frontiers | Frontiers in Sensors

TYPE Mini Review
PUBLISHED 06 November 2025
DOI 10.3389/fsens.2025.1585385

Check for updates

OPEN ACCESS

EDITED BY
Alberto Quaranta,
University of Trento, Italy

REVIEWED BY
Antonino Miceli,
Argonne National Laboratory (DOE),
United States

*CORRESPONDENCE
Paolo Cardarelli,
cardarelli@fe.infn.it

RECEIVED 28 February 2025
REVISED 24 July 2025
ACCEPTED 15 October 2025
PUBLISHED 06 November 2025

CITATION
Vladi Biesuz N, Bolzonella R, Brombal L, Cardarelli P, Cavallini V, Cerbone LA, Cimmino L, Delogu P, Feruglio A, Longo R, Mazzini V, Mettivier G, Paternò G, Rosso V, Russo P, Taibi A, Tudisco S, Velardita S and Fiorini M (2025) Review of INFN activities on characterization and applications of hybrid pixel detectors based on Timepix4 ASIC. *Front. Sens.* 6:1585385. doi: 10.3389/fsens.2025.1585385

Review of INFN activities on characterization and applications of hybrid pixel detectors based on Timepix4 ASIC

Nicolò Vladi Biesuz[1], Riccardo Bolzonella[1,2], Luca Brombal[3], Paolo Cardarelli[1]*, Viola Cavallini[1,2], Laura Antonia Cerbone[4,5], Luigi Cimmino[4], Pasquale Delogu[6], Alessandro Feruglio[6], Renata Longo[3], Vittoria Mazzini[1,2], Giovanni Mettivier[4], Gianfranco Paternò[1], Valeria Rosso[6], Paolo Russo[4], Angelo Taibi[1,2], Salvatore Tudisco[7], Simone Velardita[1] and Massimiliano Fiorini[1,2]

[1]INFN Sezione di Ferrara, Ferrara, Italy, [2]Dipartimento di Fisica e Scienze Della Terra, University of Ferrara, Ferrara, Italy, [3]Dipartimento di Fisica, Università di Trieste and INFN Sezione di Trieste, Trieste, Italy, [4]Dipartimento di Fisica "Ettore Pancini", Università di Napoli Federico II and INFN Sezione di Napoli, Napoli, Italy, [5]Scuola Superiore Meridionale, Napoli, Italy, [6]Dipartimento di Fisica, Università di Pisa and INFN Sezione di Pisa, Pisa, Italy, [7]INFN Laboratori Nazionali del Sud, Catania, Italy

The Medipix4 international collaboration represents a landmark initiative in the field of pixelated radiation imaging and detection. Building on the successes of its predecessors—the Medipix2 and Medipix3 collaborations—this effort has been pivotal in advancing hybrid pixel detector technology for a wide range of applications, including medical imaging, particle physics, and material science. The collaboration brings together a consortium of research institutions and industry partners, leveraging decades of expertise to push the boundaries of detector performance and integration. The aim of the Medipix4 collaboration is the development of two state-of-the-art application-specific integrated circuits (ASICs): Timepix4 and Medipix4. These ASICs are designed to address critical challenges in pixelated detection systems, including enhanced spatial resolution, higher data throughput, and improved energy resolution, while maintaining compatibility with a wide range of detector materials. The Italian Institute for Nuclear Physics (INFN) has been a member of the Medipix4 collaboration since 2020. This review reports the various activities that have been carried out by INFN to fully characterize the performance of detectors based on this technology. Various assemblies composed of a Timepix4 ASIC bump-bonded to Si-sensors with different thicknesses and material characteristics were manufactured and tested.

