crystals

MDPI

Review

A Survey of Crystals for SPECT Imaging

Shuyu Xu, Zijun Yan and Qingyang Wei *

Beijing Engineering Research Center of Industrial Spectrum Imaging, School of Automation and Electrical Engineering, University of Science and Technology Beijing, Beijing 100083, China; d202110348@xs.ustb.edu.cn (S.X.); m202210534@xs.ustb.edu.cn (Z.Y.)
* Correspondence: weiqy@ustb.edu.cn

Abstract: Single-photon emission computed tomography (SPECT) is an important nuclear medicine imaging tool for diagnosis and drug research. The gamma-ray detector is the core component of the SPECT system and influences the overall system performance. The detector crystals, which can be divided into scintillation crystals and semiconductor crystals, are among the main determinants of the detector's performance. The development of these crystal materials plays an important role in improving SPECT imaging. This paper provides a survey of the technological development and applications of several crystals currently used in SPECT detectors. Furthermore, it explores future research directions for the development of detector crystals.

Keywords: SPECT; scintillation crystals; semiconductor detector; performance

check for updates

Citation: Xu, S.; Yan, Z.; Wei, Q. A Survey of Crystals for SPECT Imaging. *Crystals* **2024**, *14*, 1039. https://doi.org/10.3390/cryst14121039

Academic Editor: Yutaka Fujimoto

Received: 1 November 2024
Revised: 22 November 2024
Accepted: 27 November 2024
Published: 29 November 2024

1. Introduction

Nuclear medical imaging can be used for diagnosis, treatment, and medical science research, as well as the study of the principles of drug action and the determination of drug activity. Among the methods used, positron emission tomography (PET) and single-photon emission computed tomography (SPECT) are collectively known as emission computed tomography (ECT). ECT is a functional molecular imaging technique that can reflect molecular-level changes in organisms in vivo and perform qualitative and quantitative evaluations with high sensitivity and high specificity [1].

Compared to PET, SPECT has unique advantages. SPECT is inexpensive; it has a simple structure and does not require the use of an expensive cyclotron. SPECT uses a wider variety of radionuclides, making it suitable for more organs and easier to popularize. The resolution of PET is limited by the non-collinearity of the positron's free path and annihilation photons, resulting in a limited resolution, while the resolution of SPECT is limited only by the aperture size of the collimator and the inherent resolution of the detector, which allows for a higher resolution. Micro-SPECT has a higher spatial resolution than that of PET and is more suitable for preclinical studies [2]. Although PET seems to receive more attention than SPECT, the amount of applications of SPECT in clinical nuclear medicine far exceeds that of PET. Thus, SPECT has very good prospects in the future.

The imaging principle of SPECT is the injection of radioisotope drugs (tracers) into the organism. After physiological metabolism, the drugs will concentrate in the measured site and emit gamma photons due to decay, which are captured by a scanner outside of the body. The scanner is mainly composed of a collimator, a detector, and subsequent circuitry. The role of the detector is to stop the emitted gamma rays and to produce signals with energy information, physical location information, and timing information. The performance of the detector determines the comprehensive performance and clinical diagnostic value of the imaging system. Therefore, the ideal detector would have high stopping power, high spatial resolution, good energy resolution, and high timing resolution and would be inexpensive to produce. To achieve this, the crystals are the most important of the key components. The crystals used in the current SPECT imaging systems are mainly divided into two categories:

scintillator detectors and semiconductor detectors. Scintillator detectors were developed earlier and are more widely used, while semiconductor crystals, as an emerging material with excellent characteristics, promote the development of SPECT imaging. In this paper, we review the research progress of SPECT detectors and their crystal materials and list the applications of different crystals in detectors. Finally, we predict the future development trend of detector crystals used for SPECT imaging systems.

Diagnostic radiopharmaceuticals are a type of radioactive drug used to obtain images or the functional parameters of target organs or diseased tissues within the body for disease diagnosis. In the selection of radiopharmaceuticals, their radiation safety, clinical efficacy, and impact on imaging need to be considered. Typically, drug selection is based on the half-life, type of radiation, decay products, and other physical characteristics, such as linear energy transfer, relative biological effectiveness, range, imaging properties, and radiation protection [3]. The commonly used nuclides for SPECT imaging include ^{99m}Tc (technetium), ^{131}I (iodine), ^{111}In (indium), etc. The corresponding energies of different nuclides are shown in Table 1 [4].

Table 1. Radionuclides and photon energies emitted in SPECT imaging.

Radionuclide	Energy/KeV	Half-Life
^{99m}Tc	140	6 h
^{123}I	159	13.2 h
^{131}I	364	8.02 days
^{111}In	171, 245	2.83 days
^{201}Tl	69, 71, 167	3.04 days

Among them, ^{99m}Tc decays to produce 140 KeV gamma rays with a convenient half-life of 6.02 h (long enough to handle the imaging process and short enough to limit unnecessary radiation doses to patients) [5], which is suitable for scintillation detection. ^{99m}Tc-labeled compounds and complexes can be used in imaging and hemodynamic studies on almost all organs. ^{99m}Tc is an ideal radionuclide for in vitro development, and its dosage accounts for about 90% of the total radionuclides [6].

2. Scintillation Crystals for SPECT

Scintillation crystal detectors have the advantages of high detection efficiency, high sensitivity, and high adaptability to the environment. The luminescence process of scintillation crystals is essentially a process in which electrons inside the crystal undergo excited energy level transitions to form an excited state and then emit photons of a specific wavelength through the excited radiative transition [7]. When a radiation particle enters the scintillation material, it interacts with the atoms of the material, causing some atoms to become excited. Then, these excited-state atoms transition back to the ground state, releasing energy in the form of visible scintillation light. The scintillation light is generated within the material and transmitted to a photomultiplier tube through a light guide. The light signal is converted into an electrical signal, which is then amplified, processed, and recorded for imaging purposes. Light-harvesting components, such as photoconductors and reflectors, are used to make the fluorescence hit as many photosensitive layers of the photoelectric conversion device as possible and hit the photoelectrons. These photoelectrons can be collected in the output stage directly or after multiplication to form an electrical pulse.

Different scintillators differ in physical properties, such as light yield, scintillation decay time, radiation length, irradiation hardness, density, hardness, moisture absorption, etc. The characteristics of some scintillation crystals are shown in Table 2.

Table 2. Characteristics of the scintillators.

Material	Light Output/ph/MeV	Effective Atomic Number	Density/ $g \cdot cm^3$	Hygroscopic	Decay Constant/ns	Wavelength of Emission/nm	Intrinsic Background Radiation
NaI(Tl)	39,000	51	3.67	Easily	230	415	No
CsI(Tl)	54,000	54	4.51	Slightly	800	550	No
$LaBr_3$	61,000	47	5.29	Easily	25	370	Yes
LSO	30,000	66	7.35	No	40	420	Yes
LYSO	33,800	63	7.15	No	40	420	Yes
YSO	10,000	39	4.50	No	70	420	No
GAGG:Ce	46,000	54.4	6.63	No	94 or 88	540	No

In order to meet the requirements of detection efficiency, the density and effective atomic number of scintillation crystals applied to radiation detection need to be larger in order for them to have a greater ability to stop the detected particles so that the incident particles in the crystal will lose more energy. The stopping ability of the crystals is positively correlated with the sensitivity of the system [8].

The light output is the total number of low-energy photons output by the scintillation crystal after absorbing the energy from unit gamma rays. The higher the light output, the better the energy resolution. The high energy resolution of the system is conducive to the scattering correction of SPECT systems and plays a crucial role in the simultaneous imaging of multiple isotopes. In the meantime, high energy resolution allows for the rejection of more scattered photons, yielding higher contrast images [9]. The band gap of the scintillation crystal can be adjusted by incorporating dopants into the matrix, and the relative position of the transition energy level of the luminescence center can be changed to control the light output of the scintillation crystal [10].

The crystal needs to have high irradiation hardness and resistance to radiation damage to ensure a stable light output under long-term irradiation.

The time that the crystal scintillates down after excitation by high-energy photons is the decay time, and the shorter the decay time, the higher the temporal resolution of the system will be. The decay rate is generally increased by doping the crystal with specific rare earth elements to reduce the chance of pulse stacking, obtain a higher maximum count rate, and improve the crystal time resolution.

At the same time, the scintillator crystal should have good thermal stability (luminous efficiency is less affected by temperature), good chemical stability, and no moisture absorption. It should also have excellent mechanical properties, be easy to process and shape, and not be easily broken.

