ANALYSIS OF DATA ARRAYS ON CYCLOTRON PRODUCTION OF MEDICAL RADIOISOTOPES

Yu.T. Petrusenko, A.G. Lymar', L.I. Nikolaichuk *, A.I. Tutubalin, A.G. Shepelev, T.A. Ponomarenko, O.V. Nemashkalo

National Science Center "Kharkov Institute of Physics and Technology", 61108, Kharkov, Ukraine

(Received October 10, 2008)

The paper analyzes the state of cyclotron production of radionuclides (RN) for nuclear medicine. Consideration is given to the production of ultra-short-lived (USL) and short-lived (SL) RN. The information of the IAEA Database "International Nuclear Information Systems" (INIS) for a period from 1970 to 2007 has been used for the analysis. The paper reports the data on the dynamics of works published about the cyclotron production of USL and SL RN, kinds of the works, and also, on the relative contribution of different countries to the total number of published works. Conclusions are drawn about the trends in the research of the problems considered.

PACS: 87.57.U

1. INTRODUCTION

Radioisotopes are widely used in different spheres of human activities, among which nuclear medicine appears to be the area of mass use of radioisotopes. Over 50% of the world annual production of radioisotopes are spent to meet the medical demands. In recent years, considerable attention has been focussed on radionuclide diagnostics of man's diseases through introduction of radioisotopes into the human body. Extensive application of isotopes in current medicine has created the market situation, in which the demand for the products appears much higher than their supply.

Today, medicine makes use of over 70% of world-produced stable isotopes and more than 50% of radioactive isotopes. As predicted by specialists, these figures may only escalate in the coming years. The animated interest of medical men in the isotopes is explained by a high efficiency of their application in diagnostics. It is just for diagnostic purposes that about 98% of isotopes coming to the medical sector are nowadays used. The uniqueness of isotope diagnostics consists in its accuracy, reliability, possible frequent use, and above all, in the capability to diagnose the disease even at an early stage.

As it is known, apart from 5 major elements (oxygen, hydrogen, carbon, nitrogen and calcium), the living body comprises 67 elements of Mendeleev's periodic table more. Therefore, it is now difficult to imagine a clinic (at home and abroad), that does not use various radioactive preparations and tracer-labelled compounds when diagnosing the case. Radioisotopes are used in nuclear medicine mainly in the form of radiopharmaceutical preparations (RPP) for early diagnostics of various human organ diseases and for therapy purposes.

The huge part of the world volume of radioisotope production is obtained at charged particle accelerators, which are for the most part the cyclotrons of various types.

It has been shown in the review article [1] that by 2000, among the main radionuclide-producing facilities in the world, the first place belongs to accelerators (188 machines). Of them, 178 installations are the cyclotrons, which produce radionuclides for nuclear medicine.

To elucidate the trends in the production of USL and SL radionuclides recommended by the IAEA [2] as most widely used in nuclear medicine, we have analyzed the data on the publications about the cyclotron production of USL and SL RN and their application for medical diagnostics.

The undertaken analysis of publications introduced by the IAEA countries into the automated database INIS, created in 1971, enabled us to trace the trends in the development of cyclotron production of USL and SL RN and their use in nuclear medicine for the last 35 years.

2. ANALYSIS OF INFORMATION ON CYCLOTRON PRODUCTION OF USL RADIONUCLIDES FOR NUCLEAR MEDICINE

The required amounts of USL RN are generally produced at small cyclotrons [3]. A regular use of cyclotrons for the production of medical radionuclides has begun since 1950. Small cyclotrons of medical use only, the so-called "baby cyclotrons" ($E \leq 20\,MeV$), are convenient for their location directly at the medical centers, where they serve for generating the USL RN and for PET studies with them.

*Corresponding author E-mail address: nikolaichuk@kipt.kharkov.ua

The current nuclear medicine makes use of more than 50 cyclotron radionuclides for scientific-research, diagnostic and therapeutic purposes. Their half-life is ranging from a few minutes to several years. In actual practice, to obtain RN in nuclear reactions, charged beams of protons, deuterons, ^3He, ^4He are used, protons being of most widespread use [3].