KEYWORDS

photon counting, hybrid detector, pixel detector, x-ray imaging, gamma camera

1 Introduction

Hybrid pixel detectors consist of separate sensor elements and readout electronics, each manufactured independently and later integrated using the bump-bonding interconnection technique. Such detectors enable the independent optimization of sensor and electronics to obtain the best overall performance. Initially developed for the high-energy physics community at CERN in the 1980s and 1990s, this technology was later adapted for X-ray detection and various other applications, particularly in biomedical imaging (Delpierre, 2014).

The Medipix4 international collaboration represents a landmark initiative in the field of pixelated radiation imaging and detection and was built on the successes of previous collaborations. The generation of application-specific integrated circuits (ASICs) Medipix1, Medipix2, and Medipix3 that had been developed represented a constant pivotal advance in hybrid pixel detector technology, attested by their applications in a very wide range of fields, including medical imaging, space, particle physics, and material science. The collaboration brings together a consortium of research institutions and industry partners, leveraging decades of expertise to push the boundaries of detector performance and integration. The Medipix collaborations at CERN designed several pixel detector readout chips, grown in size and complexity (Ballabriga et al. 2020; Ballabriga et al., 2018), to reach the fourth generation with the Medipix4 Collaboration. The last two ASICs are Timepix4 (Llopart et al., 2022), which provides particle detection with excellent spatial and timing precision at high rates, and Medipix4 (Sriskaran et al., 2024), which targets spectroscopic X-ray imaging at rates compatible with medical CT scans. These ASICs are designed to address critical challenges in pixelated detection systems, including enhanced spatial resolution, higher data throughput, and improved energy resolution, while maintaining compatibility with a wide range of detector materials. The Italian National Institute for Nuclear Physics (INFN) was part of the initial Medipix1 collaboration and has been a member of the Medipix4 collaboration since 2020.

In the past few years, two research projects have been funded by INFN: the National Scientific Committee 5, MEDIPIX4 (2021–2024) and the more recent TIMEPIX4 (started in 2025). These projects aim to advance the study and development of applications for these technologies, while also exploiting the INFN expertise in the characterization of hybrid photon-counting detectors (Brombal et al., 2018; Di Trapani et al., 2020).

2 Timepix4 ASIC

Timepix4 is the latest ASIC in the Timepix family, designed primarily for single-particle detection in hybrid pixel detectors. Built using 65 nm CMOS technology, Timepix4 achieves exceptional spatial and temporal resolutions while supporting high-rate data processing capabilities. This ASIC, described in detail by Llopart et al. (2022), marks a substantial advancement in time-resolved radiation imaging. Its architecture consists of a 448×512 pixel matrix with a 55-μm pitch, delivering high spatial resolution across an active area of nearly 7 cm^2. Timepix4 timestamps particle interactions with sub-100 ps precision, enabling highly accurate temporal measurements. Data output is managed through 16 configurable high-speed links operating at speeds ranging from 40 Mb/s to 10.24 Gb/s. This setup supports a maximum data throughput of 163.84 Gb/s, equivalent to approximately 2.5 Ghits/s.

Timepix4 supports two distinct operating modes:

1. Frame-based mode: any signal exceeding a programmable threshold increments a pixel-specific counter. All matrix counters are then read synchronously with the core clock. This mode primarily captures photon counts.
2. Data-driven mode: a pixel generates and transmits an output packet immediately after detecting an event. This mode can also provide additional information, such as time-of-arrival (ToA) and time-over-threshold (ToT), measured by time-to-digital converters (TDC) located in the pixels' digital front-end, based on voltage-controlled oscillators (VCO), allowing access to finer time bins. ToA is measured with a 195 ps time bin size, while ToT uses a 1.56 ns time bin size, facilitating energy calibration and discrimination at the pixel level.

The main features of Timepix4 are summarized in Table 1[1]. This unique combination of characteristics makes it suitable for different applications.