Sodium iodide (NaI) and cesium iodide (CsI) doped with thallium (Tl) have been the most common scintillators used in SPECT [11]. In addition, there are some emerging crystals, such as yttrium aluminum perovskite doped by cerium (YAP (Ce)), lutetium oxyorthosilicate doped by cerium (LSO (Ce)), lutetium yttrium oxyorthosilicate doped by cerium (LYSO (Ce)), etc., with higher light output, fast decay time, and high density. Although the cost is expensive, they have excellent performance characteristics and are ideal materials for high-energy detection.

2.1. NaI(Tl)

NaI(Tl) is currently the most widely used scintillation crystal for traditional clinical SPECT detectors. The NaI(Tl) crystal is a single crystal of sodium iodide containing about 0.1% thallium with high luminous efficiency, high crystal transparency, large light output, high energy resolution, and high spatial resolution. Moreover, NaI(Tl) has no obvious self-absorption to visible light, which is very suitable for the detection of low-energy γ photons. In addition, NaI(Tl) is cheap and cost-effective.

The crystal density is low (3.67 g/cm^3), with poor stop ability and long luminescence decay time [12]. NaI(Tl) is susceptible to deliquescence and must be stored and used under hermetic conditions; it is brittle and easily broken, making the process very difficult.

In 2000, Siemens [13] of Germany invented a directional solidification technique to grow NaI(Tl) crystals, and the light output and energy resolution of the crystal were the same as those of single crystals grown via traditional methods, thus providing a technical guarantee for the wide application of this crystal. For clinical SPECT, the NaI(Tl) thickness is usually 6–10 mm. Using StarBrite technology (Saint-Gobain crystals and detectors), grooves can be machined into the backside of 10 mm thick NaI(Tl) crystals to limit the diffusion of scintillation light, thereby improving the intrinsic spatial resolution. In 2015, the French company Saint-Gobain improved the energy resolution of NaI(Tl) crystals from 6.5% to 5.3% and accelerated the decay time from 230 ns to 170 ns by co-doping with strontium (Sr) and calcium (Ca) ions [14].

NaI(Tl) is the first crystal used in SPECT detectors. In 1958, Hal Anger used NaI(Tl) single crystal, photomultiplier tube (PMT) array, and the center of gravity position technique to develop a high-performance γ camera, named the Anger Gamma Camera, which is widely used as a probe to form a rotating γ camera SPECT. Currently, the standard dual-detector SPECT (S-SPECT) used in clinical medicine is composed of two NaI(Tl) detectors with parallel hole collimators. The SPECT research group led by Dr. Chang at Rush Medical Center in Chicago [15] successfully developed a brain imaging SPECT (McSPECT) with a rotating scanning collimator and a fixed cylindrical NaI(Tl) detector. Rastgo Hawrami et al. [12] used high-purity NaI powder as raw material and conducted the growth in a two-zone vertical furnace, with a growth rate controlled at 3 to 3.5 cm/day. The silicon photomultiplier (SiPM) of MicroFJ-60035-TSV (Onsemi, Japan) and PMT of R6231-100 Hamamatsu, Japan) was used to test the NaI(Tl) sample. At 662 KeV, the energy resolution of the newly grown NaI(Tl) crystal was 5.4%, slightly better than the 7% of existing NaI(Tl) crystals on the market. The photovoltaic yield is about 120% of the existing NaI(Tl) crystals on the market. The fast decay time constant is 234 ns. M. S. Badawi et al. [16] studied the geometry change between the source-to-detector arrangement to calibrate the "3 × 3" γ-ray NaI(Tl) detector based on the available sample shape in the laboratory. Takeuchi's team [17] constructed a NaI(Tl) detector called DALI2, which has a good angular resolution, for example, 10% energy resolution, and 20% full-energy photopeak efficiency for 1-MeVγrays emitted from fast-moving nuclei. Moreover, the researchers pointed out that the combination of the new multi-pinhole technology (MPH), Cardiac, with the triple NaI(Tl) detectors, SPECT, can significantly improve image quality. This improvement can be attributed to the increased tomographic imaging sensitivity provided by the new collimator design and the undamaged spatial resolution of the myocardial region [18].

NaI(Tl) crystal is widely used in small-animal SPECT. The A-SPECT and the improved X-SPECT developed by UNC University in collaboration with γMI consist of a 2 × 2 × 6 mm^3 NaI(Tl) crystal array; system sensitivity can reach 0.001~0.01%. The Nano-SPECT developed by BIOSCAN consists of 230 × 215 mm^3 NaI(Tl) crystals and 33 PMTs, with a spatial resolution of 0.8 mm and a system sensitivity of 1000 cps/MBq. Lei Wang MD et al. [19] reported the diagnostic value of myocardial blood flow (MBF) quantification using NaI(Tl)-based SPECT for determining coronary artery disease (CAD) defined by quantitative coronary angiography (QCA). They concluded that flow quantification using NaI(Tl) SPECT provides superior sensitivity and discriminatory capacity to myocardial perfusion imaging (MPI) in detecting significant stenosis. Dai Tiantian et al. [20] designed a small-animal SPECT imaging system based on one continuous NaI(Tl) crystal and a seven-pinhole collimator design, which could achieve an ultra-high spatial resolution of 0.5 mm on the clinical detector.

NaI(Tl) crystals can also be used in a multimode imaging system. Siemens ECAN, Philips Forte, and GE Millennium VG use thickened NaI(Tl) crystals to form a double-probe SPECT system and add conformal circuitry to develop a SPECT/PET-compatible system, which greatly reduces equipment costs compared to expensive PET systems. CIT has designed a double-layer composite crystal (Phoswich): the inner layer uses NaI(Tl) crystals to detect 140 KeV γ photons for SPECT imaging; the outer layer uses LSO crystals to detect 511 KeV γ photons for PET imaging.

2.2. CsI

CsI is another kind of scintillation crystal commonly used in SPECT detectors. CsI(Tl) has a higher density than NaI(Tl). CsI(Tl) has a density of 4.5 g/cm^3, and the high-atomic-number iodine makes up 85% of its weight, so it is particularly efficient in detecting γ-rays. It can withstand mechanical and thermal shock, and it is easy to process and shape. It is sensitive to light and has high relative luminous efficiency. In addition, the crystal has good transparency and high energy resolution. The disadvantage is that the decay time is large.

CsI(Tl) detectors can also be used in multimodal imaging systems. Z. Telikani et al. [21] use CsI(Tl) as a detector model to simulate the basic features of the scanner. They proved that collimators with finer hole sizes had superior spatial resolution and less sensitivity than the ones with larger holes, and the square hole collimators offered the optimum sensitivity and spatial resolution. M. Carminati et al. [22] developed the first SPECT-MRI (magnetic resonance imaging) system. The system consists of a static ring of 20 MRI-compatible CsI(TI) detectors and a multi-seam collimator and is coupled to arrays of silicon photomultipliers and an application-specific integrated circuit (ASIC) readout for a total of 1440 channels. The results show a sensitivity of 362 cps/MBq, an energy resolution of ~17% (at 140 keV), and a tomographic extrinsic resolution in the transaxial plane of ~8 mm across the entire field of view (FOV). The University of Sherbrooke, Quebec, Canada, has proposed the same detector system to achieve PET, SPECT, and X-CT imaging simultaneously. The detector is composed of a thin CsI(TI) layer and a thick gadolinium orthosilicate (GSO) and LSO layer and is coupled to an avalanche photodiode (APD) for photoelectrical conversion. Lisa Bläckberg [23] developed a Dynamic Cardiac SPECT (DC-SPECT) for diagnostic and theranostic applications, employing laser-processed CsI(Tl) with converging pixels to prevent blurring from the depth of interaction (DOI). Through geometry optimization, it was found that DC-SPECT exhibits a sensitivity 15 times greater than that of a gamma camera when fixed at a 15 mm resolution. Additionally, a resolution of 4.1 mm can be achieved at 0.01% sensitivity, which closely rivals the resolution of whole-body PET.

In addition, the emission of sodium-activated cesium iodide CsI(Na), which is similar to CsI(Tl), is matched to PMTs better. It is used as a detector in the Lino View small-animal SPECT system [24].