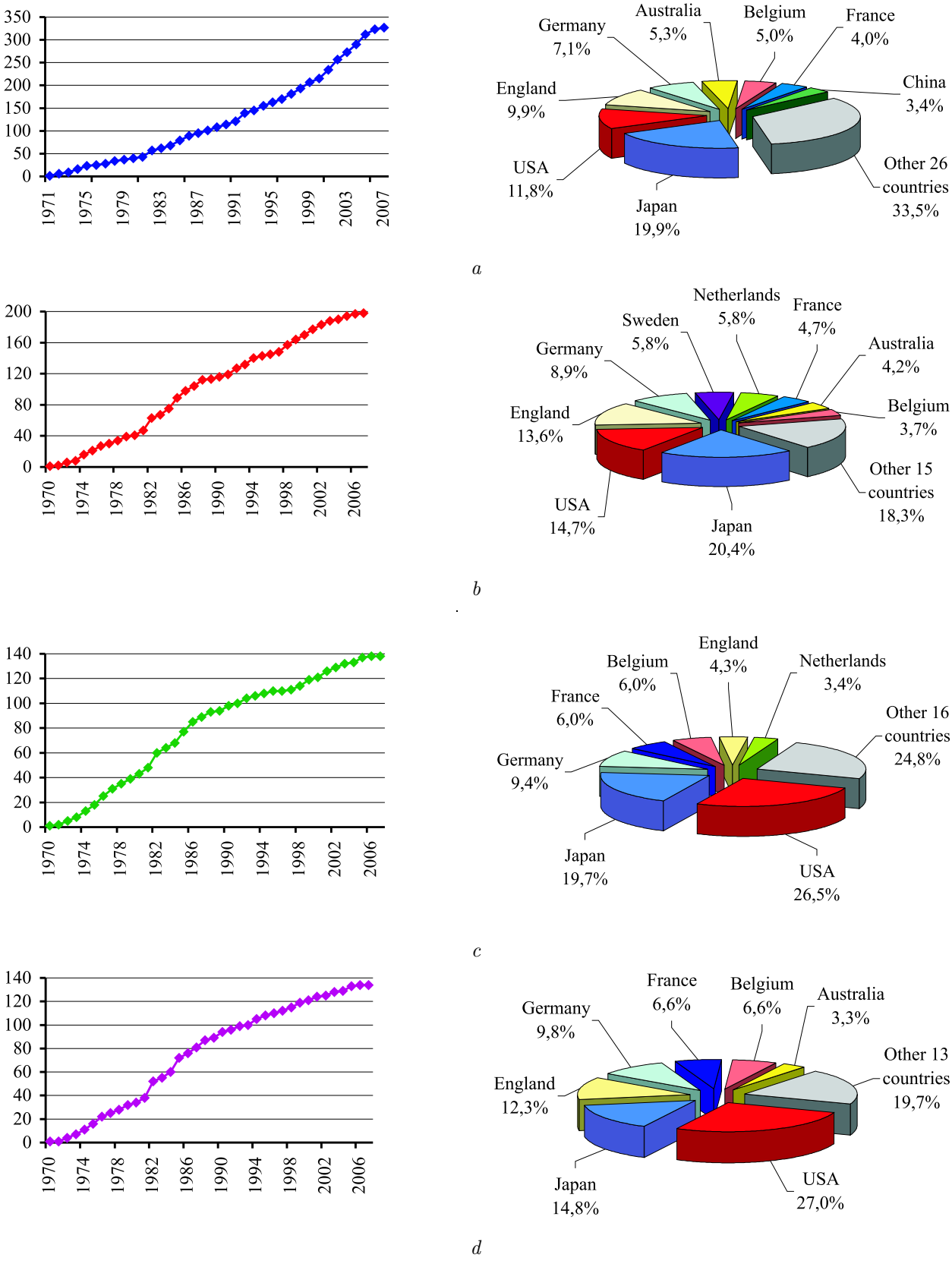

Fig.1. *Cumulative expansion in the number of publications on cyclotron production of USL radionuclides for nuclear medicine and published work distribution in the countries: a) fluorine-18, b) carbon-11, c) nitrogen 13, d) oxygen-15*

Below, we give the comparative data on the number of publications about the cyclotron production of ultra-short-lived carbon-11, nitrogen-13, oxygen-15, fluorine-18 radionuclides [4].