1. In the data-driven mode, measuring the ToT for each event allows for the evaluation of energy deposits over a continuous range without fixed energy bins based on signal thresholds. Additionally, measuring the ToA for each event enables time-based data analysis and clustering procedures. These, together with the high spatial resolution, are of great interest for spectral X-ray imaging, nuclear imaging, and beam monitoring and dosimetry.
2. Frame-based operation mode makes it a single-threshold photon-counting detector achieving very high frame rates (up to 9×10^4 frames per second at 160 Gbit/s with 8-bit counters on each pixel) for fast imaging applications.
3. Being a hybrid detection system, the sensor material and its thickness can be tailored for each specific application.

2.1 Timepix4 detector assemblies, DAQ, and software

The first Timepix4 assemblies bonded to 300-μm-thick p-on-n planar silicon sensors were delivered to the Italian collaboration at the end of the 2022. The Timepix4 ASIC is connected to a SPIDR4 system developed by the Dutch National Institute for Subatomic Physics (NIKHEF) to configure and read out the chip. In-house software was developed, allowing configuration of the system at both low and high levels, acquiring data, and monitoring the acquisitions (Cavallini et al., 2025). For the

1 https://medipix.web.cern.ch/medipix4

TABLE 1 Main features of Timepix4.

General specification		
CMOS technology		65 nm
Pixel size		55 μm × 55 μm
Pixel matrix		448 × 512 (4-side buttable)
Sensitive area		6.94 cm^2
Analog front end		
Polarity		Positive and negative
Noise		80 e^-rms
Threshold variation		40 e^-rms
Minimum operating threshold		500 e^-
Digital front end and readout		
Data-driven	Mode	ToA and ToT
	Event packet dimension	64-bit
	Maximum rate	3.58×10^6 hits $mm^{-2}s^{-1}$
	Maximum pixel rate	10.8 kHz
Frame-based	Mode	Photon-counting continuous read-write (8 or 16 bits)
	Frame	Full frame
	Maximum rate	$\sim 5 \cdot 10^9$ hits $mm^{-2}s^{-1}$
Timestamp binning		195 ps
Energy resolution		< 1 keV
Maximum readout bandwidth		163.84 Gb/s

measurements described here, the ASIC was operated in data-driven mode, providing information on the events ToA and ToT. To keep the Timepix4 at a temperature of approximately 15 °C, a custom-made liquid cooling system was realized in copper and thermally connected to the chipboard housing the Timepix4 ASIC, developed by NIKHEF. Figure 1 illustrates the assembly. The Timepix4 assembly is visible along with the copper cooling system, and the SPIDR is connected at the back via a flat ribbon cable.

3 Test and characterization of detector assemblies based on TIMEPIX4

Various activities have been conducted at INFN to characterize the performance of several available detector assemblies, consisting of Timepix4 ASICs bump-bonded to Si sensors with varying thicknesses and material properties. Three versions of the Timepix4 chip have been produced to date. Unless otherwise noted, all results presented in this review were obtained with the second version. The following provides a brief summary of the methods and results from these studies along with the published literature.

3.1 Timing performance

A characterization of the timing performance of a Timepix4 assembly bonded to a 100-μm n-on-p planar silicon detector, provided by NIKHEF and the LHCb VELO group, was performed using a picosecond pulsed infrared laser as described in Bolzonella et al. (2024). Controlled signals generated in the silicon sensors were compared to the laser trigger signal to measure the assembly timing resolution. A resolution of 107±3 ps root mean square (r.m.s.) was achieved at the single pixel level, while a value down to 33±3 ps r.m.s. was obtained using multipixel clusters by exploiting oversampling. This study investigated various factors affecting timing resolution, including time walk and an original study regarding voltage-controlled oscillator (VCO) frequency variations affecting the time bin sizes at pixel level. Calibration procedures have been implemented to correct for these effects and to calibrate the deposited charge in the pixels. Ultimately, the study demonstrates the timing capabilities of Timepix4, validating its suitability for applications like the 4DPHOTON project (Fiorini et al., 2018; Alozy et al., 2022), which aims to develop a high-performance single-photon detector capable of simultaneously reaching cutting-edge timing and spatial resolution.