Another new technique for obtaining high intrinsic spatial resolution in detectors is the direct growth of micropillar scintillators on a charge-coupled device (CCD), an electron-multiplying CCD (EMCCD), and complementary metal oxide semiconductor (CMOS) sensors [25,26].

For example, to use EMCCD to constitute a γ camera capable of imaging the incident γ photon stream with both high detection efficiency and high spatial resolution, a thin crystal of micropillar CsI(Tl) can be optically coupled with EMCCD to assemble a position-sensitive detector. Such scintillation crystals are manufactured via a vapor phase precipitation process, forming a large number of CsI(TI) filaments densely arranged in the thickness direction. The parameters of the micropillar CsI(Tl) crystal are chosen as a compromise between spatial resolution and detection efficiency. The theoretical absorption efficiency of the CsI(Tl) crystal with a thickness of 2.6 mm and a microcolumn diameter of about 30 μm can reach 70% to 140 KeV γ photons [27]. The combination of a CCD-based scintillation detector with a parallel hole or pinhole collimator creates an ultra-high spatial resolution γ camera.

This technique was first applied to the imaging of small-animal SPECT systems. The ionizing-radiation quantum imaging detector (iQID) is used in the early animal imaging system, BazucaSPECT/FastSPECT, and the human scintillation scanner [28] at the University of Arizona has an intrinsic resolution of 150–300 μm. This technique can achieve extremely spatial resolution, but the limited thickness of the grown micropillar scintillators leads to a low inherent detector sensitivity.

2.3. LSO and LYSO

LSO is widely used due to its excellent properties. The luminescence decay time of LSO is only 40 ns, which can reduce the compliance time window [29]. LSO also has good energy resolution [30]. In recent years, a co-doped LSO using calcium has been developed, with an increased light output and a shorter decay time compared to LSO(Ce) scintillators [31], which further improves the temporal resolution [32].

Rutao Yao et al. [33] demonstrated the feasibility of SPECT imaging on LSO-based animal PET. LSO/APD detectors are among the research directions undertaken in many laboratories. Nazir et al. [34] demonstrated that LSO scintillation crystals coupled with avalanche photodiodes (APDs) have good generalizability as detector modules.

LYSO is the analog of LSO with very similar properties, which may replace NaI and CsI in the future [35,36]. LYSO crystals have high spatial resolution, high density, high effective atomic number (Z-effective), high light output, and short decay time. Compared with LSO, LYSO has a relatively lower melting point, lower cost, and slightly better scintillation performance than LSO [37]. The average full width at half maximum (FWHM) of the continuous LYSO detector tested by Deprez et al. was 1.15 mm, and the center field of view (CFOV) was 0.93 mm [38].

R. Massari et al. [39] developed a new single-photon emission computed tomography (SPECT) device consisting of two detectors (a high-resolution system—HRS) combined in a rotating structure designed for preclinical imaging applications, which used the LYSO scintillator with a high light output, a medium density, a short decay time, and excellent energy resolution. The Institute for Drug and Instrument Control of PLA Beijing [40] has developed a small-animal SPECT imager based on the LYSO crystal, which can achieve small-animal whole-body imaging effectively, and the spatial resolution is about 2.5 mm.

One thing to note is that 2.6% of naturally occurring lutetium (Lu) is ^{176}Lu, which includes a β decay and three major simultaneous γ decays [41]. Detectors made with Lu-based scintillators, such as LSO and LYSO, have intrinsic background radiation due to the presence of ^{176}Lu, which introduces random events into the SPECT system and affects the system's sensitivity and other performance metrics, especially for low-activity imaging. The background radiation of LSO and LYSO is about 300 Bq/mL. Therefore, in the process of data processing, the random events caused by ^{176}Lu background radiation need to be corrected to improve the imaging quality. Setting more narrow energy acceptance windows and coincidence time windows is an effective method to reduce the effects of background radiation.

2.4. Lanthanum Halide Crystals

In 1999 and 2001, Dutch scientists successively discovered a class of excellent scintillators such as lanthanum chloride ($LaCl_3$(Ce)) and lanthanum bromide ($LaBr_3$(Ce)) crystals, both of which have high light output (46,000 ph/MeV and 61,000 ph/MeV), fast decay (25 ns and 35 ns) [42], high energy resolution (3.2% and 2.8%), and high time resolution (224 ps and 385 ps) [43,44]. It has the potential to replace NaI(Tl) as the material of choice for SPECT [45–47].

Many research groups are working on using $LaBr_3$(Ce) in SPECT experimental systems, such as the University of Surrey [48] and the Bhabha Atomic Research Centre [49]. Cuilan Zhao et al. [50] achieved a spatial resolution of 1.5 mm based on a continuum-type lanthanum bromide ($LaBr_3$) crystal with an H8500 position-sensitive photomultiplier tube. But, $LaBr_3$ is still expensive and only as good at blocking gamma photons as NaI(Tl), with deliquescence problems and some background radiation.

Lanthanum halide crystals also exhibit a certain level of intrinsic background radiation, primarily originating from the naturally radioactive isotope ^{138}La in lanthanum. During detection, this background radiation can significantly increase noise. The interference from background radiation can be effectively reduced through measures such as setting energy acceptance windows and signal correction techniques.

2.5. Gadolinium Aluminum Gallium Garnet (GAGG)

The special features of garnet scintillators are as follows: (1) they have a cubic structure, which allows for faster crystal growth at lower temperatures using ceramic techniques; (2) the possibility of fabricating scintillators of different shapes and sizes without cutting makes it possible to achieve cost-effective manufacturing. The development of non-lutetium-based garnet scintillators may be cost-effective in the long run [51]. Martinazzoli et al. [52] demonstrated that the Czochralski method, heavily doped with a cerium activator and a magnesium codopant at different concentrations, can accelerate the afterglow and improve the timing resolution [53]. The newly developed cerium-doped rare earth garnets—$Gd_3Al_2Ga_3O_{12}$(GAGG) [54], $Gd_3(Al,Ga)_5O_{12}$(GGAG), and $(Gd,Lu)_3(Al,Ga)_5O_{12}$ (GLuGAG) [55]—have shown a performance comparable to LSO or LYSO.

GAGG has become a popular scintillation crystal for SPECT due to its high light yield, fast decay time, and high stop power, along with the lack of background radiation and no deliquescence, as well as the outstanding advantage of being able to have different luminescence decay times [56], which has significant potential for application in the detectors of nuclear medicine imaging systems.

Wei et al. [57] proposed a detector with a side-by-side LYSO/GAGG composite crystal array coupled to an SiPM array, achieving a resolution of 1.35 mm in one direction. An innovative self-collimating SPECT design concept was proposed by Ma et al. [58] from Tsinghua University. This concept utilizes a multi-layer interspaced mosaic detector architecture known as MATRICES, where spatially distributed sensitive scintillators (GAGG) serve as collimators instead of the traditional absorptive heavy-metal materials. By adopting this design approach, the conventional interdependency between resolution and sensitivity in a SPECT system is overcome, leading to a simultaneous enhancement of both features.

2.6. $Cs_3Cu_2I_5$

$Cs_3Cu_2I_5$ is an emerging radiation detection material, particularly for X-ray and γ-ray detection, with excellent scintillation performance. Recent studies have highlighted $Cs_3Cu_2I_5$ as a promising SPECT detector material due to its various advantages, which include high light output, high energy resolution, moisture resistance, high density, low toxicity, and high chemical and mechanical stability [59–61].

Current research on $Cs_3Cu_2I_5$ focuses on enhancing its scintillation performance by doping with elements like Li^+ and K^+. Li^+ doping improves light output, energy resolution, and stability. Its stability reduces long-term degradation under radiation exposure [62]. K^+ doping accelerates the flicker decay time, while the improved radiation fluorescence efficiency enhances light output [63]. Recent studies have also shown that incorporating Sb into $Cs_3Cu_2I_5$ boosts light output, radiation resistance, and stability in high-humidity environments, demonstrating its potential for single-photon detection in challenging conditions [64].

However, $Cs_3Cu_2I_5$ still faces challenges, such as immature application technology and high crystal preparation costs. As a result, it has not yet gained widespread application in clinical and commercial SPECT detectors, requiring further research and development.