Figure 1 (*a*-*d*) shows the general growth of works on the problems of cyclotron production of the above-mentioned USL radionuclides, which were published by all IAEA member countries for a period of 1970 to 2007 (e.g., [5]-[9]) and were introduced into the INIS Database. Of certain interest is the information about the relative contribution of different countries to the total number of published works and about the type of publications on the problem under discussion, and also the particulars on the languages, in which the information was published.

From the data shown in Fig.1 (*a*, *b*, *c*, *d*) it follows that the number of publications on cyclotron production of nitrogen (^{13}N) and oxygen (^{15}O) for 1971 to 2006 has increased practically by a factor of 140, on the production of ^{11}C - by a factor of approximately 200, and on the production of ^{18}F - by a factor of more than 300. This fact points to considerably increased-in-recent-years demands for medical-purpose isotopes, particularly, ^{18}F for radionuclide diagnostics with the use of positron-emission tomographs (PET). The data presented in Fig.1 (*a*, *b*, *c*, *d*) illustrate the contribution of different countries to the number of publications about the production of USL RN for nuclear medicine. Here, Japan (20.4%), USA (14.7%) and Germany (8.9%) occupy a prominent place in carbon-11 production. The production of fluorine is characterized by the following distribution in different countries: Japan (19.9%), USA (11.8%), England (9.9%).

The main types of publications on the production of USL radioisotopes for nuclear medicine are the articles (≈ 40%), proceedings of conferences (≈ 30%), reports (15%) and books (15%). Naturally, the overall picture of USL RN production is also characterized by the increased number of publications in the mentioned countries.

English is the prevailing language of the works published on all the USL RN produced.

3. ANALYSIS OF INFORMATION ON CYCLOTRON PRODUCTION OF SHORT-LIVED RADIONUCLIDES FOR NUCLEAR MEDICINE

According to IAEA recommendations [2], a number of SL radionuclides also hold promise for nuclear medicine.

We have analyzed the data about publications concerned with the problems of SL RN production and medical diagnostic application, which were introduced by the IAEA member countries into the automated INIS Database.

Figures 2 to 4 show the dynamics of the total number of publications of all IAEA member countries on the above-mentioned problems over a period from 1970 to 2007.

The information is given on the relative contribution of different countries to the total number of publications, on the type of these publications, and also on the languages, in which the publications were published. The data are presented for palladium-103, iodine-124, iodine-123, strontium-89, copper-64, copper-67, ytterbium-169 [[10]-[15]].

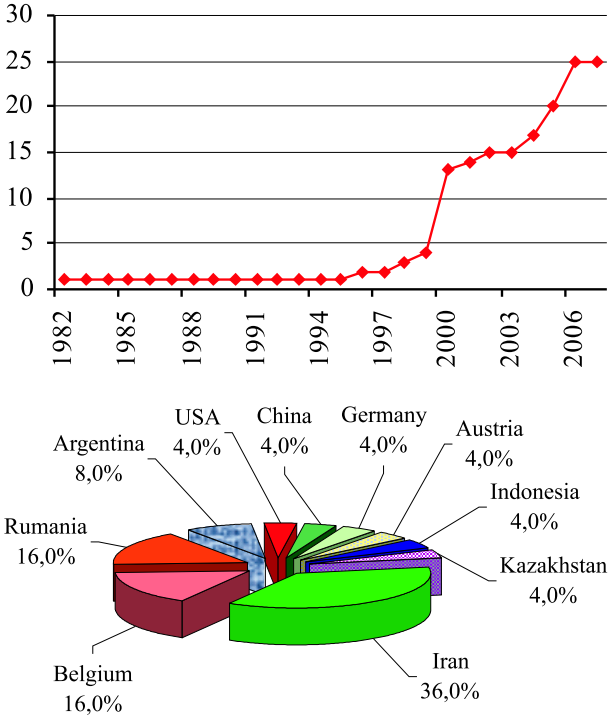

Fig.2. *Cumulative expansion of the number of publications on cyclotron production of ^{103}Pd radionuclide for nuclear medicine (1970-2007)*

From the data shown in Fig.2 it can be seen that the number of publications on cyclotron production of palladium for medical diagnostics during 1997 to 2005 has increased. This is explained by the use of palladium for brachytherapy and for ever-growing application of PET diagnostics.

In production of palladium, Iran (≈ 36%), Belgium (≈ 19%) and Roumania (16%) are among the leaders. Most publications (92%) are written in English.