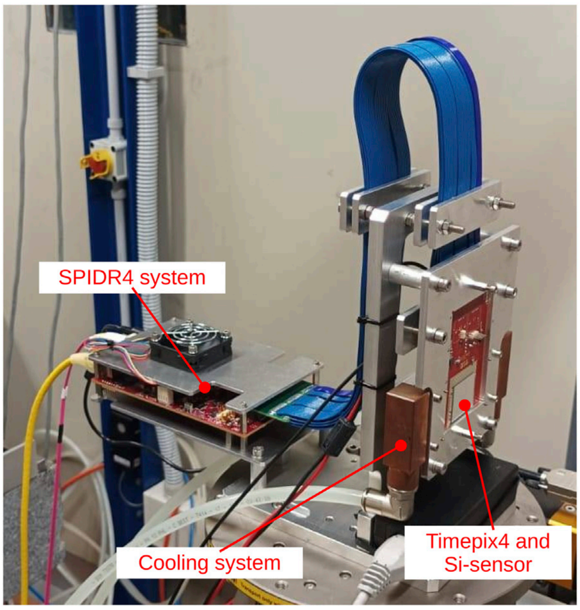

FIGURE 1
Detector setup used during the activities at ELETTRA synchrotron. On the right, the Timepix4 assembly with a bump-bonded Si-sensor, the copper cooling system, and the SPIDR4 readout system connected at the back via a flat ribbon cable.

3.2 Energy response calibration and characterization

For operation in the data-driven mode, a calibration of the measured ToT signals is necessary for the energy to be deposited in each pixel by the incident radiation. Several experimental configurations have been adopted for the calibration of the available detection systems, with a focus on X-ray imaging applications. All the Timepix4 assemblies studied were based on silicon sensors that varied in thickness; the X-ray generators used differed because the data were collected in various laboratories. A first calibration, based on test pulses internally generated by the ASIC, was performed for all the available detection systems. This procedure allowed the response of the 229k pixels of the ASIC to be partially uniform and enabled the measurement of X-ray photon energy with an accuracy of the order of a few keV.

The Timepix4 assembly based on a 500-µm-thick p-on-n silicon detector was preliminarily calibrated with X-rays on a limited number of pixels to limit the volume of acquired data and their analysis time. This setup, installed at the University of Ferrara, features an XM-12 mammographic X-ray tube coupled to a mosaic crystal; through it, Bragg's diffraction quasi-monochromatic X-ray beams with energy tunable between 8 and 35 keV were generated. Energy measurements were performed starting from 10 keV up to 35 keV in 5 keV steps. Over the whole detector surface, three areas of 5 × 5 pixels were selected and irradiated; after data acquisition, the resulted spectra for the six quasi-monochromatic X-ray beams were analyzed, and an asymmetric Gaussian fit was applied to each peak to determine the mean energy value and the standard deviation. The analysis revealed an energy shift of a few keV between the reconstructed energy spectra, calibrated with the test-pulses, and the X-rays' nominal values. More detailed results are reported in Mazzini et al. (2025) and Velardita et al. (2025). Results with this partial surface irradiation allowed the evaluation of the necessary photon statistics to achieve a pixel-to-pixel calibration across the whole matrix.