The current development direction of the scintillation detector technology is to seek to obtain better spatial, temporal, and energy resolution and higher detection efficiency. Therefore, the future development trend of scintillation crystals will continue to focus on high light output, fast response, high density, and other properties in order to investigate the comprehensive characteristics of excellent scintillators. In addition to selecting scintillation crystal materials with better performance, the essence of performance optimization of the scintillation detector is to reasonably design and optimize the transport process of scintillation photons in the crystal so as to obtain a higher comprehensive performance of the detector. There are three effective methods to design the transport process of scintillation photons, specifically designing the surface treatment of the scintillation crystal, changing the detection process of scintillation photons, and changing the geometric structure of the scintillation crystal. Methods such as ion substitution in the original high-temperature scintillation crystals can improve the shortcomings of the existing scintillation crystals, thus improving the scintillation performance of the crystal, as can searching for optimized methods and processes for growing high-temperature scintillation crystals [65].

3. Semiconductor Detector for SPECT

The semiconductor detector is a solid-state device that converts the absorbed ray energy directly into an electrical signal [66]. Commonly used semiconductor detectors include P-N junction semiconductor detectors, lithium drift semiconductor detectors, and high-purity germanium semiconductor detectors [67]. The basic principle of semiconductor detectors is that charged particles generate electron–hole pairs in the sensitive volume of the semiconductor detector (one pair is generated every 3–10 eV). The electron–hole pairs drift, multiply, and collect under the action of the external electric field and then output a signal proportional to the energy of the particle. The characteristics of some semiconductors are shown in Table 3.

Table 3. Characteristics of the semiconductors.

Material	Atomic Number	Density/ $g{\cdot}cm^3$	Band Gap Width/(eV)	Generating an Electron–Hole Pair Requires Deposition Capacity/(eV)
Si	14	2.33	1.12	3.60
Ge	32	5.33	0.67	2.90
CdTe	48.52	5.85	1.44	4.43
CZT	48.52	5.81	1.60	4.60

Semiconductor detectors have the advantages of high sensitivity, high spatial resolution, fast response speed, and wide linear range [68]. At the same time, the high detection efficiency of semiconductor detectors facilitates the rejection of small-angle scattering events, improves imaging quality, and makes it possible to perform more accurate scattering corrections. Since the intermediate high-gain amplification stage is not required, the device is compact, operates at low voltage, and achieves higher precision in signal output compared to scintillators, resulting in better energy resolution. But, the manufacturing cost of the semiconductor detector is high [69].

With the development of material technology, several new semiconductor materials working at room temperature have been developed, such as cadmium telluride (CdTe), cadmium zinc telluride (CZT), etc. [70,71]. These materials have the advantages of high energy resolution and high absorption cross-section. The semiconductors currently used in SPECT equipment mainly include CZT, CdTe, etc. [72,73]. In recent years, SPECT scanners with newly designed racks, combined with semiconductor detectors, have entered the market. Compared with traditional scanners, the volume of semiconductor detectors and racks is significantly reduced, easy to integrate, and requires less physical space.

3.1. CZT

A major advance in nuclear medicine is the introduction of cadmium zinc telluride (CZT) detector technology to SPECT. Compared with traditional SPECT, CZT detector SPECT is based on a multi-pinhole design and pixel array detector, which can simultaneously collect in multiple directions and improve the sensitivity and the spatial resolution of the detector [74]. With higher energy resolution, CZT is very suitable for simultaneous multi-nuclide imaging [75], and it can reduce the dose of the radiographic imaging agent and shorten the scanning time. Another advantage is that the CZT detector has excellent photoelectric performance without a photomultiplier tube and a photoelectric conversion process and can directly convert X-rays and gamma rays into photons and electrons at room temperature [76]. By directly digitizing the photons, the image quality can be improved to a certain extent, achieving high intrinsic spatial resolution (pixel size in D-SPECT is $2.46 \times 2.46 \times 5$ mm^3). The compactness of the CZT detector allows for a smaller detector module, combined with the elimination of the photomultiplier tube and improved collimator design, resulting in a reduced footprint compared to conventional SPECT [77].

Commercialized CZT-SPECT, such as Discovery NM 530c (Chicago, IL, USA) and D-SPECT (Spectrum Dynamics Medical, Caesera, Israel), can complete the SPECT myocardial perfusion image at a low dose with high efficiency and high time resolution [78]. The Discovery NM530cTM and Discovery NM/CT 570cTM, from GE, are the first SPECT devices in the world to use semiconductor detectors, with greatly accelerated acquisition speed and improved spatial resolution. The Discovery NM 530c has an inherent spatial resolution of up to 2.46 mm, and the energy resolution is higher, up to 6.2%. The sensitivity is also increased by 2~5 times, along with being more compact and lighter. D-SPECT adopts the most advanced all-digital CZT solid-state detector. The probe consists of nine strip-shaped CZT detectors; each block is 4 cm $\times$ 16 cm, composed of 16×64 CZT detector units (2.46 mm $\times$ 2.46 mm $\times$ 5 mm), with a wide-angle parallel hole collimator installed in front of each detector block. With a 10-fold increase in sensitivity, a 2-fold increase in resolution, and a 10-fold increase in scanning speed, the blood perfusion of the heart and the functional status of the myocardium can be observed with very high diagnostic accuracy [79]. Michel Hesse et al. [80] used a GE StarGuide SPECT/CT camera with a CZT rotating detector ring for dynamic SPECT imaging. The maximum likelihood expectation maximization (MLEM) algorithm was used for reconstruction, with a maximum of 20 iterations, both with and without attenuation correction. The results demonstrate the feasibility of using the CZT rotating detector ring camera for dynamic SPECT imaging and are consistent with the standard dynamic plane imaging results of traditional gamma cameras. Dynamic SPECT imaging can conduct regional organ analysis and achieve a temporal resolution as low as 1 s. Hong Song et al. [81] have suggested that the new StarGuide system can enable fast whole-body post-therapy SPECT/CT scans based on CZT detectors, enhancing patient experience and compliance while facilitating image-based treatment assessment and personalized dosimetry for targeted radionuclide therapies.

The advantage of CZT-SPECT technology in energy resolution affords it significant potential in cerebral perfusion, dopaminergic imaging, and therapeutic monitoring. Antoine Verger [82] proposed that the CZT-SPECT system has image quality at least comparable to traditional systems but with shorter acquisition time, thus having advantages in workflow management and patient acceptance. The results showed that CZT-SPECT MPI significantly shortens the imaging time, significantly reduces the dose of ^{99m}Tc-labeled contrast agent used, and decreases the radiation dose to the patient [83]. Duan [84] showed that the CZT-based multidetector SPECT/CT demonstrated superior image quality compared to both traditional NaI-based SPECT/CT and other CZT-based two-head detectors. The University of Shanghai for Science and Technology, in conjunction with the University of California [85], developed a SPECT/CT device for small-animal imaging using a SPECT system with a multi-probe CZT flat panel detector and a high-resolution, microfocus, cone-beam X-ray CT system that enables slip-ring helical scanning and dual-nucleus SPECT imaging. Yoonsuk Huh [86] proposed a variable aperture full-loop SPECT system using a combination of pixelated CZT and energy-optimized parallel hole collimator modules, using a full-ring SPECT system design, including eight large-area CZT detectors, which can be used for a broad spectrum of SPECT radiopharmaceuticals. Experiments have shown that the new full-loop CZT-SPECT design has the potential to reduce acquisition time and improve sensitivity, with a volume sensitivity of about 1.7 times higher than traditional scanners while maintaining an acceptable carrier-to-noise ratio (CNR) and spatial resolution. GE uses 10 CZT arrays to form a ring detector to develop a multi-spatial resolution dynamic small-animal SPECT imaging system, which can adapt to the different needs of imaging large and small mice.

The current bottleneck in the development of CZT-SPECT mainly lies in the expensive cost of CZT. Therefore, it is not yet widely used. But, with its high performance in all aspects, as well as the further improvement of the CZT production process, its hardware cost is expected to be significantly reduced in the future. We anticipate that it will have a positive future in the field of nuclear medicine imaging.

3.2. CdTe

Cadmium telluride (CdTe) has a high optical absorption coefficient (>5 × 10^5/cm). The CdTe film with a thickness of only 2 µm has an optical absorption rate of more than 90% under standard AM1.5 conditions, with a maximum theoretical conversion efficiency of 28%. CdTe detectors have higher energy resolution, higher spatial resolution, and smaller detector module size than traditional scintillator detectors while highly fault-tolerant with respect to magnetic fields.

