https://doi.org/10.15407/scine19.05.043

DANYLENKO, Yu. A. (https://orcid.org/ 0000-0002-7251-7071),
and NEPOKUPNA, T. A. (https://orcid.org/0000-0002-2987-4671)
Institute for Scintillation Materials of the National Academy of Sciences,
60, Nauky Ave., Kharkiv, 61072, Ukraine,
+380 57 341 0161, info@isma.kharkov.ua

ANALYSIS OF SCINTILLATION MATERIALS FOR NUCLEAR MEDICINE ON THE BASIS OF PATENT ANALYTICS

Introduction. *It is known that the object of intellectual property is an important source of technological information that can be used for assessing the industry development and the prospects for further study of scintillation materials, finding competitors, etc.*

Problem Statement. *Today, nuclear medicine is very popular all over the world. Scintillation crystals are one of the main materials used in modern diagnostic devices. Therefore, the development of highly efficient scintillation materials for medical imaging systems is a relevant task.*

Purpose. *The patent activity analysis for nuclear medicine is purposed to find out the dynamics of patenting scintillation materials used in this field for the period 1992—2022 as well as to determine the most priority and important research directions.*

Material and Methods. *The patent search has been made with the help of special search programs: information database Lens.org and specialized database Inventions (Utility models) in Ukraine. While doing the research, we used the methods of analysis, systematization, and comparison.*

Results. *Assessing the development of scintillation materials for nuclear medicine based on patent analysis allows us to analyse the available scintillation materials for this industry, to find new materials for it, and to identify more promising directions for its development.*

Conclusions. *American companies have the largest number of patents on scintillation materials used in nuclear medicine, but in the Ukrainian market, there are similar patents. The main scintillators for nuclear medicine are BGO, $CdWO_4$, $ZnWO_4$, LSO, LYSO, GSO, NaI, CsI, BaF_2, $LaBr_3$, LuAP, LuAG, GGAG, LGSO, CaF_2 : Eu, ZnSe : Te, Gd_2O_2S : Tb or mixed scintillators such as $NaBaLaBr_6$, $Cs_2NaLaCl_6$, etc. in the design of pixels. They are used as bulk crystals, ceramics, films and others. There appear patents on new materials, such as $MAPbBr_3$, $CeBr_{3+x}$, $Tl_2LiLaBr_6$, the properties and prospects for application of which have been currently being studied.*

Keywords: nuclear medicine, scintillation material, object of intellectual property, and analytical data.

Citation: Danylenko, Yu. A., and Nepokupna, T. A. (2023). Analysis of Scintillation Materials for Nuclear Medicine on the Basis of Patent Analytics. *Sci. innov.*, 19(5), 43—56. https://doi.org/10.15407/scine19.05.043

Today, nuclear medicine is very popular all over the world. Inorganic scintillators are one of the main materials for scintillation detectors, which are used in modern diagnostic devices. So currently, the development of highly efficient scintillation materials that simultaneously provide a high sensitivity of medical devices and a low radiation dose to the patient remains very relevant.

It is known that the main diagnostic methods in nuclear medicine are [1, 2] as follows:

1. X-ray computed tomography (CT), for which the scintillator should have a high light output and registration efficiency of X-ray, a low afterglow, a high density, and a significant stopping power, etc.

2. Single-photon emission computed tomography (SPECT) that uses scintillators with a high light output to provide a significant sensitivity of the device and its high spatial and energy resolution.

3. Positron-emission computed tomography (PET) that needs crystals with a high gamma ray registration efficiency that is associated with a high density and a high atomic number, and also with a fast decay time for better image contrast. In addition, there are special PET scanners for mammography, which should have an improved resolution (positron emission mammography (PEM)).

It should be noted that intellectual property objects (patents) are one of important source of technological information that can be used for assessing the trends in the industry development and the prospects for further study of scintillation materials, finding competitors, etc.

In view of the above, we can say that the analysis of patent activity in the field of nuclear medicine, the identification of the dynamics of patenting the scintillation materials that can be used in medical diagnostic devices, and the determination of the most priority areas of research are very important and, therefore, are the purpose of this research.

Patent activity is the number of intellectual property objects, namely patents on inventions or utility models, obtained over a certain period of time.

We have formed the patent search task, defined the keywords and search characteristics, selected the CPC classification codes for the patent search, for example, G01T1/00: Measuring X-radiation, gamma radiation, A61B6/00: Apparatus for radiation diagnosis, e.g. combined with radiation therapy devices, etc. The patent search is carried out with the help of special search programs: information databases Lens.org and specialized databases Inventions (utility models) in Ukraine (base.uipv.org). During the research, the methods of analysis, systematization, and comparison have been used.

The geographic concentration of patents is spread over the whole world, the retrospect of the patent search is 30 years. During the research, we have used the methods of analysis, systematization, and comparison.

Figure 1 shows a diagram as a ratio of the number of filed, granted, published patents for scintillation detectors for nuclear medicine by years.

As we can see from the diagram (Fig. 1), the patent activity in the field of the development of scintillation detectors for nuclear medicine started to increase in the 1990s and reached its peak in terms of the number of patents in 2002–2012. This is due to the possibility of manufacturing large-area scintillation detectors, the improvement of electronic devices for scintillation signal processing, changes in the policy of insurance medicine in the USA. All this had led to a significant increase in funding of research in this field and, as a result, to an increase in the number of patents in the field of medicine. However, nowadays, the number of filed applications, like the number of published patents, has halved as compared with 2002–2012. This means the market has been oversaturated with patented solutions, although at this time these materials are still widely used in nuclear medicine. We can also see from the diagrams, more than half of the patents are not maintained, while since 2012, the number of the valid ones has decreased from 1,500 to about 700. Within the period from 2012 to 2022, this number was constant, so we may suggest that these patents are still relevant today.

The main patent applicants for new scintillation devices in nuclear medicine are representa-

 ISSN 2409-9066. Sci. innov. 2023. 19 (5)

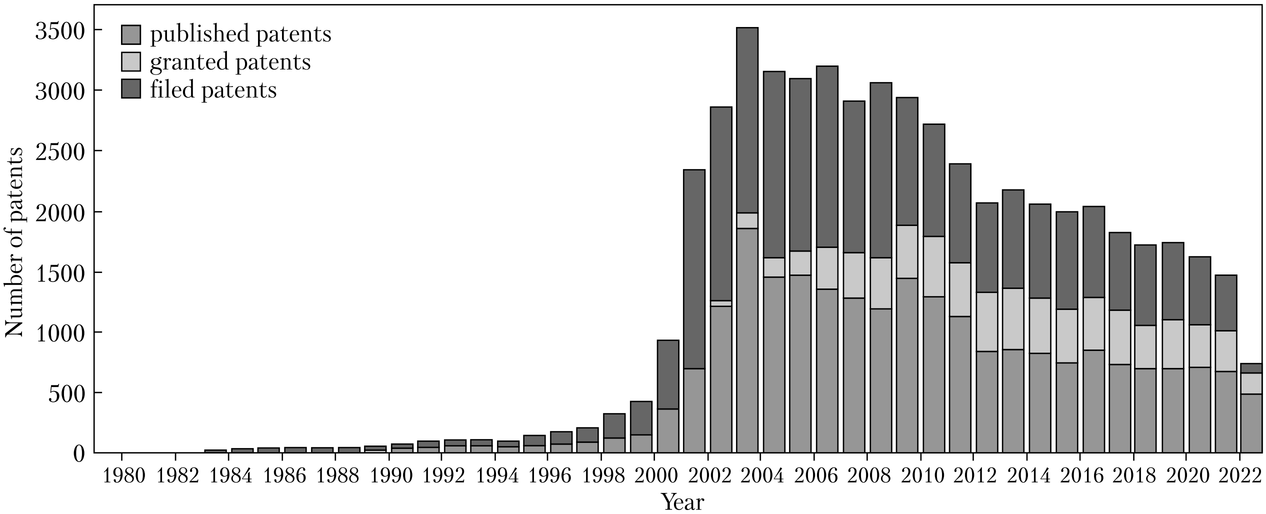

Fig. 1. The dynamics of the number of patents on scintillation detectors for nuclear medicine