The other available assembly is based on a 300-µm-thick p-on-n silicon detector and was fully characterized in two data-collection campaigns, where the whole detector surface (~ 7 cm^2) was irradiated. During the first data taking, performed at the INFN and Physics Department of the University of Pisa laboratory, a micro-focus X-ray tube from Hamamatsu was used to produce fluorescence photons from various metal foils. The foils were located at approximately a 40-degree angle with respect to the direction of the micro-focus X-ray beam. The detector was placed outside the primary beam so that only fluorescence photons hit the detector's surface. By varying the material foils, eight irradiations in the energy range of 6.40–25.19 keV were performed. The data acquired were clustered using information on the ToA and on the location of the hits. The calibration procedure required a pixel-by-pixel analysis, and only photons with a fully collected charge in a single pixel were considered. The ToT spectra acquired were asymmetric with a long tail toward energies lower than the photopeak value. To evaluate the means and the standard deviations, Gaussian fits were performed considering only a limited region of the ToT photopeak, excluding the events not fully collected. For each pixel, the ToT values obtained for all the acquired energies were plotted as a function of energy and fitted with Equation 1, a four-parameter calibration function already available (Jakubek et al., 2007):

$$ToT = aE + b + \frac{c}{E - t} \tag{1}$$

Once the calibration procedure on a pixel basis was performed, the obtained calibrated energy spectra were analyzed, calculating both the mean measured energy corresponding to each photopeak and the standard deviation. The energy resolution, defined as FWHM/E, and the energy accuracy, defined as $|E_{nominal} - E_{measured}|/E_{nominal}$, were calculated. Accuracy was found to be better than 1.6%, while the detector's energy resolution, evaluated at 32.28 keV, was 9%. More details on the measurements were reported by Feruglio et al. (2024b).

The other experimental campaign was conducted at the SYRMEP (SYnchrotron Radiation for Medical Physics) beamline of the ELETTRA Synchrotron (Trieste, Italy), which has been instrumental in previous INFN experiments on advanced X-ray imaging techniques utilizing hybrid detector technology (Longo et al., 2019; Brombal et al., 2024). Detector irradiation was performed with monochromatic X-ray beams at 18 energy levels ranging from 8.5 keV to 40 keV. The laminar beam shape, characteristic of synchrotron radiation, required a specific set-up to fully irradiate the sensor. The Timepix4 detection system was moved vertically at a constant speed to obtain a uniform irradiation across the sensor surface. Moreover, the data acquired were clustered for the analysis, and only the photons with charges fully collected in a single pixel were considered. The ToT data were converted into energy adopting the same four parameter calibration function adopted in Feruglio et al. (2024b) and using only nine flat-field irradiations. Due to the non-linear behavior of the Timepix4 calibration curve in the low energy region, test-pulse data were used to extend the calibration range beyond the one characterized with X-rays. Seventeen points were sampled in a nominal energy range between 4.7 keV and 50.7 keV. The data acquired via test-pulse were analyzed by repeating the same procedure followed for the X-ray data. The integration of the X-ray data with test-pulse data required the specific procedure reported in Delogu et al. (2024) and Feruglio et al. (2024a). Analyzing the X-ray spectra, the energy resolution values obtained were slightly better than those obtained with fluorescence photons calibration, and the shift of the photopeak position was reduced, resulting in an accuracy better than 1.2%. Moreover, the detector's energy resolution was calculated for each energy measurement, and the data were then fitted with a Gaussian energy broadening function (Amoyal et al. (2020); Eftekhari Zadeh et al. (2014)). The calculated energy resolution function indicates that for X-ray beams above 22 keV, the relative energy resolution of the system is better than 9%.

3.3 Spatial resolution for X-ray imaging

The spatial response of the Timepix4 detection system, based on a 300-µm-thick p-on-n silicon detector, was also studied during data taking at the SYRMEP beamline, in terms of the line spread function (LSF). The system was energy-calibrated, as described in the previous section, and the edge spread function (ESF) was obtained by the moving edge method. The detector spatial response was characterized through multiple acquisitions with the synchrotron X-ray beam of 10 keV and 20 keV.