The Department of Nuclear Medicine, Royal Surrey County Hospital, U.K. [87], developed a CdTe detector for multi-radioisotope SPECT imaging with a detector size of 2 cm × 2 cm, energy resolution of 0.75% at 159 KeV, and spatial resolution of 2 mm for SPECT systems. S. Takeda et al. [88] proposed a new small-animal SPECT system named CdTe-DSD SPECT-I, which is based on a cadmium telluride double-sided strip detector (CdTe-DSD). It has an energy resolution of 1–2 KeV (FWHM) at 10–100 KeV and 1.6% (FWHM) at 140 KeV. They also showed through experiments with small animals that the high energy resolution and the crosstalk subtraction technique effectively minimize image noise and spectral crosstalk.

3.3. Si

Another semiconductor detector with high spatial resolution is the silicon (Si) detector. Due to its low atomic number (Z = 14) and density (2.3 g/cm^3), silicon is not useful for conventional X-ray imaging of most medium- and high-energy rays. However, it is suitable for very low energy rays and X-ray emitters, and silicon detectors have good spatial resolution and are well suited for Compton cameras [89]. Si has a higher band gap than Ge, allowing Si(Li) detectors to operate at room temperature.

Choong et al. [90] designed a high-resolution animal SPECT using a pixelated lithium drift silicon [Si(Li)] detector with high interaction probability (>90%), good energy resolution [<15% full width half maximum (FWHM)], and good intrinsic spatial resolution. At an imaging distance of 20 mm, the system has a spatial resolution of 1.6 mm half-width and a sensitivity of 6.7 cps/Ci.

Solid-state detectors can also be used with scintillation crystals to record the light emitted by the scintillation crystals and thus detect photon signals indirectly. Digirad [91] adopted this approach in the Cardius camera by using CsI(Tl) scintillation crystals and photodiodes (instead of photomultiplier tubes). Each detector head contains an array of 768 CsI(Tl) crystals (6.1 mm × 6.1 mm × 6 mm) coupled to a single Si photodiode, which converts the light output from the crystals into electrical pulses. Then, the electrical pulses are digitally processed to form an image. This design is more compact than conventional Anger cameras.

In addition, SiC and GaN have also been applied in nuclear radiation detection. With the characteristics of breakdown electric field strength, low intrinsic carrier concentration, good irradiation resistance, and being easy to produce commercially, the ultra-wideband gap semiconductor Ga_2O_3 is a research hot spot for application in the field of high-performance nuclear radiation detectors [92].

4. Conclusions and Discussion

In this paper, the crystals used in SPECT detectors were reviewed and compared with an emphasis on the scintillation crystal detectors and semiconductor detectors, and their development and applications were also discussed. The key to improving the performance of nuclear medicine imaging systems is to improve the main indicators, such as spatial resolution, sensitivity, and signal-to-noise ratio. Therefore, the detector crystal used needs to have high stop power, high spatial resolution, high energy resolution, and high temporal resolution. At present, scintillation crystals still occupy the mainstream market of nuclear medicine imaging system detectors due to their high-cost performance. At the same time, semiconductor detectors are gradually being used more and more by virtue of their excellent energy resolution and detection characteristics that can directly facilitate photoelectric conversion.

The development of detectors with excellent performance is an important research element in the field of nuclear medicine imaging, which plays an important role in improving image quality and imaging efficiency and is of great research significance. SPECT has a bright future both in clinical imaging and research due to its modest infrastructure requirements, correspondingly low costs, and the large number of approved and in-development radiotracers. The sizable clinical market and the unique challenges of preclinical imaging will continue to inspire further exploration and innovation of SPECT detector technology in the future.

New detector research and development will explore higher energy resolution, higher spatial resolution, higher temporal resolution, and higher detection efficiency; will continue to search for new crystals with faster response speed, higher stop power, higher density, higher light yield, and lower cost; and will develop detectors that can meet the needs of multimodal synchronous imaging. The future research direction in the field of SPECT scintillation crystals is to explore new crystals suitable for depth of interaction (DOI) information. Research on the new SPECT detector crystals still has significant potential for future development.

Author Contributions: Conceptualization, S.X.; formal analysis, S.X. and Z.Y.; investigation, S.X. and Z.Y.; data curation, S.X.; writing—original draft preparation, S.X.; writing—review and editing, Z.Y. and Q.W.; visualization, Z.Y.; supervision, Q.W.; project administration, Q.W.; funding acquisition, Q.W. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the National Natural Science Foundation of China, grant number 12375337, and the National Key R&D Program of China, grant number 2022YFC2402001.

Data Availability Statement: Data are contained within the article.

Conflicts of Interest: The authors declare no conflicts of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Rowe, S.P.; Pomper, M.G. Molecular imaging in oncology: Current impact and future directions. *CA Cancer J. Clin.* **2022**, *72*, 333–352. [CrossRef] [PubMed]
2. Vargas, C.S.; Struelens, L.; D'Huyvetter, M.; Caveliers, V.; Covens, P. Assessment of mouse-specific pharmacokinetics in kidneys based on 131I activity measurements using micro-SPECT. *EJNMMI Phys.* **2022**, *9*, 13. [CrossRef] [PubMed]
3. Stokke, C.; Kvassheim, M.; Blakkisrud, J. Radionuclides for targeted therapy: Physical properties. *Molecules* **2022**, *27*, 5429. [CrossRef] [PubMed]
4. Fan, P. Studies on Positioning and Energy Performance Optimization of Advanced Detector for Nuclear Medicine Imaging Systems. Master's Thesis, Tsinghua University, Beijing, China, 2016.
5. Mohan, A.-M.; Beindorff, N.; Brenner, W. Nuclear medicine imaging procedures in oncology. *Metastasis Methods Protoc.* **2021**, *2294*, 297–323. [CrossRef]
6. Jin, Y.J. *Nuclear Medical Instrument and Method*; Harbin Engineering University Press: Harbin, China, 2010.
7. Lecoq, P.; Gektin, A.; Korzhik, M.; Lecoq, P.; Gektin, A.; Korzhik, M. Scintillation mechanisms in inorganic scintillators. In *Inorganic Scintillators for Detector Systems: Physical Principles and Crystal Engineering*; Springer: Berlin/Heidelberg, Germany, 2017; pp. 125–174. [CrossRef]
8. Bell, Z.W. Scintillators and Scintillation Detectors. In *Handbook of Particle Detection and Imaging*; Springer: Berlin/Heidelberg, Germany, 2021; pp. 413–449. [CrossRef]
9. Wagenaar, D.J.; Zhang, J.; Kazules, T.; Vandehei, T.; Bolle, E.; Chowdhury, S.; Parnham, K.; Patt, B.E. In vivo dual-isotope SPECT imaging with improved energy resolution. In Proceedings of the 2006 IEEE Nuclear Science Symposium Conference Record, San Diego, CA, USA, 29 October–1 November 2006; Volume 6, pp. 3821–3826. [CrossRef]