tives of the USA, which account for about 8,000 patents, namely: Merck Sharp & Dohme Corp., Human Genome Sciences INC, Bristol-Myers Squibb Company, General Electric Company, Astrazeneca Ab, The Regents of the University of California, Millennium Pharmaceuticals INC, National Institutes of Health (NIH), Janssen Pharmaceutica Nv, Siemens Medical Solutions Usa INC, etc. The distribution of the number of patents for these applicants is given in Fig. 2.

There have been many simple and extended patent families in this region. For example, the US extended patent family [3] includes 19 patents, 18 of which are valid today. The applicant is Minnesota Imaging and Engineering LLC. Patent describes the detector module designs for radiographic imaging, which include the first and the second layers of scintillator rods or pixel arrays oriented in the first and the second directions.

It is known that the most significant discovery in the scintillation field is the obtainment of the NaI:Tl crystal in the mid-1940s. This scintillator has a significant light output that is higher than that of many available scintillation materials [4]. There are also industrial technologies for growing large-sized NaI : Tl crystals. However, this scintillator is hygroscopic and has a high afterglow, which can significantly affect the intensity of pulse counting. In addition to NaI : Tl that is commonly used in SPECT, there is CsI:Tl that is also used in CT, SPECT, and PET systems. This scintillator has a light output of 54000 photons/MeV and a weak hygroscopicity [5—7].

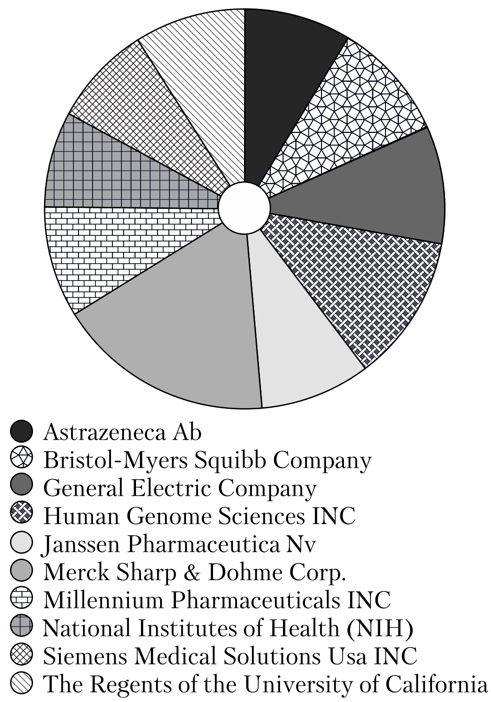

Fig. 2. The number of patents hold by the main applicants for patents on new scintillation devices for nuclear medicine

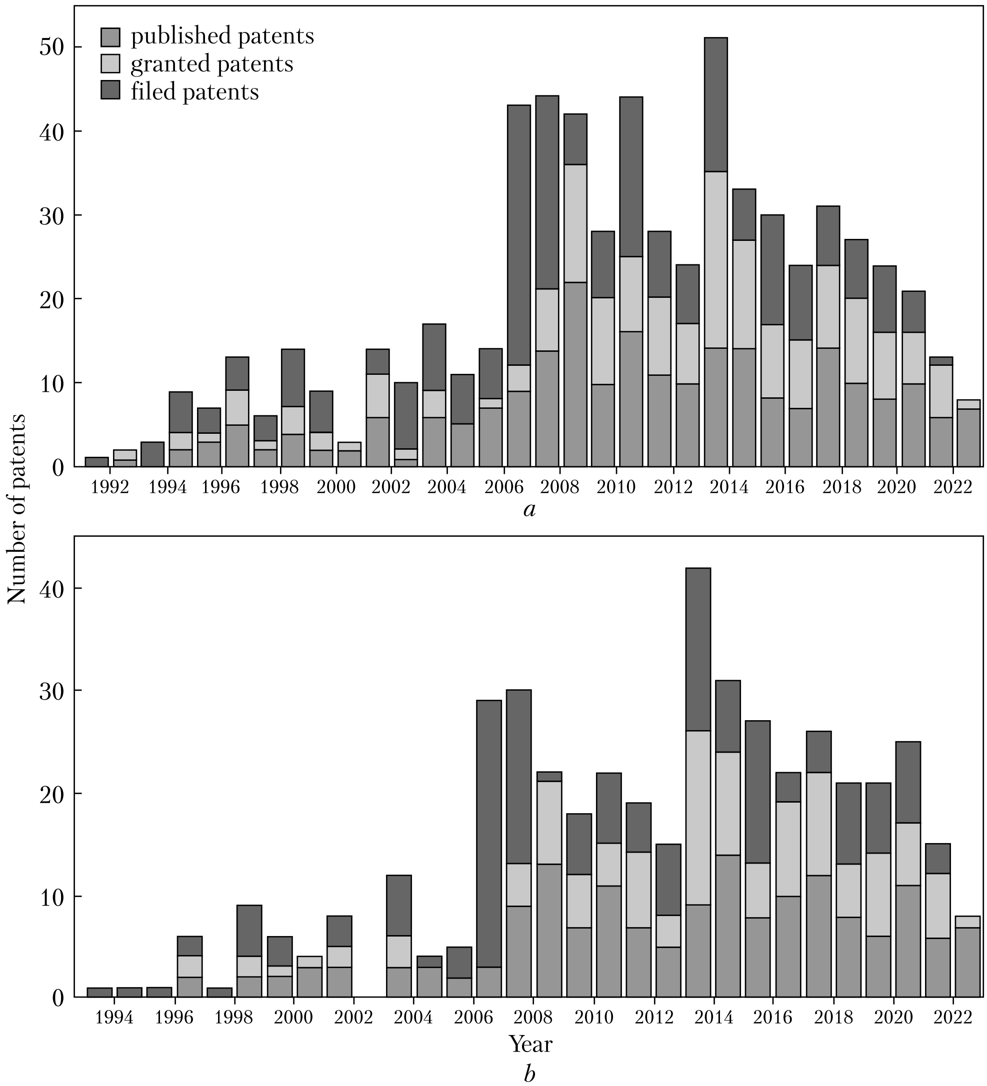

Fig. 3. The dynamics of the number of patents on scintillation materials with alkali halide crystals for nuclear medicine

The main global holders of patents on medical devices in which alkali-halide crystals are used are American companies: Spectrum Dynamics LLC, Biosensors Group International LTD, and Spectrum Dynamics Medical Limited.

There are also Ukrainian patents UA 87792 [8] and UA 93840 [9] for a scintillation material based on cesium iodide doped by thallium iodide, as well as UA108798 [10] for a method of obtaining alkali-halide scintillation crystals (the applicant is the Institute for Scintillation Materials of the National Academy of Sciences of Ukraine (hereinafter referred to as ISMA of the NAS of Ukraine).