Figures 3 and 4 illustrate the increase in the total number of publications by all IAEA member-countries on the problems of cyclotron production of SL radionuclides (iodine-123, iodine-124, copper-64, copper-67, ytterbium-169, strontium-89) for nuclear medicine over a period from 1972 to 2007. Much as in the analysis of publications on USL radionuclides, Figs.3 and 4 give the data on the relative contribution of different countries to the total number of publications and the type of these publications on the above-mentioned problem. The data on the languages, in which the information was published, are also presented.

It can be seen from the data presented in the figures that the number of publications on iodine-123 and iodine-124 has increased for the mentioned period by factors of 200 and 30, respectively. The lead-

ing position in the number of publications on iodine-123 belongs to Belgium (13.7%) and USA (10.9%), while Germany (23.3%) and the USA (13.3%) are the leaders in the number of publications on iodine-124. The main kinds of publications on the above-mentioned RN are the articles (31%) and the proceedings of conferences (≈ 37%). English is the predominant language of publications: 70% for iodine-123 and 90% for iodine-124.

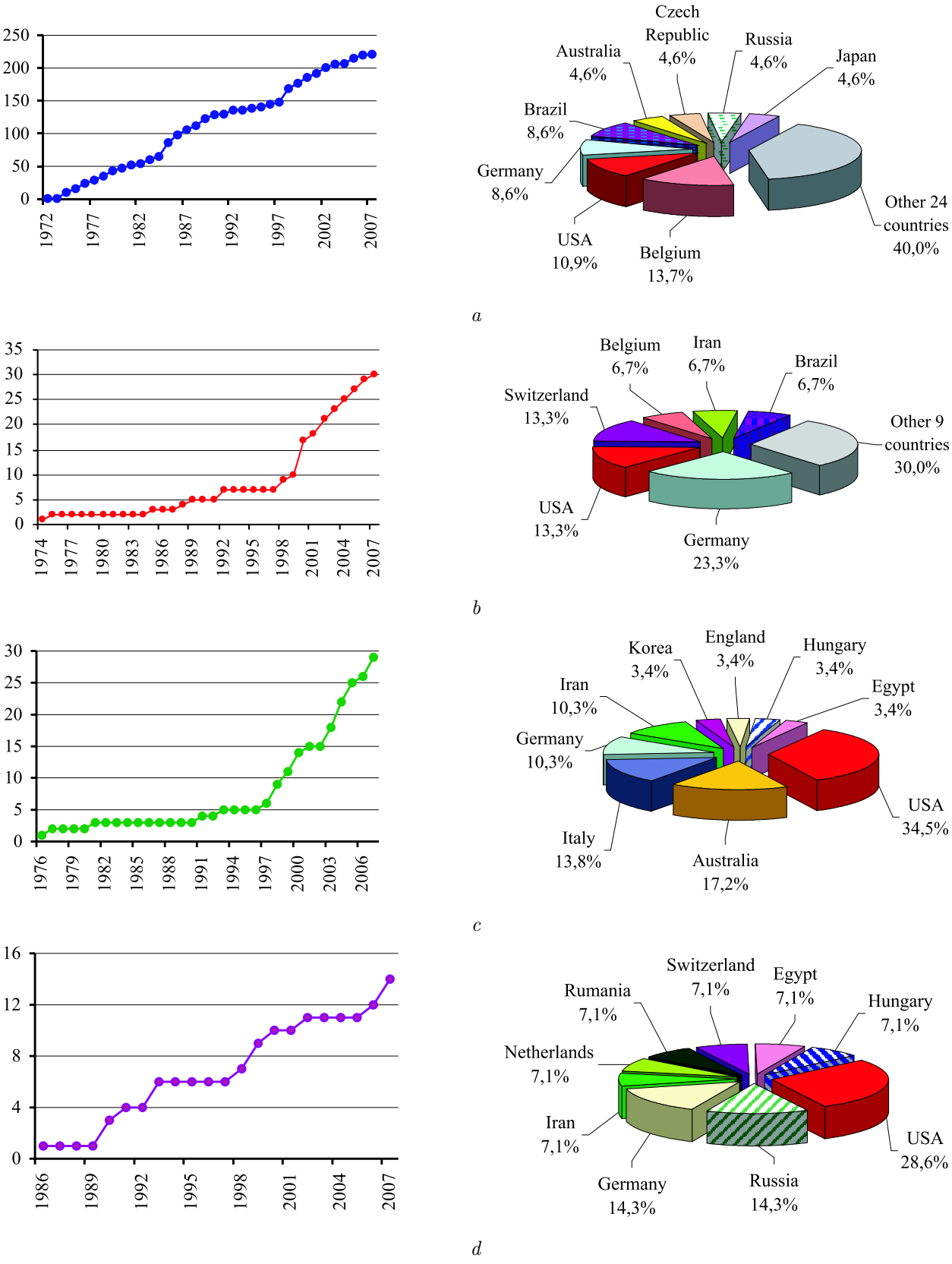

Fig.3. *Cumulative growth in the number of publications on cyclotron production of SL radionuclides for nuclear medicine (1970-2007): a) iodine-123, b) iodine-124, c) copper-64, d) copper-67*

The analysis of Fig.3 (c, d) shows that the number of publications on copper-64 and copper-67 has increased for the 1970-2007 period by factors of 30 and 15, respectively. The leading position in the number of publications belongs in both cases to the USA. The language of publications is mainly English ($\approx 95\%$).

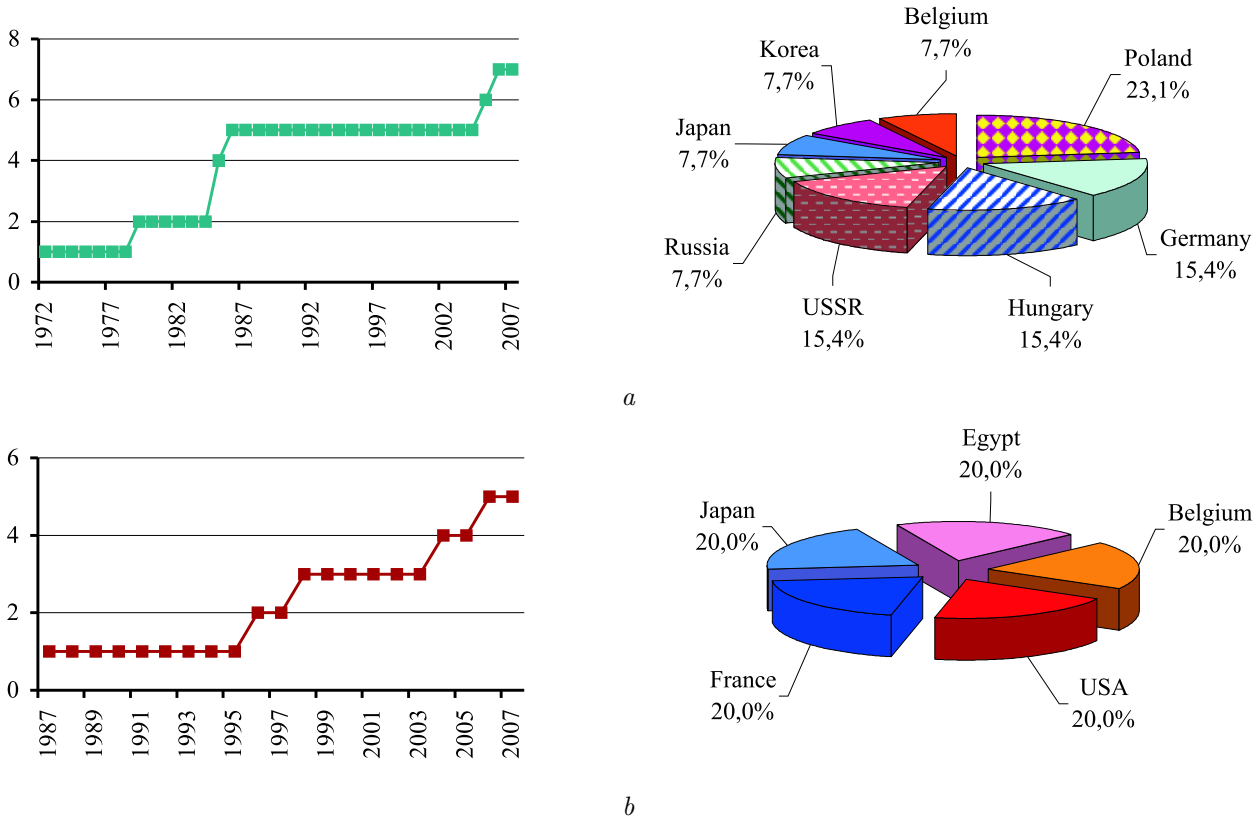

Fig.4. *Cumulative growth in the number of publications on cyclotron production of SL radionuclides for nuclear medicine (1970-2007): a) ytterbium-169, b) strontium-89*

The data on ytterbium are presented in Fig.4(a).