10. Vaněček, V.; Děcká, K.; Mihóková, E.; Čuba, V.; Král, R.; Nikl, M. Advanced halide scintillators: From the bulk to nano. *Adv. Photon. Res.* **2022**, *3*, 2200011. [CrossRef]
11. Usanase, N.; Uzun, B.; Ozsahin, D.U.; Ozsahin, I. A look at radiation detectors and their applications in medical imaging. *J. Radiol.* **2024**, *42*, 145–157. [CrossRef]
12. Hawrami, R.; Ariesanti, E.; Farsoni, A.; Szydel, D.; Sabet, H. Growth and evaluation of improved CsI: Tl and NaI: Tl scintillators. *Crystals* **2022**, *12*, 1517. [CrossRef]
13. Berthold, T.; Böninger, H.; Stielfried, J. Growth of single crystalline NaI plates. *J. Cryst. Growth* **2000**, *217*, 441–448. [CrossRef]
14. Yang, K.; Menge, P.R. Improving γ-ray energy resolution, non-proportionality, and decay time of NaI: Tl^+ with Sr^{2+} and Ca^{2+} co-doping. *J. Appl. Phys.* **2015**, *118*, 21. [CrossRef]
15. Jin, Y.; Liu, J.; Chang, W.; Liu, Y.; Huang, G. Calibrations and corrections of a modular cylindrical SPECT system (McSPECT-II). *IEEE Trans. Nucl. Sci.* **1995**, *42*, 2275–2280. [CrossRef]
16. Badawi, M.S.; Thabet, A.A. Measurements correlated to efficiency studies of NaI (Tl) scintillator with vertical hexagonal radioactive source. *J. Instrum.* **2021**, *16*, P07011. [CrossRef]
17. Takeuchi, S.; Motobayashi, T.; Togano, Y.; Matsushita, M.; Aoi, N.; Demichi, K.; Hasegawa, H.; Murakami, H. DALI2: A NaI (Tl) detector array for measurements of γ rays from fast nuclei. *Nucl. Instrum. Methods Phys. Res. Sect. A* **2014**, *763*, 596–603. [CrossRef]
18. Krizsan, A.K.; Kukuts, K.; Al-Muhanna, W.; Szoboszlai, Z.; Balazs, L.; Szabo, B.; Kiss, J.; Nekolla, S.; Barna, S.; Garai, I. Performance evaluation of a novel multi-pinhole collimator on triple-NaI-detector SPECT/CT for dedicated myocardial imaging. *EJNMMI Phys.* **2023**, *10*, 24. [CrossRef] [PubMed]
19. Wang, L.; Zheng, Y.; Zhang, J.; Wang, M.; Wu, D.; Wang, Y.; Qiu, H.; Hsu, B.; Fang, W. Diagnostic value of quantitative myocardial blood flow assessment by NaI (Tl) SPECT in detecting significant stenosis: A prospective, multi-center study. *J. Nucl. Cardiol.* **2023**, *30*, 769–780. [CrossRef]
20. Dai, T.; Liu, Y.; Ma, T.Y.; Xia, Y.; Wang, S.; Wei, Q.; Jin, Y. Design and performance evaluation of high-resolution small animal SPECT system. *At. Energy Sci. Technol.* **2011**, *45*, 369–373. [CrossRef]
21. Telikani, Z.; Sadremomtaz, A. A Monte Carlo simulation study of optimization for collimator in a pixelated SPECT camera. *J. Med. Imaging Radiat. Sci.* **2019**, *50*, 163–170. [CrossRef]
22. Carminati, M.; D'Adda, I.; Morahan, A.J.; Erlandsson, K.; Nagy, K.; Czeller, M.; Tölgyesi, B.; Nyitrai, Z.; Savi, A.; van Mullekom, P. Clinical SiPM-based MRI-compatible SPECT: Preliminary characterization. *IEEE Trans. Radiat. Plasma Med. Sci.* **2019**, *4*, 371–377. [CrossRef]
23. Bläckberg, L.; Sajedi, S.; Anderson, O.A.; Feng, Y.; El Fakhri, G.; Furenlid, L.; Sabet, H. Dynamic Cardiac SPECT for diagnostic and theranostics applications: Latest results. In Proceedings of the 2020 IEEE Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), Boston, MA, USA, 31 October–7 November 2020; pp. 1–3. [CrossRef]
24. Massari, R.; D'Elia, A.; Soluri, A.; Soluri, A. Super Spatial Resolution (SSR) method for small animal SPECT imaging: A Monte Carlo study. *Nucl. Instrum. Methods Phys. Res. Sect. A* **2020**, *982*, 164584. [CrossRef]
25. Nagarkar, V.V.; Gaysinskiy, V.; Shestakova, I.; Taylor, S. Microcolumnar CsI(Tl) films for small animal SPECT. In Proceedings of the IEEE Symposium Conference Record Nuclear Science 2004, Rome, Italy, 16–22 October 2004; Volume 5, pp. 3334–3337. [CrossRef]
26. Beekman, F.J.; de Vree, G.A. Photon-counting versus an integrating CCD-based gamma camera: Important consequences for spatial resolution. *Phys. Med. Biol.* **2005**, *50*, N109. [CrossRef]
27. Nagarkar, V.V.; Shestakova, I.; Gaysinskiy, V.; Tipnis, S.V.; Singh, B.; Barber, W.; Hasegawa, B.; Entine, G. A CCD-based detector for SPECT. *IEEE Trans. Nucl. Sci.* **2006**, *53*, 54–58. [CrossRef]
28. Han, L.; Miller, B.W.; Barrett, H.H.; Barber, H.B.; Furenlid, L.R. Applications of iQID cameras. In Proceedings of the SPIE: Radiation Detectors in Medicine, Industry, and National Security XVIII, San Diego, CA, USA, 9–10 August 2017; SPIE: Bellingham, WA, USA, 2017; Volume 10393, pp. 165–170. [CrossRef]
29. Zheng, R.; Wang, L.; Liu, Y.; Chen, J.; Xiao, P.; Xie, Q. Optical and scintillation properties of modified LSO crystals with different ions doping grown by a rapid CZ system. *J. Cryst. Growth* **2024**, *627*, 127523. [CrossRef]
30. Reilly, R.M. Nuclear Medicine Imaging Technology. In *Medical Imaging for Health Professionals: Technologies and Clinical Applications*; John Wiley & Sons: Hoboken, NJ, USA, 2019; pp. 27–43.
31. Laguta, V.; Havlak, L.; Babin, V.; Barta, J.; Pejchal, J.; Nikl, M. Charge transfer and charge trapping processes in Ca- or Al-Co-doped Lu_2SiO_5 and $Lu_2Si_2O_7$ scintillators activated by Pr^{3+} or Ce^{3+} ions. *Materials* **2023**, *16*, 4488. [CrossRef] [PubMed]
32. Gundacker, S.; Turtos, R.M.; Kratochwil, N.; Pots, R.H.; Paganoni, M.; Lecoq, P.; Auffray, E. Experimental time resolution limits of modern SiPMs and TOF-PET detectors exploring different scintillators and Cherenkov emission. *Phys. Med. Biol.* **2020**, *65*, 025001. [CrossRef] [PubMed]
33. Yao, R.; Ma, T.; Shao, Y. Lutetium oxyorthosilicate (LSO) intrinsic activity correction and minimal detectable target activity study for SPECT imaging with a LSO-based animal PET scanner. *Phys. Med. Biol.* **2008**, *53*, 4399. [CrossRef]
34. Nazir, A.; Matthews, R.; Chimpiri, A.; Henretta, M.; Varughese, J.; Franceschi, D. Fluorodeoxyglucose positron-emission tomography-magnetic resonance hybrid imaging: An emerging tool for staging of cancer of the uterine cervix. *World J. Nucl. Med.* **2021**, *20*, 150–155. [CrossRef]