As one can see, for more than 20 years, these scintillation materials for medical devices are associated with a very high patent activity (Fig. 3, *a, b*), but in recent years, this patent activity has been showing a downward trend.

However, the further development of alkali-halide scintillators is associated with their compositions with other compounds. For example, patent [11] for a radiation monitoring device (the holder

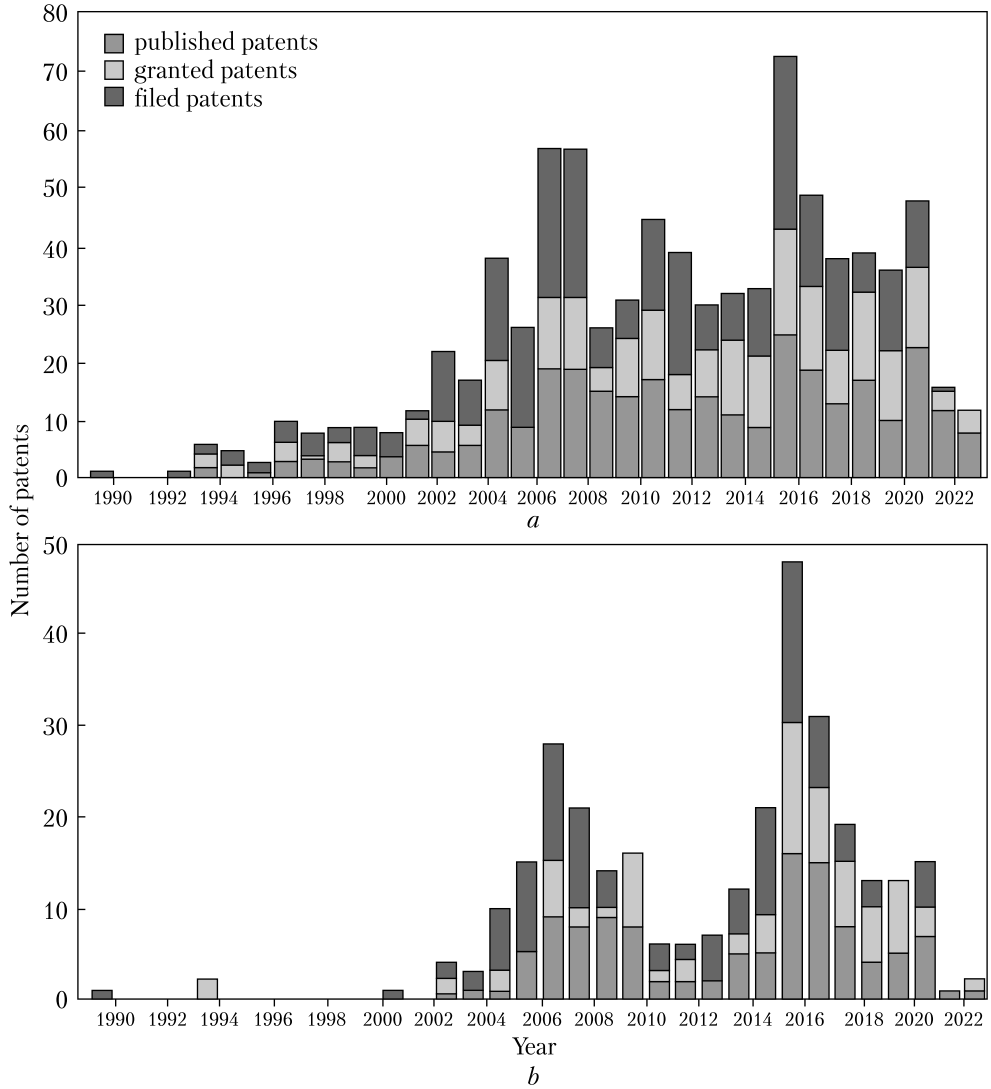

Fig. 4. The dynamics of the number of patents on scintillation devices with BGO (*a*) and GSO (*b*) for nuclear medicine

is Radiation Monitoring Devices Inc) includes a mixed halide scintillator composition that contains at least two different Cs, Na, La halide compounds (Cs_2NaLaF_6, $Cs_2NaLaBr_6$, $Cs_2NaLaCl_6$, Cs_2NaLaI_6) and Ce as a dopant, in which the scintillator may have crystalline, ceramic, or polycrystalline ceramic structure.

Simple family [12] by the same US holder consists of 4 patents, where the scintillator composition may include, for example, a scintillation compound and a dopant. The scintillation compound has the formula, x_1-x_2-x_3-x_4 where x_1 is Cs; x_2 is Na; x_3 is La, Gd, or Lu; and x_4 is Br or I, and a dopant or mix of dopants Ce, Lu, La, Eu, Pr, Sm, Sr, Tl, Cl, F, or I (for example, $Cs_2NaGdI_6 : Ce$, $Cs_2NaLaI_6 : Ce$, or $Cs_2NaLuI_6 : Ce$).

The following oxide scintillators have application as a scintillation material in nuclear medicine devices: $Bi_4Ge_3O_{12}$ (BGO), $Gd_2SiO_5 : Ce$ (GSO), and $Lu_2SiO_5 : Ce$ (LSO).

For example, the combined Nuclear and Sonographic Imaging Apparatus [13] comprises nuclear

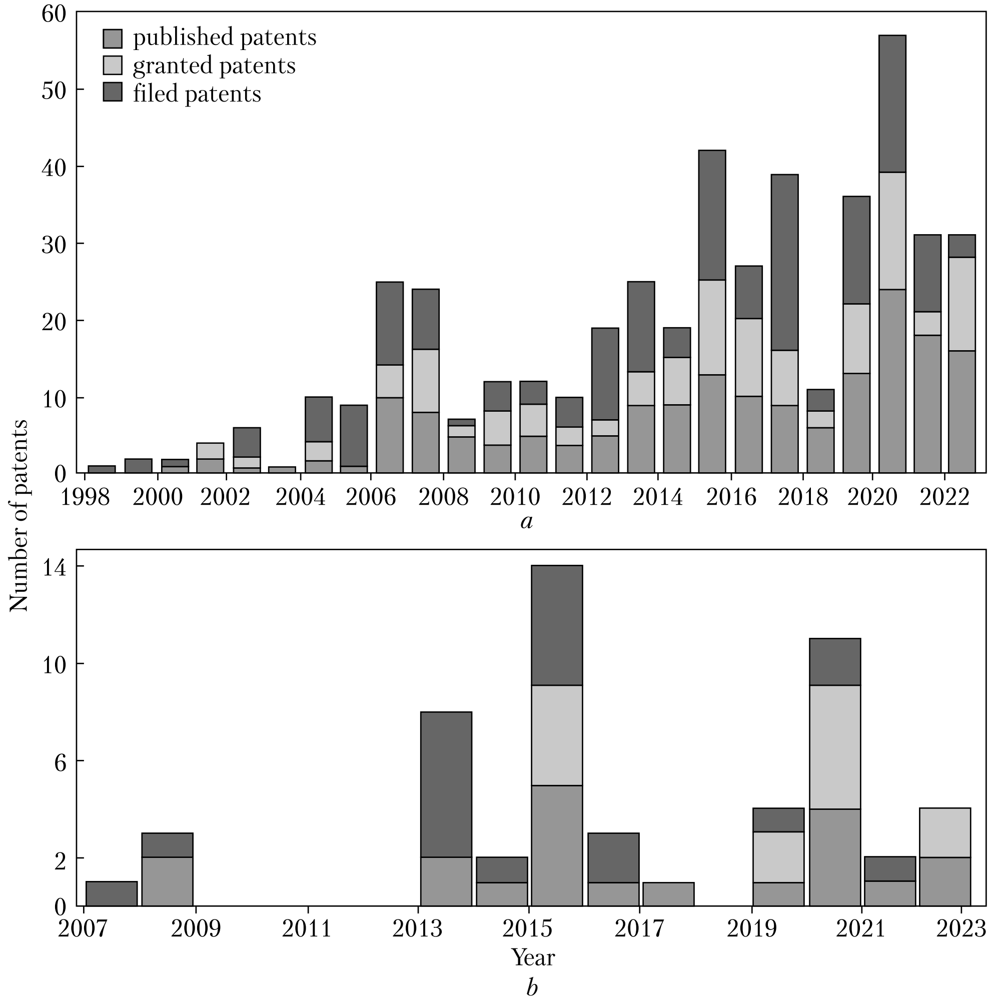

Fig. 5. The dynamics of the number of patents on scintillation materials with LSO (*a*) and LYSO (*b*) for nuclear medicines