The spatial response is strongly affected by the charge sharing—the spread of the signal over multiple pixels due to the diffusion of the electrical charge cloud produced in the sensor. To mitigate this effect, events triggering multiple nearby pixels due to charge sharing can be clustered by using the ToA information. For this reason, the response of the detection system was studied by analyzing the data clustered in four ways: i) non clustered events; ii) clustered events, considering all cluster sizes events; iii) clustered events, considering only size = 1 clusters; iv) clustered events, considering only size = 2 clusters parallel to the shift direction. The LSFs were calculated using two methods: a direct differentiation and an analytical analysis; more details are reported in Delogu et al. (2025). The results obtained adopting the two methods agree with each other and show how charge sharing degrades the system spatial resolution, with the entity depending on the energy of the X-ray beam. The degradation can be recovered by applying the clusterization of the events, and the spatial resolution is determined only by the pixel pitch (55 µm). Moreover, the LSFs observed for cluster size = 2 events show that charge sharing occurs only when photons interact at the edges of the pixels, in an area approximately 10 µm wide.

4 Gamma camera and coded masks

In past years, INFN developed MediPROBE2, a compact gamma camera (CGC) for nuclear medicine procedures (sentinel lymph node imaging and radioguided surgery) based on the Medipix2/Timepix2 readout circuits, and a CdTe pixel detector coupled to pinhole collimators (Russo et al., 2011; Russo et al., 2020). Recently, within the MEDIPIX4 INFN project, the group designed and realized a new CGC prototype, MediPROBE4, based on the new Timepix4 readout ASIC and a high-resolution coded aperture (CA) collimator. With the availability of the larger ASIC (approximately 7 cm^2 for Timepix4 vs. approximately 2 cm^2 for Timepix2), the CA imaging probe can be operated with a significantly larger image field of view (88 mm × 88 mm) at a source–collimator distance of 50 mm. Correspondingly, Geant4 Monte Carlo simulations with a Tc-99m radioactive source (140.5 keV) —carried out for device performance analysis and optimization—indicated a system sensitivity as good as 0.22 cps/kBq and a lateral spatial resolution of 1.7 mm FWHM, with a 2-mm thick CdTe detector and an antisymmetric 62 × 62 MURA CA collimator with 0.25 mm apertures. The estimated axial (longitudinal) spatial resolution—as permitted by the specific 3D imaging capability of the CA collimator—was 8.2 mm FWHM for a radioactive source at 40 mm from the collimator face (Cerbone et al., 2023; Cerbone, 2023). Laboratory tests with a 300-µm-thick Silicon pixel detector bump-bonded to a Timepix4 v1 chip, and a high-resolution CA collimator, showed ToT and ToA capabilities with Am-241 and Ba-33 gamma radioactive sources and reasonable agreement with Monte Carlo simulated performance (Cerbone et al., 2023; Cerbone, 2023). The simulated imaging performance was tested using a Timepix3 silicon detector and a high resolution CA collimator, showing the capability of localizing the 3D-position of a gamma source with a mean localization error of 0.77 mm on the simulated image and 2.64 mm on the experimental data in the imaging range of 10–200 mm (Meißner et al., 2024b). Correspondingly, the axial resolution of 5.3 mm and 1.8 mm at 12 mm using standard MURA decoding or innovative 3D-MLEM decoding, respectively, were measured with a Am-241 source (Meißner et al., 2024a).

5 Conclusion

This review reports the various activities that have been carried out by INFN to characterize the performance of detectors based on the Timepix4 technology. Various assemblies composed of a Timepix4 ASIC bump-bonded to Si-sensors with different thicknesses and material characteristics have been manufactured and tested. Timing performance has been investigated through controlled laser-generated signals, providing insights into time resolution and the influence of systematic effects such as time walk and oscillator frequency variations. Energy response calibration has been carried out using different X-ray sources and experimental setups, allowing for precise correlation between detector signals and deposited energy. Spatial resolution has been analyzed through synchrotron-based studies, focusing on charge-sharing effects and event clustering techniques to improve imaging accuracy. The results of this characterization demonstrate that Timepix4-based detectors are promising for X-ray imaging applications.