The number of publications on production of ytterbium-169 has substantially increased for the above-mentioned period. Among the countries leading in the number of publications we mention the former Soviet Union (15%), Hungary (15%), Germany (15%), Poland ($\approx$ 23%). The main kinds of publications are as follows: articles (30%), reports (30%), and proceedings of conferences (30%). The language of publications is mainly English (42%).

The foregoing data demonstrate that the investigations concerned with the application of cyclotrons to production of radionuclides for nuclear medicine are steadily advancing. A particularly noticeable growth (200- to 300-fold increase) can be observed in the case of cyclotron production of ultrashort-lived isotopes of carbon-11, nitrogen-14, oxygen-15 and fluorine-18, this being due to the use of USL RN in PET diagnostics. As it is known, by 2005, only in the USA there were 2000 PET centers, 5 PET centers in Russia and none in Ukraine.

4. CONCLUSIONS

The analysis of publications on cyclotron production of USL and SL radionuclides for nuclear medicine, taken from the INIS Database, testifies to a continuous growth of their number in different countries, and hence, to the urgency of the problematics.

The main cyclotron radionuclides are intended for medicine, industry and scientific purposes. Medicine is the area, where the cyclotron radionuclides are in most common use for diagnostic and therapeutic purposes.

It is known that radionuclide diagnostics methods are widely used in current world clinical practice. Of particular importance has been the recent appearance of medical techniques and apparatus, which enable the use of USL radionuclides, most optimum from the viewpoint of diagnostics and radiation safety. Due to the fact that most of them present the isotopes of chemical elements, which actively participate in the body life activity, the arsenal of current practical medicine has acquired, owing to PET, a unique possibility of patient examination at the functional level, at the level of metabolic activity and vital actions occurring in the living body. This provides a complete and, what is of importance, early diagnostics of many main diseases of the man (oncological, cardiovascular diseases, etc.), and also, their individual characteristics and special features.

In developed countries, radionuclide examinations of people are carried out every 3-5 years. In the USA,

for example, in 1990 there were ten million diagnostic procedures performed with radionuclides.

The potential requirements for nuclear medicine technologies are enormous in Ukraine. The nuclear medicine is at a new level of development in the whole world. This concerns, first of all, the PET and radionuclide therapy. Ukraine must not be an exception in this respect. The cyclotron CV-28 to be commissioned at the NSC KIPT [16] can indeed become the manufacturer of cyclotron products for nuclear medicine in Ukraine and adjacent regions of Russia, Byelorussia and Moldova.

References

1. A.N. Dovbnya, N.P. Dikiy, O.V. Nemashkalo, A.I. Tutubalin, V.L. Uvarov. A.G. Shepelev, B.I. Shramenko, L.D. Yurchenko. The status of the problem of accelerator/reactor production of various-purpose radionuclides // *Visnyk Kharkivs'kogo Natsional'nogo Universitetu N619, series fis. "Yadra, chastynky, polya", 2004, iss. 1(23), p.58-64* (in Russian).

2. Nuclear Date for Production of Therapeutic Radionuclides, Summary Report of Second Research Coordination Meeting // *IAEA.* Viena, 2004.

3. V.Yu. Baranov. *"Isotopes": properties, production and application.* Moscow: "Nauka", "Fizmat. Lit.", 2005, p.328 (in Russian).

4. Yu.T. Petrusenko, L.I. Nikolaichuk, A.I. Tutubalin, A.G. Shepelev, T.A. Ponomarenko. Production of ultrashort- and short-lived isotopes at the cyclotron CV-28 for nuclear medicine // *PAST. Series "Nuclear Physics Investigations".* 2009, N3(51), p.75-81.

5. N.S.MacDonald, J.S.Cook, R.L.Birdsall, et al. Proc. of the 27th conference on remote systems technology. La Grange Park, IL. American Nuclear Society, 1980, p. 314-315.

6. H.B.Hupf, S.D.Tischer, F.Al-Watban // *Nuclear Instrument and Methods in Physics Research.* Section B. 1985, v.10/11 (pt.2) p.967-968.