medicine imaging means including detector, where scintillator crystals consist of individual pixels or monolithic blocks made of one or more of the following scintillating materials: LSO, LYSO, LuAP, LuYAP, BGO, GSO, LGSO, $LaCl_3$, and $LaBr_3$.

The BGO crystals are non-hygroscopic and have a fast decay time, a high density and a high atomic number, which allows significantly reducing the size of crystals in detectors. However, the disadvantage of BGO is a long afterglow and a low light output (15% of NaI : Tl), which results in a reduction in the energy resolution and a decrease in the refractive index, which leads to the loss of scintillation light because of internal reflection [14].

The GSO crystals are non-hygroscopic and high-density fast scintillators, but their light output is 20% that of NaI : Tl. The BGO [15, 16] and the GSO [17, 18] crystals are used in gamma radiation detectors for PET systems.

The main holders of patents on BGO are American companies: General Electric Company, Minnesota Imaging and Engineering LLC, Toshiba Medical Systems Corporation, Kabushiki Kaisha Toshiba, Radiation Monitoring Devices INC, and Siemens Medical Solutions USA INC. The main package of patents on GSO scintillation materials is held by General Electric Company (the USA).

Figure 4, *a, b* shows that in the last 20 years, the BGO and GSO scintillation materials have been widely used in detectors for nuclear medicine. About 20 patents are filed annually for the last fifteen years. That is, the BGO and GSO materials, which were developed in the 1990s, are still quite relevant today.

Patents UA 77593 [19] for the method of growing BGO monocrystals (the applicant is ISMA of the NAS of Ukraine) and UA 9942 [20] for the method of heat treatment of BGO crystals (the applicant is Institute of Monocrystals of the NAS of Ukraine) have represented Ukraine in the market of scintillators.

The LSO crystal has been widely used due to the fact that it has a high density, is non-hygroscopic, its light output is close to 75% of that of NaI:Tl, and the decay time is 42 ns, which makes it possible to produce large crystals and to use them in PET. However, the long decay of the radioactive isotope Lu^{176} can affect the parameters of highly sensitive detectors due to the fact that the crystal has very deep capture centers [21]. The dynamics of patenting LSO is shown in Fig. 5, *a* that shows how many patents have been issued for this material since 2012.

The crystal scintillators based on cerium-doped rare-earth oxyorthosilicate (LFS, LSO, LYSO, LGSO, and GSO) have defects in comparison with the ideal crystal structure. These defects change the optical transmission and absorption spectra in the range of approximately 200—340 nm. They underlie the invention that is subject of application [22] (the applicant is Zecotek Imaging Systems Singapore Pte Ltd) and can be useful for PET scanners, SPECT, positron emission tomography with magnetic resonance imaging. The invention deals with improving the scintillation materials that have the emission maximum in the range of about 400—450 nm.

There is an extended family of five patents [23], which comprises the positron emission tomography detector in which the scintillator is any of BGO, LSO, LYSO, LuAP, LuYAP, $LaBr_3$, LuI_3, GSO, LGSO, and LuAG (the holder is Sogang University Research Foundation).

The LYSO scintillation crystal has a high light output, a fast decay time, a high density, and stable physical and chemical properties [24]. Therefore, LYSO : Ce is well suitable for the devices that require the best energy resolution. The number of patents with this material is not as significant as that for the above mentioned materials (Fig. 5, *b*), but the material is used for PET scanners and SPECT.

The scintillators based on $LuGdSiO_5$: Ce (LGSO) crystal have a high light output, but at the same time, a high afterglow, which can affect the energy resolution of scintillation detectors [25]. The number of patents on the devices that use this scintillation material is shown in Fig. 6. One can see, the peak of the use of this material in the patents has already been passed.

ISMA of the NAS of Ukraine is the applicant for inventions UA 87767 [26] (the nanocrystalline lutetium oxyorthosilicate glow powder activated by rare earth metals, which has the general formula $Lu_{2-x-z}Ce_xRe_zSiO_5$, where Re is Yb or Dy, $0.0002 \le x \le 0.1$ and $0 \le z \le 0.001$), UA 108932 [27] (the method for surfacing a crucible with a charge for growing high-temperature oxides), and UA 92705 [28] (the method for obtaining a melt for growing crystals of lutetium and gadolinium oxyorthosilicates doped with cerium).

The extended patent families relates to a set of multi-doped cerium-activated scintillation materials of the solid solutions on the basis of the rare earth silicate that comprises lutetium and have compositions represented by the chemical formulas: Lu2-w-x+2yAwCexSi1-y)1-zMexJjOq and (Lu2-w-x-2yAwCexSi1+y)1-zMezJjOq. The invention is useful for TOF PET and DOI PET scanners, SPECT, PET/MR, and for X-ray computer fluorography.

The scintillation materials Lu_2SiO_5:Ce, $LaBr_5$: Ce, LuYAP : Ce, and $LuAlO_3$: Ce are used in scintillation elements of X-ray radiation detector module, e.g. X-ray-computer tomography-device [30]; the applicant is Siemens AG.