In addition to characterization, this review reported the development of a compact gamma camera for nuclear medicine. By integrating the Timepix4 ASIC with coded aperture collimators, the system can enhance imaging sensitivity and spatial resolution.

Monte Carlo simulations and experimental tests have been conducted to optimize its performance for clinical applications. MediPROBE4 is now being implemented with a 2-mm-thick CdTe Timepix4 v2 ASIC and ergonomic handling for field operation in the clinic, with lab tests performed in 2025 and clinical tests planned for 2026.

The results of these activities highlight the ongoing efforts within the INFN community to advance hybrid pixel detector technology and expand its applications. Future research will extend the characterization to alternative high atomic-number sensor materials, such as CdTe or GaAs, which have recently become available to the INFN community. This will further broaden the impact of these detectors in high-precision radiation imaging and detection. The particle tracking and spectroscopic characteristics of these detection systems will also enable their application for the dosimetric characterization of X-ray, proton, and electron beams, adopting suitable configurations.

Author contributions

NV: Writing – review and editing. RB: Writing – review and editing, Visualization, Writing – original draft. LB: Writing – original draft, Writing – review and editing. PC: Writing – review and editing, Conceptualization, Visualization, Writing – original draft. VC: Writing – review and editing. LaC: Writing – review and editing. LuC: Writing – review and editing. PD: Writing – review and editing. AF: Visualization, Writing – review and editing. RL: Conceptualization, Writing – original draft, Writing – review and editing. VM: Writing – review and editing. GM: Conceptualization, Writing – original draft, Writing – review and editing. GP: Writing – review and editing. VR: Conceptualization, Writing – original draft, Writing – review and editing. PR: Writing – review and editing. AT: Writing – review and editing. ST: Writing – review and editing. SV: Visualization, Writing – review and editing. MF: Conceptualization, Writing – review and editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This work was carried out in the context of the Medipix4 Collaboration based at CERN and supported by the INFN-CSN5 (MEDIPIX4 project) and by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (Grant agreement No. 819627, 4DPHOTON project).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

References

Alozy, J. A., Biesuz, N. V., Campbell, M., Cavallini, V., Cotta Ramusino, A., Fiorini, M., et al. (2022). Development of a single-photon imaging detector with pixelated anode and integrated digital read-out. *J. Instrum.* 17, C06007. doi:10.1088/1748-0221/17/06/C06007

Amoyal, G., Ménesguen, Y., Schoepff, V., Carrel, F., Michel, M., Angélique, J.-C., et al. (2020). Evaluation of timepix3 si and cdTe hybrid-pixel detectors' spectrometric performances on x-and gamma-rays. *IEEE Trans. Nucl. Sci.* 68, 229–235. doi:10.1109/TNS.2020.3041831

Ballabriga, R., Campbell, M., and Llopart, X. (2018). Asic developments for radiation imaging applications: the medipix and timepix family. *Nucl. Instrum. Methods Phys. Res. Sect. A Accel. Spectrom. Detect. Assoc. Equip.* 878, 10–23. doi:10.1016/j.nima.2017.07.029

Ballabriga, R., Campbell, M., and Llopart, X. (2020). An introduction to the medipix family asics. *Radiat. Meas.* 136, 106271. doi:10.1016/j.radmeas.2020.106271

Bolzonella, R., Alozy, J., Ballabriga, R., van Beuzekom, M., Biesuz, N., Campbell, M., et al. (2024). Timing resolution performance of timepix4 bump-bonded assemblies. *J. Instrum.* 19, P07021. doi:10.1088/1748-0221/19/07/P07021

Brombal, L., Donato, S., Brun, F., Delogu, P., Fanti, V., Oliva, P., et al. (2018). Large-area single-photon-counting CdTe detector for synchrotron radiation computed tomography: a dedicated pre-processing procedure. *Synchrotron Radiat.* 25, 1068–1077. doi:10.1107/s1600577518006197