7. S.C.Yones, W.M.Buselewich, R.A.Brissette, et al // *International Journal Applied Radiation and Isotopes.* 1977, v.28(1-2), p.25-28.

8. R.Finn, P.Plascjak, Y.Sheh, et al. // *Nuclear Instruments and Methods in Physics Research.* Section B. 1987, v.24/25 (pt. 2), p.954-956.

9. M.De-Bruin, G.De-Haas, G.Hogenhius, et al. // *Radioactive isotopes in clinic and research, Gastein international symposium 1984*, (Hoefer,-R.; Bergmann,-H., eds.), Vienna, Egermann 1984. v.16, (pt.1), p. 101-108.

10. R.Bett, J.G.Cuninghame // *Computer assisted functional analysis.* Stuttgart, 1982, p.289-293.

11. G.J.Beyer, G.Pimentel, O.Solin, et al. // *Isotopenpraxis* (Aug 1988), v.24(8), p.297-303.

12. D.Graham, I.C.Trevena, et al // *Journal of Nuclear Medicine.* 1984, v.25(5) p.32.

13. V.A.Ageev, A.I.Bezruk, V.I.Bykov. Proceedings of International conference on cyclotrons and their application // *Join. Inst. For Nuclear Research.* Dubna (USSR). 1985, p.294-298.

14. R.M.Lambrecht, M.Sajjad, R.H.Syed, et al // *Nuclear Instruments and Methods in Physics Research.* Section A. 1989, v.282(1), p.296-300.

15. S.A.C.Mestnic, J.Mengatti, W.Nieto, et al. // *Proc. 1 National Forum of Science and Technology on Health.* (Costa,-E.T.; Martins,-H.L.; Muehlen,-S.S. et. al, eds), MG (Brazil). 1992, p.467-469.

16. A.M. Yegorov, A.G. Lymar', I.M. Neklyudov, Yu.T. Petrusenko. A compact cyclotron CV-28 and the prospects of its use at NSC KIPT // *Voprosy atomnoj nauki i tekhniki. Ser. "Yadernofizicheskie issledovaniya".* 2008, N5(50), p.12-15 (in Russian).

АНАЛИЗ МАССИВА ПУБЛИКАЦИЙ ПО ПРОИЗВОДСТВУ МЕДИЦИНСКИХ РАДИОИЗОТОПОВ НА ЦИКЛОТРОНАХ

Ю.Т. Петрусенко, А.Г. Лымарь, Л.И. Николайчук, А.И. Тутубалин, А.Г. Шепелев, Т.А. Пономаренко, О.В. Немашкало

Дан анализ состояния производства на циклотронах радионуклидов (РН) для ядерной медицины. Рассматривается проблема получения ультрокороткоживущих (УКЖ) и короткоживущих (КЖ) РН. При анализе использовалась информация, содержащаяся в Международной Базе Данных МАГАТЭ "International Nuclear Information System"(INIS) за период с 1970 по 2007 г. Приводятся сведения о динамике публикаций по производству циклотронных УКЖ и КЖ РН, о виде публикаций, а также об относительном вкладе различных стран в общее число публикаций. Сделаны заключения о тенденции развития исследований по рассмотренным вопросам.

АНАЛІЗ МАСИВУ ПУБЛІКАЦІЙ ПО ВИРОБНИЦТВУ МЕДИЧНИХ РАДІОІЗОТОПІВ НА ЦИКЛОТРОНАХ

Ю.Т. Петрусенко, А.Г. Лимарь, Л.І. Ніколайчук, А.І. Тутубалін, А.Г. Шепелєв, Т.О. Понамаренко, О.В. Немашкало

Наведено аналіз стану виробництва на циклотронах радіонуклідів (РН) для ядерної медицини. Розглядається проблема отримання ультрокороткоживучих (УКЖ) та короткоживучих (КЖ) РН. При аналізі використовувалася інформація, що міститься у Міжнародній Базі Даних МАГАТЕ "International Nuclear Information System"(INIS) за період з 1970 по 2007 р. Приведено результати відносно динаміки публікацій з виробництва циклотронних УКЖ і КЖ РН, відносно вигляду публікацій, а також відносно вкладу різних країн в загальне число публікацій. Зроблено висновки відносно тенденції розвитку досліджень з розглянутих питань.