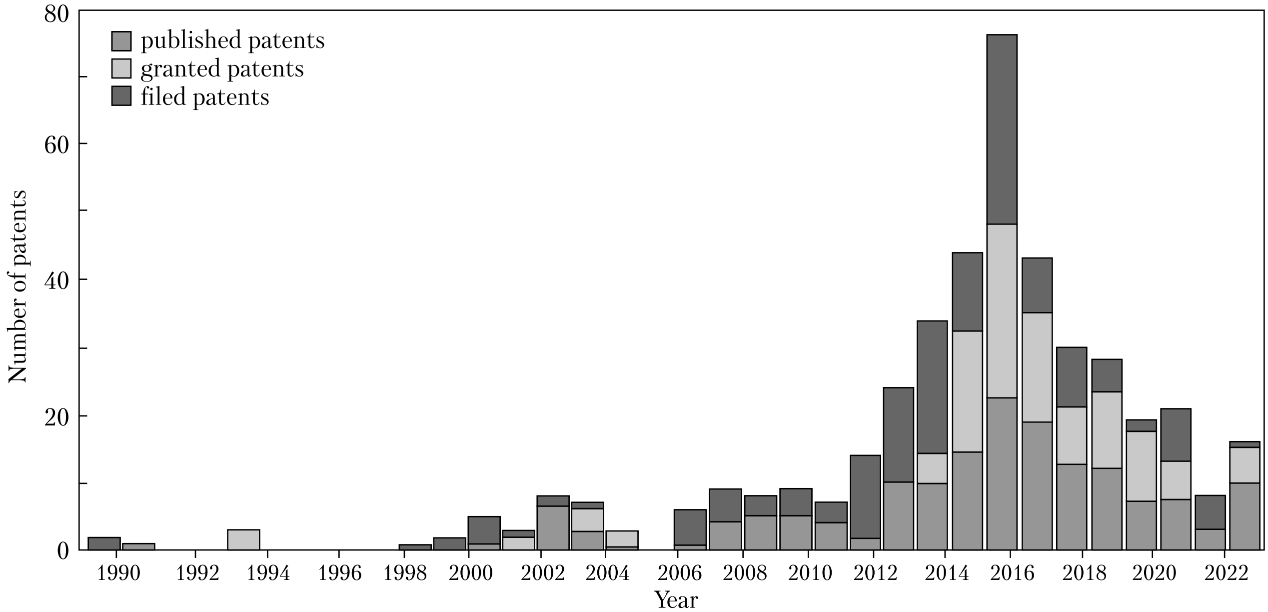

Fig. 6. The dynamics of the number of patents on scintillation devices with LGSO

$YAlO_3$: Ce (YAP) is also used in X-ray medical systems. It is a non-hygroscopic, mechanically stable scintillator with a relatively high density and light output, has a fast decay time of about 27—28 ns [31]. Figure 7 shows the number of patents obtained for YAP scintillation material. One can see that the number of patented solutions for this material has significantly decreased over the last five years.

The extended patent family [32] consists of 20 patents, 14 of which have been published; the holder is Dkfz Deutsches Krebsforschungszentrum. Currently, these patents have been employed by 26 companies. The invention relates to the optical imaging detector and the method for fluorescence and bioluminescence imaging of an imaged object, which that can be employed for tomographic imaging. The invention is purposed for providing a highly compact optical imaging detector with a high detection sensitivity, a high intrinsic spatial resolution, and a high time resolution. The PET detectors consist of the most advanced materials in the form pixelized crystals optically mounted to position-sensitive photo multiplier tubes.

There is also another extended family of 11 patents US 8923588 B2 [33] for pixelated scintillators, non-pixelated or homogeneous scintillators of LSO, LYSO : Ce, LuYAP : Ce, LuAP : Ce, LGSO, LaBr, LaCl, GSO, BGO, and mixes thereof.

Patent [34] (the holder is ISMA of the NAS of Ukraine) deals with the technology for growing oxide crystals activated by cerium, in particular garnets ($Y_3Al_5O_{12}$:Ce, $Lu_3Al_5O_{12}$: Ce, $Tb_3Al_5O_{12}$: Ce, etc.) and perovskites ($YAlO_3$: Ce, $LuAlO_3$: Ce, etc.) from molybdenum or tungsten crucibles by the methods of Chochralsky, Kiropoulos, EFG (Edge Defined Film Fed Growth), TGT (Temperature Gradient Technique), VGF 5 (Vertical Gradient Freeze), and others, in a protective reducing atmosphere.

$LaCl_3$:Ce scintillation crystal [21] has a stable light output similar to NaI:Tl, but a much better energy resolution and a fast decay time. $LaCl_3$: Ce is a promising scintillation crystal for various applications, including gamma radiation detection and nuclear medicine imaging (PET, SPECT).

One of the most promising from the point of view of efficiency and energy resolution is the $LaBr_3$: Ce scintillator [21]. These crystals have a light output that is 1.3—1.7 times higher than that of

NaI:TI, a fast decay time, a high density and a high atomic number, but they are hygroscopic and have a significant intrinsic background. Usually, it can be employed in medicine in PET and SPECT.

The scintillation material based on rare earth elements with reduced radioactive background has been patented by Saint-gobain cristaux et detecteurs, UA 87683 [35]. Another applicant for the method of obtaining bromide scintillation single crystals of high purity is ISMA of the NAS of Ukraine [36].

US 2022/0206168 A1 [37] (the holders are Universitat Politecnica De Valencia, Consejo Superior De Investigaciones Cientificas (Csic), family of 5 patents) deals with the device for detecting Gamma Rays with the following scintillators:

- the organic crystal scintillators: antracene, stilbene, and/or naphthalene;
- the inorganic crystal scintillators: CsI, CsI : Tl, BGO, NaI:Tl, BaF_2, CaF_2:Eu, $CdWO_4$, $LaBr_3$: Ce, ZnS : Ag, LYSO, CsF, KI : Tl, CaF_2 : Eu, GSO and/or LSO;
- the liquid scintillators: p-terphenyl ($C_{18}H_{14}$), 2-(4-biphenylyl)-5-phenyl-1,3,4-oxadiazole PBD ($C_{20}H_{14}N_{20}$), butyl PBD ($C_{24}H_{22}N_{20}$), PPO ($C_{15}H_{11}NO$) dissolved in such solvents as toluene, xylene, benzene, phenylcyclohexane, triethylbenzene or decalin; and
- the gaseous scintillators: nitrogen, helium, argon, krypton, and/or xenon.

There is known patent family US 2007/0284534 consisting of 9 patents (the holder is General Electric Company), where the radiation detector for a positron emission tomography device includes a crystal scintillator that has the following composition: an array material, at least with one element selected from the group consisting of alkaline earth metals and lead; at least one lanthanide halide; an activator for the array material that contains cerium, praseodymium, or a mix of cerium and praseodymium; for example, $BaGdCl_5$, Ba_2GdCl_7, Ba_2LaBr_7, Ba_2LaI_7, Sr_2YCl_7, $BaSrYCl_7$, $BaSrLuBr_7$, Ca_2YBr_7, $NaBaLaBr_6$, $CsCaGdCl_6$, etc.

The next scintillator with a high density, a high atomic number, and a relatively high light output is $CdWO_4$. The crystals have stable mechanical properties, a low afterglow, are non-hygroscopic, and easy to work with. The light output varies within 30—50% of that of NaI:Tl. The high density makes $CdWO_4$ an effective absorber, especially for high-energy X-rays, and is optimal at this time.

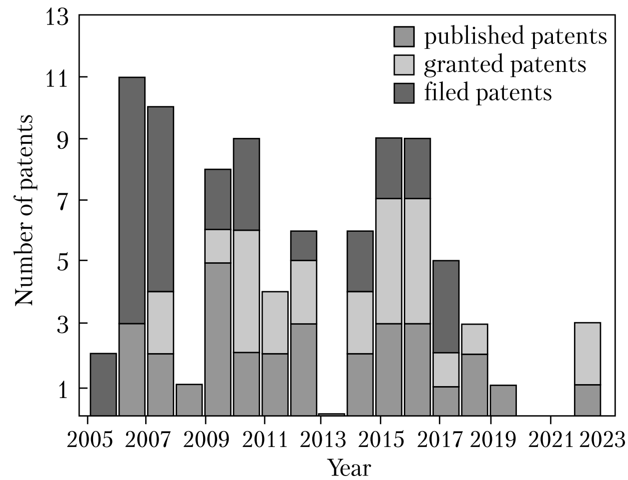

Fig. 7. The dynamics of the number of patents on YAP scintillation material

In the market, there are the following Ukrainian patents: UA77543 [39] for the method of growing scintillation monocrystals of doped $CdWO_4$, UA86104 [40] for the method of thermal treatment of scintillation monocrystals $CdWO_4$, and UA105335 [41] for scintillation monocrystals based on $ZnWO_4$. The applicant for these patents is ISMA of the NAS of Ukraine.