35. Enríquez-Mier-y-Terán, F.E.; Ortega-Galindo, A.S.; Murrieta-Rodríguez, T.; Rodríguez-Villafuerte, M.; Martínez-Dávalos, A.; Alva-Sánchez, H. Coincidence energy spectra due to the intrinsic radioactivity of LYSO scintillation crystals. *EJNMMI Phys.* **2020**, *7*, 1–17. [CrossRef]
36. Nakanishi, K.; Yamamoto, S.; Kataoka, J. Performance comparison of finely pixelated LYSO- and GAGG-based Si-PM gamma cameras for high resolution SPECT. *Nucl. Instrum. Methods Phys. Res. Sect. A* **2017**, *872*, 107–111. [CrossRef]
37. Dujardin, C.; Auffray, E.; Bourret-Courchesne, E.; Dorenbos, P.; Lecoq, P.; Nikl, M.; Vasil'Ev, A.N.; Yoshikawa, A.; Zhu, R.-Y. Needs, trends, and advances in inorganic scintillators. *IEEE Trans. Nucl. Sci.* **2018**, *65*, 1977–1997. [CrossRef]
38. Deprez, K.; Van Holen, R.; Vandenberghe, S. A high resolution SPECT detector based on thin continuous LYSO. *Phys. Med. Biol.* **2013**, *59*, 153. [CrossRef]
39. Massari, R.; D'elia, A.; Soluri, A. Preliminary results on a small animal SPECT system based on H13700 PSMPT coupled with CRY018 array. *Nucl. Instrum. Methods Phys. Res. A* **2019**, *940*, 296–301. [CrossRef]
40. Zhang, Q.; Li, S.; Xie, Z.; Lu, Y.; Yang, K.; Ren, Q. Development of a small animal SPECT imager with LYSO scintillator arrays and PSPMTs. In Proceedings of the 6th 2013 Biomedical Engineering International Conference, Krabi, Thailand, 23–25 October 2013; pp. 1–5. [CrossRef]
41. Wei, Q. Intrinsic radiation in lutetium based PET detector: Advantages and disadvantages. *arXiv* **2015**, arXiv:1501.05372. [CrossRef]
42. Ferri, T.; Caracciolo, A.; Borghi, G.; Carminati, M.; Altieri, S.; Protti, N.; Fiorini, C. Imaging Study and First Measurements of a $LaBr_3$ Gamma Detector for BNCT Applications. *IEEE Trans. Nucl. Sci.* **2024**, *71*, 1019–1025. [CrossRef]
43. Tseremoglou, S.; Michail, C.; Valais, I.; Ninos, K.; Bakas, A.; Kandarakis, I.; Fountos, G.; Kalyvas, N. Optical Photon Propagation Characteristics and Thickness Optimization of $LaCl_3$: Ce and $LaBr_3$: Ce Crystal Scintillators for Nuclear Medicine Imaging. *Crystals* **2023**, *14*, 24. [CrossRef]
44. van der Sar, S.J.; Leibold, D.; Brunner, S.E.; Schaart, D.R. $LaBr_3$: Ce and silicon photomultipliers: Towards the optimal scintillating photon-counting detector. In Proceedings of the 7th International Conference on Image Formation in X-Ray Computed Tomography, Baltimore, MD, USA, 12–16 June 2022; Volume 12304, pp. 55–60. [CrossRef]
45. Ji, Y.-Y.; Lim, T.; Choi, H.-Y.; Chung, K.H.; Kang, M.J. Development and performance of a multipurpose system for the environmental radiation survey based on a $LaBr_3$(Ce) detector. *IEEE Trans. Nucl. Sci.* **2019**, *66*, 2422–2429. [CrossRef]
46. Hou, Y.; Liu, S.; Yuan, H.; Gui, Q.; Zhang, C.; Fang, Z.; Zhang, M. Study on high-temperature performance of $LaBr_3$ (Ce) scintillators. IOP Conf. *Ser. Mater. Sci. Eng.* **2019**, *678*, 012084. [CrossRef]
47. Feng, P.-Y.; Sun, X.-L.; An, Z.-H.; Deng, Y.; Wang, C.-E.; Jiang, H.; Li, J.-J.; Zhang, D.-L.; Li, X.-Q.; Xiong, S.-L. The energy response of $LaBr_3$(Ce), $LaBr_3$(Ce, Sr), and NaI(Tl) crystals for GECAM. *Nucl. Sci. Technol.* **2024**, *35*, 23. [CrossRef]
48. Alzimami, K.S.; Spyrou, N.M.; Sassi, S.A. Investigation of $LaBr_3$: Ce and $LaCl_3$: Ce scintillators for SPECT imaging. In Proceedings of the 2008 5th IEEE International Symposium on Biomedical Imaging: From Nano to Macro, Paris, France, 14–17 May 2008; pp. 1243–1246. [CrossRef]
49. Roy, T.; Ratheesh, J.; Sinha, A. Three-dimensional SPECT imaging with $LaBr_3$: Ce scintillator for characterization of nuclear waste. *Nucl. Instrum. Methods Phys. Res. Sect. A* **2014**, *735*, 1–6. [CrossRef]
50. Zhao, C.L.; Li, Y.P.; Chen, L.H.; Yuan, C.; Qi, Y.J. The experimental study of lanthanum bromide detector in the gamma ray imaging. *Appl. Mech. Mater.* **2013**, *336*, 373–378. [CrossRef]
51. Wang, Z.; Guo, H.; Qian, S.; Zhu, Y.; Hu, P.; Wu, Q.; Chen, P.; Ma, L.; Peng, S.; Zhang, L. Performance study of GAGG: Ce scintillator for gamma and neutron detection. *J. Instrum.* **2020**, *15*, C06031. [CrossRef]
52. Martinazzoli, L.; Nargelas, S.; Boháček, P.; Calá, R.; Dušek, M.; Rohlíček, J.; Tamulaitis, G.; Auffray, E.; Nikl, M. Compositional engineering of multicomponent garnet scintillators: Towards an ultra-accelerated scintillation response. *Mater. Adv.* **2022**, *3*, 6842–6852. [CrossRef]
53. Park, C.; Kim, S.; Melis, A.; Seo, J.; Cho, S.; Yeom, J.-Y. Time-resolved photoluminescence analysis of ceramic Ce: GAGG scintillators. *Opt. Express* **2023**, *31*, 34677–34687. [CrossRef] [PubMed]
54. Martinazzoli, L.; Kratochwil, N.; Gundacker, S.; Auffray, E. Scintillation properties and timing performance of state-of-the-art $Gd_3Al_2Ga_3O_{12}$ single crystals. *Nucl. Instrum. Methods Phys. Res. Sect. A* **2021**, *1000*, 165231. [CrossRef]
55. Bárta, J.; Müllerová, E.; Kuzár, M.; Procházková, L.; Kučerová, R.; Jakubec, I.; Čuba, V. Photochemical synthesis and characterization of multi-component $(Gd, Lu)_3(Ga, Al)_5O_{12}$: Ce garnet powders. *Radiat. Meas.* **2019**, *124*, 98–102. [CrossRef]
56. Murata, I.; Kusaka, S.; Minami, K.; Saraue, N.; Tamaki, S.; Kato, I.; Sato, F. Design of SPECT for BNCT to measure local boron dose with GAGG scintillator. *Appl. Radiat. Isot.* **2022**, *181*, 110056. [CrossRef]
57. Wei, Q.; Ma, T.; Jiang, N.; Xu, T.; Lyu, Z.; Hu, Y.; Liu, Y. A side-by-side LYSO/GAGG phoswich detector aiming for SPECT imaging. *Nucl. Instrum. Methods Phys. Res. Sect. A Accel. Spectrometers Detect. Assoc. Equip.* **2020**, *953*, 163242. [CrossRef]
58. Ma, T.; Wei, Q.; Lyu, Z.; Zhang, D.; Zhang, H.; Wang, R.; Dong, J.; Liu, Y.; Yao, R.; He, Z.-X. Self-collimating SPECT with multi-layer interspaced mosaic detectors. *IEEE Trans. Med. Imaging* **2021**, *40*, 2152–2169. [CrossRef]
59. Wu, Y. Crystal growth, scintillation mechanism, and radiation detection applications of $Cs_3Cu_2I_5$: Tl single crystals. In Proceedings of the 2024 IEEE Nuclear Science Symposium (NSS), Medical Imaging Conference (MIC) and Room Temperature Semiconductor Detector Conference (RTSD), Tampa, FL, USA, 26 October–2 November 2024; p. 1. [CrossRef]

