based on user input and the databases of nuclear reactions

²⁶ Copper-64 radiopharmaceuticals for theranostic applications. <https://www.iaea.org/projects/crp/f22067>

²⁷ Nanosized delivery systems for radiopharmaceuticals. <https://www.iaea.org/projects/crp/f22064>

²⁸ Production of Zirconium-89 and the development of Zr-89 radiopharmaceuticals. <https://www.iaea.org/projects/crp/f22071>

²⁹ Production of cyclotron-based Gallium-68 radioisotope and related radiopharmaceuticals. <https://www.iaea.org/projects/crp/f22073>

³⁰ Production and quality control of Ac-225 radiopharmaceuticals. <https://www.iaea.org/projects/crp/f22075>

curated by the Agency. The Medical Isotope Browser can be used by medical scientists and the radiopharmaceutical industry to discover radioisotope production routes not yet explored³¹. The production of medical isotopes for therapy or diagnosis depends on complex nuclear reaction processes, which are only available to nuclear physicists via measurements and nuclear reaction theories. The Medical Isotope Browser makes this fundamental information accessible to many non-specialist users through its graphical user interface. The first version is restricted to isotopes produced by charged-particle accelerators. Users can specify the characteristics of the accelerator, such as the projectile (proton, deuteron, tritium, helium-3 or alpha particle), current in microamperes and the incident and exit energy, as well as the target material and the desired produced radioisotope. The required isotopic yield as a function of irradiation and cooling time as well as a complete description of all the produced impurities can be obtained almost instantly. The simulations are based on the TENDL nuclear data library augmented with evaluated cross sections from the IAEA medical isotope database. The next version will also include medical isotope production using research reactors and electron beams.

IAEA-WHO collaborative activities

The IAEA and WHO collectively support Member States through different activities, including those in radiopharmaceuticals. Nuclear medicine is an indispensable modality in current clinical settings that fully depends on the availability of suitable radiopharmaceutical products. The quality and safety standards of radiopharmaceuticals, being drugs, are significantly important. The IAEA support its Member States through various activities to ensure availability of good quality radiopharmaceuticals, and hence also address heterogeneous situations among its various Member States related to health regulations. The new developments in radiopharmaceuticals, especially for detection and treatment of cancer, are benefiting patients, hence there is increasing interest in producing and using such products. The pharmacopoeias are the publications that specify applicable drug quality standards; however many radiopharmaceuticals products are currently not included many of the national/regional pharmacopoeia's. The International Pharmacopoeia: (Ph. Int.) is published by WHO with the aim to provide specifications and test methods for priority

medicines of major public health importance and is widely refereed by drug producers, regulators, and health care providers, policy makers, etc. from different Member States. The IAEA is working with WHO for inclusion of radiopharmaceutical product specifications in the section on radiopharmaceuticals in the Ph.Int. Similarly, combined efforts are underway for publishing guidelines for manufacturing radiopharmaceutical products. The general guidelines on good manufacturing practices for radiopharmaceutical products is published in Ph.Int. Annex 2³². The drafts for specific guidelines for cold kit production and investigational radiopharmaceuticals are under review by expert committees.

Network of women in radiopharmaceutical sciences

the IAEA being an international organization, emphasizes the need to be inclusive, which includes nurturing an unbiased multicultural environment and gender equality. Women professionals are engaged in the radiopharmaceuticals field in different regions of the World; even though the IAEA always supports their participation in their various events, the proportion of women is significantly lower than that of the men. Enhanced efforts are therefore needed to bring together women scientists and professionals from different Member States through the IAEA platform. Thus, with the goal of networking among professionals, the 'IAEA Network of Women in Radiopharmaceutical Sciences, WRS' was established during IAEA symposium ISTR2019. This Network is also the first interest group under Women in Nuclear (WiN Global). WRS currently has 166 members from 34 countries spread across the globe and seven expert women professionals in the field as an advisory group. The WRS network includes physicists, chemists, biologists, pharmacists, and members with profiles ranging from young researchers to senior professionals and program leaders, spanning academic institutions, regulatory agencies, nuclear establishments, and commercial companies. The WRS network aims at knowledge sharing, mentoring young professionals, and helping/advising members in specific challenging situations related to their work in the area of radiopharmaceuticals, recognizing the support needed for advancement and advocacy of women to ascend to higher professional roles in their careers.

³¹ Dixit A. On the spot: IAEA launches its first android app-isotope browser. 2013. <https://www.iaea.org/newscenter/news/spot-iaea-launches-its-first-android-app-isotope-browser>

³² International Atomic Energy Agency and World Health Organization guideline WHO Technical Report Series No. 1025, 2020, 93–108. [https://apps.who.int/gb/ebwha/pdf_files/EB147/B147_1\(draft\)-en.pdf](https://apps.who.int/gb/ebwha/pdf_files/EB147/B147_1(draft)-en.pdf)

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AUTHORS / ОБ АВТОРАХ

Amirreza Jalilian, Ph. D.

ORCID: <https://orcid.org/0000-0002-1948-0580>
A.Jalilian@iaea.org

Aruna Korde, Ph. D.

ORCID: <https://orcid.org/0000-0002-9539-5521>
A.Korde@iaea.org

Valeriia Starovoitova, Ph. D.

ORCID: <https://orcid.org/0000-0003-1442-1853>
V.Starovoitova@iaea.org

Joao Osso Jr., Ph. D.

ORCID: <https://orcid.org/0000-0002-6672-1631>
j.a.osso-junior@iaea.org

Arjan Koning, Ph. D.

ORCID: <https://orcid.org/0000-0001-7253-0455>
a.koning@iaea.org

Nuno Pessoa Barradas, Ph. D.

ORCID: <https://orcid.org/0000-0001-7795-8573>
N.Pessoa-Barradas@iaea.org

Celina Horak, Ph. D.

ORCID: <https://orcid.org/0000-0003-4130-0395>
C.Horak@iaea.org

Melissa Denecke, Ph. D.

ORCID: <https://orcid.org/0000-0003-0210-1844>
m.denecke@iaea.org

Джалилиан Амирреза, Ph. D.

ORCID: <https://orcid.org/0000-0002-1948-0580>
A.Jalilian@iaea.org

Корде Аруна, Ph. D.

ORCID: <https://orcid.org/0000-0002-9539-5521>
A.Korde@iaea.org

Старовойтова Валерия, Ph. D.

ORCID: <https://orcid.org/0000-0003-1442-1853>
V.Starovoitova@iaea.org

Оссу-мл. Жоау, Ph. D.

ORCID: <https://orcid.org/0000-0002-6672-1631>
j.a.osso-junior@iaea.org

Конинг Аръян, Ph. D.

ORCID: <https://orcid.org/0000-0001-7253-0455>
a.koning@iaea.org

Песoa Баррадаш Нуну, Ph. D.

ORCID: <https://orcid.org/0000-0001-7795-8573>
N.Pessoa-Barradas@iaea.org

Хорак Селина, Ph. D.

ORCID: <https://orcid.org/0000-0003-4130-0395>
C.Horak@iaea.org

Денеке Мелисса, Ph. D.

ORCID: <https://orcid.org/0000-0003-0210-1844>
m.denecke@iaea.org

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