Aluminium-gallium garnet $Gd_3Al_2Ga_3O_{12}$: Ce, (GaGG : Ce) is recently decomposed scintillator that has a high density, a high photon emission, a high energy resolution and is non-hygroscopic. The authors of [42] have found that GaGG : Ce crystal is an excellent candidate for the further development of visualization systems (PET, PEM, SPECT, CT), especially those based on the Compton distribution and depends critically on energy resolution.

Ukrainian patent [43] (the holder is ISMA of the NAS of Ukraine) deals with the technology for obtaining oxide single crystals. The invention can be used for preparing iridium crucibles before growing single crystals with a melting point above 1700 °C, such as: $Gd_3Ga_5O_{12}$, $YAlO_3$, Gd_2SiO_5, $Y_3Al_5O_{12}$, Lu_2SiO_5, when the use of platinum crucibles is impossible.

Ukrainian patent [44] (the holder is ISMA of the NAS of Ukraine) refers to the technology of obtaining a melt for growing single crystals of complex oxides with melting points under 500 °C ($Bi_4Ge_3O_{12}$, $Bi_4Si_30_{12}$, $CdWO_4$, $PbWO_4$) and above 1500 °C ($Y_3Al_5O_{12}$, Lu_2SiO_5, Gd_2SiO_5, $YAlO_3$, $Gd_3Ga_5O_{12}$).

The lutetium aluminum garnets are a good choice for medical scanning systems (PET, PEM) and tomography. In particular, LuAG : Ce has such advantages as a high density and a fast decay time, which is suitable for thin image screens. LuAG : Ce crystal has a high density and a high light output, a fast decay time, and a good energy resolution, which makes it suitable for fast imaging for PET, PEM, etc.

CsI : Tl, CsI : Na, NaI : Tl, ZnS або ZnO, YAP : Ce, YAG : Ce, BGO, CaF : Eu, LuAG : Ce, GSO : Ce, $CdWO_4$, $PbWO_4$, $NaBi(WO_4)_2$, ZnSe : Te, $LaBr_3$: Ce, $CeBr_3$, and $LaCl_3$: Ce are used in patent US 7612342 B1 [45]; the holder is Radiation Monitoring Devices Inc. The patent deals with the devices for increasing the light output of a scintillator, which have a tremendous potential in many important applications, such as computed tomography (CT), SPECT, diagnostic digital radiology, etc.

Patent US6630077B2 [46] (the holder is General Electric Company) is for the scintillator compositions that have a garnet crystal structure suitable for the detection of high-energy photons, X-rays and gamma quanta, as well as beta radiation and contain at least one of terbium and lutetium. The scintillator has at least one rare earth metal and at least one of Al, Ga, and In. Terbium or lutetium may be partially substituted with Y, La, Gd, and Yb. In particular, the scintillator composition contains both terbium and lutetium. The scintillators are characterized by a high light output, a reduced afterglow, a fast decay time, and a high X-ray stopping power.

Ceramic scintillator Gd_2O_2S : Tb with a grain size from 3 to 50 μm is widely used in radiation detectors for medical diagnostics. For example, there is the method for preparation and application of gadolinium oxysulfide scintillation ceramic where gadolinium oxysulfide polycrystalline scintillation ceramic doped with at least one element of Pr, Eu, Tb, Sm, Yb, and Tm has been efficiently obtained [47]. Improved $(Gd_{1-x}Tb_x)_2O_2S$ X-ray glow powder, where x ranges from 0.0003 to 0.0045, possesses an increased brightness in the blue region of the spectrum and, at the same time, an acceptable resistance for X-ray intensifying screens [48]. An X-ray receiver with a plate X-ray optical converter based on materials of rare earth elements, cesium iodide or gadolinium oxysulfide has been developed [49, 50].

A PET scanning imager [51] (the applicants are Grirem Hi-Tech Co. Ltd, Rare Earth Functional Materials (Xiong 'An) Innovation Center Co. Ltd, and Grirem Advanced Materials Co. Ltd) contains the scintillation detector with a rare earth halide scintillation material $CeBr_{3+x}$, where $0.0001 \leq x \leq 0.1$. The rare earth halide scintillation material has excellent scintillation properties, including a high light output, a high energy resolution, and a fast decay time.

The system for gamma ray and/or neutron detection, which contains a scintillator material comprising a thallium-based halide composition (the formula is $Tl_2LiLaBr_6$) with one or more dopants selected from the group consisting of Ce, Pr, Eu, Sr, Ca, Ba, Mg, and Cd wherein the density of the composition is greater than 4 g/cm^3 (the applicant is Radiation Monitoring Devices Inc) has been patented in [52].

Multiwave Metacrystal S.A. has offered a device for detecting gamma radiation for PET applications, which uses the scintillating materials comprising BGO, LSO, LYSO, GSO, NaI, CsI, BaF_2, $LaBr_3$, LuAP, LuAG, GGAG, CdSe, polyvinyl toluene-p-terphenyl PVT-PPP, methyl ammonium lead bromide perovskite $MAPbBr_3$, or a combination thereof [53].

There is family of 10 patents [54] for low-temperature perovskite scintillators and devices with them; the holder is Deep Science Llc, Saliba

Michael. The device is configured to be operated as part of PET scanner and CT scanner. It has been determined that the light output of CsI is 100,000 ph/MeV, at 77 K, while that of MAPbBr3 is 90,000 ph/MeV and 116,000 ph/MeV, at 77 K and 8 K, respectively.

Family of 6 patents [55] for scintillating nanocrystalline compositions deals with the scintillator nanocrystalline structure of a perovskite material with a diameter from about 25 nm to about 300 nm, in which the scintillator nanocrystal contains $(Y_{1-x}Pr_x)_3Al_5O_{12}$, (YAG : Pr), where x is 0.0075, 0.01, 0.0125, 0.015, and 0.0175. This structure is a fragment of the chemical agent that is a component of drugs for treatment of infections or cancer (the applicant is the Regents of the University of California).

Increasingly, patents on new devices specify the properties the scintillation material has to possess. This allows us to extend the list of scintillation materials suitable for a certain device and to use any new scintillator that appears over time and meet the required properties.

CONCLUSIONS

1. Nowadays, the number of filed applications for patents has halved as compared with 2002—2012. The main patent applicants for new scintillation devices in nuclear medicine are representatives of the USA, but in the Ukrainian market, there are similar patents.

2. In recent years, the patent activity associated with the use of scintillation crystals CsI : Tl, CsI : Na, and NaI : Tl in medical equipment has been showing a downward trend. However, alkali-halide scintillators have been developed in compositions with other compounds such as Cs_2NaLaF_6, $Cs_2NaLaBr_6$, $Cs_2NaLaCl_6$, and Cs_2NaLaI_6.

3. The oxide scintillators are often used as a scintillation material in nuclear medicine devices: BGO, GSO, and LSO crystals have been relevant since the beginning of the 1990s. $CdWO_4$ is an optimal and effective absorber for high-energy X-ray radiation. GaGG : Ce is an excellent candidate for the further development of imaging systems (PET, PEM, SPECT, and CT). LuAG : Ce has such advantages as a high density and a short decay time, which is makes it suitable for thin display screens.

4. Ceramic scintillator Gd_2O_2S : Tb with a grain size from 3 to 50 μm has been widely used in radiation detectors for medical diagnostics.