60. Liu, Z.; Li, W.; Wang, L.; Zhang, F.; Wang, S.; Liu, J.; Zhang, C.; Yin, L.; Jia, G.; Shi, Z. Uniform nucleation and growth of $Cs_3Cu_2I_5$ nanocrystals with high luminous efficiency and structural stability and their application in white light-emitting diodes. *Nanoscale* **2023**, *15*, 11491–11496. [CrossRef]
61. Wang, P.; Meng, M.; Nie, M.; Hu, X.; Cai, P.; Cai, M.; Lei, L.; Calvez, L.; Zhang, X.; Xu, S. Fabrication of Highly Stable $Cs_3Cu_2I_5$-in-Glass Composite for X-Ray Imaging by SPS Technique. *Adv. Opt. Mater.* **2024**, *12*, 2400813. [CrossRef]
62. Xiang, P.; Wei, Q.; Wang, C.; Cai, P.; Tong, Y.; Tang, G.; Sun, X.; Yang, F.; Shi, H.; Liu, Z.; et al. An all-inorganic Li-doped $Cs_3Cu_2I_5$ single crystal for dual gamma ray and neutron detection applications. *J. Mater. Chem. C* **2022**, *10*, 15400–15407. [CrossRef]
63. Wu, T.; Shi, Y.; Wu, H.; Chen, M.; Ran, H.; Zheng, J.; Li, X.; Chen, J.; Tang, Y. Potassium-regulated lead-free cesium copper iodide $Cs_3Cu_2I_5$ perovskites with enhanced scintillation properties and their application in high-resolution X-ray imaging. *J. Mater. Chem. C* **2024**, *12*, 1002–1011. [CrossRef]
64. Li, Y.; Tang, H.; Yu, B.; Wang, Z.; He, G.; Lin, Q. Sb-enhanced $Cs_3Cu_2I_5$ scintillators for ionizing radiation detection. *J. Mater. Chem. C* **2024**, *12*, 6841–6848. [CrossRef]
65. Kim, C.; Lee, W.; Melis, A.; Elmughrabi, A.; Lee, K.; Park, C.; Yeom, J.-Y. A review of inorganic scintillation crystals for extreme environments. *Crystals* **2021**, *11*, 669. [CrossRef]
66. Błaszczyk, M.; Adamczewski, Z.; Płachcińska, A. Capabilities of Modern Semiconductor Gamma Cameras in Radionuclide Diagnosis of Coronary Artery Disease. *Diagnostics* **2021**, *11*, 2130. [CrossRef] [PubMed]
67. Johns, P.M.; Nino, J.C. Room temperature semiconductor detectors for nuclear security. *J. Appl. Phys.* **2019**, *126*, 040901. [CrossRef]
68. Venkataraman, R. Semiconductor detectors. In *Handbook of Radioactivity Analysis*; Elsevier: Amsterdam, The Netherlands, 2020; pp. 409–491. [CrossRef]
69. Farnworth, A.L.; Bugby, S.L. Intraoperative gamma cameras: A review of development in the last decade and future outlook. *J. Imaging* **2023**, *9*, 102. [CrossRef]
70. Owens, A. Semiconductor materials and radiation detection. *J. Synchrotron Radiat.* **2006**, *13*, 143–150. [CrossRef]
71. Iniewski, K. CZT detector technology for medical imaging. *J. Instrum.* **2014**, *9*, C11001. [CrossRef]
72. Murata, I.; Nakamura, S.; Manabe, M.; Miyamaru, H.; Kato, I. Characterization measurement of a thick CdTe detector for BNCT-SPECT—Detection efficiency and energy resolution. *Appl. Radiat. Isot.* **2014**, *88*, 129–133. [CrossRef]
73. Abbene, L.; Principato, F.; Buttacavoli, A.; Gerardi, G.; Bettelli, M.; Zappettini, A.; Altieri, S.; Auricchio, N.; Caroli, E.; Zanettini, S. Potentialities of high-resolution 3-D CZT drift strip detectors for prompt gamma-ray measurements in BNCT. *Sensors* **2022**, *22*, 1502. [CrossRef]
74. Zavadovsky, K.V.; Mochula, A.V.; Maltseva, A.N.; Shipulin, V.V.; Sazonova, S.I.; Gulya, M.O.; Liga, R.; Gimelli, A. The current status of CZT SPECT myocardial blood flow and reserve assessment: Tips and tricks. *J. Nucl. Cardiol.* **2022**, *29*, 3137–3151. [CrossRef]
75. Panjer, M.; Dobrolinska, M.; Wagenaar, N.R.L.; Slart, R.H.J.A. Diagnostic accuracy of dynamic CZT-SPECT in coronary artery disease. A systematic review and meta-analysis. *J. Nucl. Cardiol.* **2022**, *29*, 1686–1697. [CrossRef] [PubMed]
76. Abbene, L.; Principato, F.; Gerardi, G.; Benassi, G.; Zambelli, N.; Zappettini, A.; Bettelli, M.; Seller, P.; Veale, M.C. Digital CZT detector system for high flux energy-resolved X-ray imaging. In Proceedings of the 2016 IEEE Nuclear Science Symposium, Medical Imaging Conference and Room-Temperature Semiconductor Detector Workshop (NSS/MIC/RTSD), Strasbourg, France, 29 October–6 November 2016; pp. 1–7. [CrossRef]
77. Kim, Y.; Lee, T.; Lee, W. Radiation measurement and imaging using 3D position sensitive pixelated CZT detector. *Nucl. Eng. Technol.* **2019**, *51*, 1417–1427. [CrossRef]
78. Favero, M.S.; Marques da Silva, A.M. Image Quality Performance of a Dedicated Cardiac Discovery NM 530c SPECT: Impact of Time Acquisition and Reconstruction Parameters. In Proceedings of the World Congress on Medical Physics and Biomedical Engineering 2018, Prague, Czech Republic, 3–8 June 2018; Volume 3, pp. 703–707. [CrossRef]
79. Sajedi, S.; Bläckberg, L.; Vittum, B.; Sabet, H. Dynamic Cardiac SPECT system for diagnostic and theranostics applications: Design optimization and experimental data. *J. Nucl. Med.* **2020**, *61*, 308.
80. Hesse, M.; Dupont, F.; Mourad, N.; Babczenko, P.; Beaurin, G.; Xhema, D.; Bonaccorsi-Riani, E.; Jamar, F.; Lhommel, R. Kidney dynamic SPECT acquisition on a CZT swiveling-detector ring camera: An in vivo pilot study. *BMC Med. Imaging* **2024**, *24*, 94. [CrossRef]
81. Song, H.; Ferri, V.; Duan, H.; Aparici, C.M.; Davidzon, G.; Franc, B.L.; Moradi, F.; Nguyen, J.; Shah, J.; Iagaru, A. SPECT at the speed of PET: A feasibility study of CZT-based whole-body SPECT/CT in the post 177Lu-DOTATATE and 177Lu-PSMA617 setting. *Eur. J. Nucl. Med. Mol. Imaging* **2023**, *50*, 2250–2257. [CrossRef]
82. Verger, A.; Cecchin, D.; Guedj, E.; Albert, N.L.; Brendel, M.; Fraioli, F.; Tolboom, N.; Traub-Weidinger, T.; Yakushev, I.; Van Weehaeghe, D.; et al. EANM perspectives for CZT SPECT in brain applications. *Eur. J. Nucl. Med. Mol. Imaging* **2024**, *51*, 3680–3684. [CrossRef]
83. Fang, W.; Liu, S. New 99mTc radiotracers for myocardial perfusion imaging by SPECT. *Curr. Radiopharm.* **2019**, *12*, 171–186. [CrossRef]
84. Duan, H.; Ferri, V.; Castaneda, P.; Visser, T.; Luong, K.; Davidzon, G.; Aparici, C.M.; Iagaru, A. Head-to-head Comparison of a Conventional or CZT-based SPECT/CT with a Next Generation Multidetector CZT-based SPECT/CT System. *J. Nucl. Med.* **2022**, *28*, 3323–3324. [CrossRef]

85. Lai, X.; Meng, L.-J. Simulation study of the second-generation MR-compatible SPECT system based on the inverted compound-eye gamma camera design. *Phys. Med. Biol.* **2018**, *63*, 045008. [CrossRef]
86. Huh, Y.; Yang, J.; Dim, O.U.; Cui, Y.; Tao, W.; Huang, Q.; Gullberg, G.T.; Seo, Y. Evaluation of a variable-aperture full-ring SPECT system using large-area pixelated CZT modules: A simulation study for brain SPECT applications. *Med. Phys.* **2021**, *48*, 2301–2314. [CrossRef]
87. Scuffham, J.W.; Wilson, M.D.; Seller, P.; Veale, M.C.; Sellin, P.J.; Jacques, S.D.M.; Cernik, R.J. A CdTe detector for hyperspectral SPECT imaging. *J. Instrum.* **2012**, *7*, P08027. [CrossRef]
88. Takeda, S.; Orita, T.; Yagishita, A.; Katsuragawa, M.; Yabu, G.; Tomaru, R.; Moriyama, F.; Sugawara, H.; Watanabe, S.; Mizuma, H. CdTe-DSD SPECT-I: An ultra-high-resolution multi-isotope tomographic imager for mice. *IEEE Trans. Radiat. Plasma Med. Sci.* **2023**, *7*, 860–870. [CrossRef]
89. Roser, J.; Hueso-González, F.; Ros, A.; Llosá, G. Compton cameras and their applications. In *Radiation Detection Systems*; CRC Press: Boca Raton, FL, USA, 2021; pp. 161–198.
90. Choong, W.-S.; Moses, W.W.; Tindall, C.S.; Luke, P.N. Design for a high-resolution small-animal SPECT system using pixellated Si(Li) detectors for in vivo 125I imaging. *IEEE Trans. Nucl. Sci.* **2005**, *52*, 174–180. [CrossRef]
91. Hawman, P.C.; Haines, E.J. The cardiofocal collimator: A variable-focus collimator for cardiac SPECT. *Phys. Med. Biol.* **1994**, *39*, 439. [CrossRef] [PubMed]
92. Datta, A.; Mei, H.; Lebedinsky, A.; Halasyamani, P.S.; Motakef, S. Gallium oxide semiconductor-based large volume ultrafast radiation hard spectroscopic scintillators. *J. Appl. Phys.* **2024**, *136*, 064503. [CrossRef]