5. $LaBr_3$: Ce and $LaCl_3$: Ce, as well as $CeBr_{3+x}$, where $0.0001 \le x \le 0.1$, are promising scintillators; $Tl_2LiLaBr_6$ doped with Ce, Pr, Eu, Sr, Ca, Ba, and Mg can be used for gamma and/or neutron detection.

6. Other materials for nuclear medicine are $ZnWO_4$, LYSO, BaF_2, LuAP, LGSO, CaF_2 : Eu, ZnSe : Te or mixed crystals, such as $NaBaLaBr_6$, $Cs_2NaLaCl_6$, which are used as pixels, bulk crystals, ceramics, films, etc.

7. There appear patents that involve new materials ($MAPbBr_3$, Cs_2NaGdI_6 : Ce, and YAG : Pr) whose properties and prospects for application have been currently being studied.

The authors express their gratitude to Prof. Borys Grynyov and Prof. Oleg Sidletskiy for helpful comments during the preparation of the article.

REFERENCES

1 Paul Lecoq. (2016). Development of new scintillators for medical applications. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, pectrometers, Detectors and Associated Equipment*, 809, 130—139. https://doi.org/10.1016/j.nima.2015.08.041.

2. Moses, William W. (1999). Scintillator requirements for medical imaging. *International Conference on Inorganic Scintillators and Their Applications: SCINT99* (*16—20 Aug 1999, Moscow*). Moscow.

3. *US 2021/0333417 A1*. Nelson Robert Sigurd, Nelson William Bert. Structured Detectors and Detector Systems for Radiation Imaging.

4. Hofstadter, R. (1948). Alkali Halide Scintillation Counters. *Phys. Rev.*, 74, 100.

5. *US 7696482 B1*. Nagarkar V., Gaysinskiy V. High spatial resolution radiation detector.
6. *US 7361901 B1*. Gaysinskiy V. Scintillator detector fabrication.
7. *EP 2847617 B1*. Valentino Frank Charles. Spect/pet Imaging System.
8. *Patent of Ukraine № 87792*. Zaslavskyi B. H., Kudin Ol. M., Hryniov B. V., Vasetskyi S. I., Kolesnikov Ol. V., Mitichkin A. I. Ovcharenko N. V. Scintillation material based on caesium iodide, activated with thallium iodide and method for obtaining thereof [in Ukrainian].
9. *Patent of Ukraine №* 93840. Vasetskyi S. I., Zaslavskyi B. H., Kolesnikov Ol. V., Tymoshenko M. M. Method for growth of monocrystalls based on sodium iodide and cerium iodide [in Ukrainian].
10. *Patent of Ukraine №* 108798. Taraniuk V. I., Kolesnikov O. V. Hektin O. V. Method for producing crystals, in particular large area crystalline plates [in Ukrainian].
11. *US 8242452 B1*. Shah Kanai S., Higgins William M., Van Loef Edgar V., Glodo Jaroslaw. Cesium and sodium-containing scintillator compositions.
12. *US 8575553*. Shah Kanai S., Higgins William M., Van Loef Edgar V., Glodo Jaroslaw. Cesium and sodium-containing scintillator compositions.
13. *US 2008/0208044 A1*. Lecoq Paul, Mundler Olivier, Cohen-Bacrie Claude. Combined Nuclear and Sonographic Imaging Apparatus and Method.
14. C. Chai, Bruce and Ji, Yangyang (2005). Lutetium Yttrium Orthosilicate Single Crystal Scintillator Detector. UCF Patents. 737.
15. *US 4664744 A*. Le Gal Herve, Damelet Jean L. Process for the production of bismuth germanate monocrystals with a high scintillation response.
16. *CN103695994A*. Hu Zhixiang, Zhu Liu, Wen Chongbin, Luo Tao. Growth method of bismuth germanate single crystal.
17. *WO 2020/242331 A2*. O'doherty Jim William, Bouhali Othmane, Toufique Yassine. Coincidence Detection System for Measuring Arterial Blood Time-Activity Curves and Methods of Using Same.
18. *US 2007/0181814 A1*. Crosetto Darlo B. Method and apparatus for determining depth of interactions in a detector for three-dimensional complete body screening.
19. *Patent of Ukraine №* 77593. Bondar V. H., Hriniov B. V., Kryvoshein V. I., Pyrohov Y. M., Ryzhykov V. D. Method for growing monocrystals of bismuth germanate [in Ukrainian].
20. *Patent of Ukraine №* 9942. Kukhtina N. M., Ryzhykov V. D., Pyrohov Y., Borodenko Y. A., Burachas S. F. Method for heat treatment of crystals of bismuth germanate [in Ukrainian].
21. Sidletsky, O. Ts., Grynyov, B. V. (2019). *Scintillation crystals based on solid substitution solutions*. Kharkov [in Ukrainian].
22. *WO 2015/185988 A1*. Zagumennyi Alexander Iosifovich. Cerium Doped Rare-Earth Ortosilicate Materials Having Defects for Improvement or Scintillation Parameters.
23. *US 9529100 B2*. Choi Yong, Choe Hyeok Jun. Positron emission tomography detector and positron emission tomography system using same.
24. Melcher, Charles L. (2000). Scintillation crystals for pet. *Nuclear medicine,* 41(6), 1051—1055.
25. Moszynski, M. A., Nassalski, W., Czarnacki, A., Syntfeld-Kazuch, D., Wolski, T., Batsch, H. Ishibashi. (2007). Energy resolution of LGSO scintillators. *Ieee Transactions on Nuclear Science,* 54(3), 725—731.
26. *Patent of Ukraine № 87767*. Velikhov Y. M., Viahin O. H., Hanina I. I., Zhmurin P. M., Maliukin Y. V., Masalov A. O. Nanocrystalline luminophor of lutecium oxyorthosilicate activated with metals of rare-earth elements and film scintillator based thereon [in Ukrainian].
27. *Patent of Ukraine № 108932*. Voloshyna Ol. V., Bondar V. H., Kurtsev D. O., Kononets V.V., Arkhypov P. V., ..., Tkachenko S. A. Method for welding deposition of crucible by charge, in particular for growing of high temperature oxides [in Ukrainian].
28. *Patent of Ukraine № 92705*. Bondar V. H., Voloshyna Ol. V., Hryniov B. V., Zhukov L. S., Kurtsev D. Ol., Sidletskyi Ol. T. Metod for producing melt for growing crystals of lutecium AND gadolinium oxyorthosilicates [in Ukrainian].
29. *EP 2836628 A4*. Zagumennyi A. I., Zavartev Y. D., Kutovoi S. A., Kozlov V. A., Zerrouk F. A., Zavertyaev M. V. Multi-Doped Lutetium Based Oxyorthosilicate Scintillators Having Improved Photonic Properties.
30. *DE 102008033960 A1*. Heismann B., Henseler D. Radiation detector module i.e. X-ray radiation detector module, for e.g. X-ray-computer tomography-device, has photo-detection unit connected with scintillation elements, detecting light, and including silicon-photomultiplier.
31. Baccaro, S., Blaiek, K., Notaristefani, F., Maly, P., Mares, J. A., Pani, R., Pellegrini, R., Soluri, A. (1995). Scintillation properties of YAP:Ce. *Nuclear Instruments and Methods in Physics Research,* A 361, 209—215.
32. *EP 1875210 B1*. Peter Jörg, Schulz Ralf, Unholtz Daniel. Optical Imaging Detector.

33. *US 8923588 B2*. Laurence T., Griesmer J. J., Kolthammer J. A., Thon A., Brinks R., Degenhardt C. Method and system for improved TOF PET reconstruction.
34. *Patent of Ukraine №*123344. Gerasimov Ya. V., Sidletskyi O. Ts., Arkhipov P. V., Tkachenko S. A.. Method of growing oxide crystals activated by cerium [in Ukrainian].
35. *Patent of Ukraine №*87683. Iltis Alain. Material-scintillator on basis of rare earth elements with decreased radioactive phone noise, method to obtain it, detector and its application [in Ukrainian].
36. *Patent of Ukraine №139789*. Rebrova N. V., Grippa O. Yu., Rebrov O. L., Kononets V. V., Horbachova T. E., Cherginets V. L. Method of obtaining high-purity bromide scincillation single crystals [in Ukrainian].
37. *US 2022/0206168 A1*. Benlloch B. J. M., Gimenez A. V., Gonzalez M. A. J., Ilisie V. Method and Device for Detecting Gamma Rays With the Ability to Determine Multiple Interactions and Their Corresponding Time Sequence.
38. *US 2007/0284534*. Srivastava A. M., Duclos S. J., Comanzo H. A. Scintillators for detecting radiation, and related methods and articles.
39. *Patent of Ukraine №* 77543. Nagorna L. L., Vostretsov Y. Y., Hriniov B. V., Tupitsyna I. A. Method for growing scintillation monocrystals of alloyed cadmium tungstate [in Ukrainian].
40. *Patent of Ukraine № 86104*. Tupitsyna I. A., Nahorna L. L., Hryniov B. V. Method for heat treatment of scintillation monocrystals of cadmium tungstate [in Ukrainian].
41. *Patent of Ukraine № 105335*. Tupitsyna I. A., Hryniov B. V., Dubovik Ol. M., Yakubovska H. H. Scintillation single crystal on the basis of ZINC tungstate [in Ukrainian].
42. Makek, M., Bosnar, D., Kožuljevi, A.-M., Paveli, L. (2020). Investigation of GaGG:Ce with TOFPET2 ASIC Readout for Applications in Gamma Imaging Systems. *Crystals*, 10, 1073. https://doi.org/10.3390/cryst10121073.
43. *Patent of Ukraine № 86154*. Bondar V. H., Kryvoshein V. I. Method for reduction of crucibles from precious metals, in particular from iridium [in Ukrainian].
44. *Patent of Ukraine № 88507*. Bondar V. H., Kryvoshein V. I. Method for fusing of charge of monocrystals of compound oxydes (variants) [in Ukrainian].
45. *US 7612.342 B1*. Nagarkar Vivek V. Very bright scintillators.
46. *US6630077B2*. Shiang J. J., Setlur A. A., Srivastava A. M., Comanzo H. Ann. Terbium- or lutetium — containing garnet phosphors and scintillators for detection of high-energy radiation.
47. *CN114031403A*. An Ning, Yu. Jinfeng, Di Juqing. Preparation method and application of gadolinium oxysulfide scintillation ceramic.
48. *US4507560A*. Mathers James E., Yale Ramon L. Terbium-activated gadolinium oxysulfide X-ray phosphor.
40. *Patent of Ukraine №106004*. Miroshnychenko S. I., Nevhasymyi A. O. Compound optical fiber connector and x-ray detector based thereon [in ukrainian].
50. *Patent of Ukraine № 60818*. Miroshnychenko S. I., Nevhasymyi A. O. X rays receiver for x-rays apparatus [in Ukrainian].
51. *US 2022/0259496*. Yu Jinqiu, Luo Liang, Diao Chengpeng, Cui Lei, Wu Hao, He Huaqiang. Rare Earth Halide Scintillation Material.
52. *US 11254867 B1*. Hawrami Rastgo, Pandian Lakshmi Soundara, Shah Kanai S. Thallium-based scintillator materials.
53. *EP 4033271 A1*. Zhang Lei, Konstantinou Georgios, Antonakakis Tryfon, Lecoq Paul René Michel. Devices and Methods for Detecting Gamma Radiation.
54. *US 11269090 B2*. Saliba Michael. Low-temperature perovskite scintillators and devices with low-temperature perovskite scintillators.
55. *US 11224656 B2*. Makale Milan T., Wrasidlo Wolfgang J., Kesari Santosh, Mckittrick Joanna, Hirata Flores Gustavo A., Graeve Olivia. Scintillator nanocrystal-containing compositions and methods for their use.

Received 06.12.2022
Revised 22.02.2023
Accepted 22.03.2023

Ю.А. Даниленко (https://orcid.org/ 0000-0002-7251-7071),
Т.А. Непокупна (https://orcid.org/0000-0002-2987-4671)

Інститут сцинтиляційних матеріалів Національної академії наук України,
просп. Науки, 60, 61072, Харків, Україна,
+380 57 341 0161, info@isma.kharkov.ua

АНАЛІЗ СЦИНТИЛЯЦІЙНИХ МАТЕРІАЛІВ ДЛЯ ЯДЕРНОЇ МЕДИЦИНИ НА ОСНОВІ ПАТЕНТНОЇ АНАЛІТИКИ

Вступ. Об'єкти інтелектуальної власності є найбільш важливим джерелом технологічної інформації, яку можливо використовувати для оцінювання напрямків розвитку галузі, перспективності подальшого вивчення сцинтиляційних матеріалів, знаходження конкурентів тощо.

Проблематика. На сьогодні ядерна медицина має величезну популярність в усьому світі. Сцинтиляційні кристали є одними з основних матеріалів, які використовують у сучасному діагностичному обладнанні, тому розроблення високоефективних сцинтиляційних матеріалів для систем медичної візуалізації є актуальним завданням.

Метою аналізу патентної активності для ядерної медицини було виявлення динаміки патентування сцинтиляційних матеріалів, які використовуються для цієї галузі за період 1992—2022 рр., а також визначення найбільш пріоритетних та важливих напрямків досліджень.

Матеріали й методи. Патентний пошук проводився за допомогою спеціальної пошукових програм — інформаційних баз Lens.org та спеціалізованих баз даних "Винаходи (корисні моделі) в Україні"; використано методи аналізу, систематизації та порівняння.

Результати. Оцінювання розвитку сцинтиляційних матеріалів для ядерної медицини на основі патентного аналізу дозволило проаналізувати наявні сцинтиляційні матеріали для цієї галузі, знайти нові матеріали для неї та виділити найбільш перспективні напрямки її розвитку.

Висновки. Найбільшу кількість патентів на сцинтиляційні матеріали для ядерної медицини мають американські компанії, але аналогічні патенти представлені й на українському ринку. Основними сцинтиляторами, які використовують для ядерної медицини, є BGO, $CdWO_4$, $ZnWO_4$, LSO, LYSO, GSO, NaI, CsI, BaF_2, $LaBr_3$, LuAP, LuAG, GGAG, LGSO, CaF_2 : Eu, ZnSe : Te, Gd_2O_2S : Tb або змішані сцинтилятори, такі як $NaBaLaBr_6$, $Cs_2NaLaCl_6$, $SrAl_{12}O_{16}$ тощо у вигляді пікселів, об'ємних кристалів, кераміки, плівок та інших. З'являються патенти з новими матеріалами, наприклад, $MAPbBr_3$, $CeBr_{3+x}$, $Tl_2LiLaBr_6$, властивості та перспективи використання яких наразі вивчають.

Ключові слова: ядерна медицина, сцинтиляційний матеріал, об'єкт інтелектуальної власності, аналітика.