Brombal, L., Arfelli, F., Brun, F., Di Trapani, V., Endrizzi, M., Menk, R. H., et al. (2024). Edge-illumination spectral phase-contrast tomography. *Phys. Med. and Biol.* 69, 075027. doi:10.1088/1361-6560/ad3328

Cavallini, V., Biesuz, N. V., Bolzonella, R., Calore, E., Fiorini, M., Gianoli, A., et al. (2025). DataPix4: a C++ framework for Timepix4 configuration and read-out. *Comput. Phys. Commun.* 314, 109658. doi:10.1016/j.cpc.2025.109658

Cerbone, L. (2023). Towards a timepix4 compact gamma camera for coded aperture 3D imaging. *IL NUOVO CIMENTO* 100, 46. doi:10.1393/ncc/i2023-23128-4

Cerbone, L. A., Cimmino, L., Sarno, A., Biesuz, N. V., Bolzonella, R., Mettivier, G., et al. (2023). Monte carlo and experimental evaluation of a timepix4 compact gamma camera for coded aperture nuclear medicine imaging with depth resolution. *Phys. Medica* 113, 102663. doi:10.1016/j.ejmp.2023.102663

Delogu, P., Biesuz, N. V., Bolzonella, R., Brombal, L., Cavallini, V., Brun, F., et al. (2024). Validation of Timepix4 energy calibration procedures with synchrotron X-ray beams. *Nucl. Instrum. Methods Phys. Res. A* 1068, 169716. doi:10.1016/j.nima.2024.169716

Delogu, P., Biesuz, N., Bolzonella, R., Brombal, L., Brun, F., Cardarelli, P., et al. (2025). Timepix4 spatial response characterization with X-ray monochromatic synchrotron beam. *J. Instrum.* 20, C02047. doi:10.1088/1748-0221/20/02/C02047

Delpierre, P. (2014). A history of hybrid pixel detectors, from high energy physics to medical imaging. *J. Instrum.* 9, C05059. doi:10.1088/1748-0221/9/05/c05059

Di Trapani, V., Bravin, A., Brun, F., Dreossi, D., Longo, R., Mittone, A., et al. (2020). Characterization of the acquisition modes implemented in Pixirad-1/Pixie-III X-ray detector: effects of charge sharing correction on spectral resolution and image quality. *Nucl. Instrum. Methods Phys. Res. Sect. A Accel. Spectrom. Detect. Assoc. Equip.* 955, 163220. doi:10.1016/j.nima.2019.163220

Eftekhari Zadeh, E., Feghhi, S., Bayat, E., and Roshani, G. (2014). Gaussian energy broadening function of an hpge detector in the range of 40 kev to 1.46 mev. *J. Exp. Phys.* 2014, 1–4. doi:10.1155/2014/623683

Feruglio, A., Biesuz, N., Bolzonella, R., Brombal, L., Brun, F., Cardarelli, P., et al. (2024a). Timepix4 characterization with monochromatic x-rays at the elettra synchrotron facility. *Nucl. Instrum. Methods Phys. Res. Sect. A Accel. Spectrom. Detect. Assoc. Equip.* 1069, 169844. doi:10.1016/j.nima.2024.169844

Feruglio, A., Biesuz, N., Bolzonella, R., Cavallini, V., Fiorini, M., Rosso, V., et al. (2024b). Timepix4 calibration and energy resolution evaluation with fluorescence photons. *Il Nuovo Cimento C* 47. doi:10.1393/ncc/i2024-24314-6

Fiorini, M., Alozy, J., Bolognesi, M., Campbell, M., Ramusino, A. C., Llopart, X., et al. (2018). Single-photon imaging detector with o(10) ps timing and sub-10 μm position resolutions. *J. Instrum.* 13, C12005. doi:10.1088/1748-0221/13/12/C12005

Jakubek, J., Dammer, J., Holy, T., Jakubek, M., Pospisil, S., Tichy, V., et al. (2007). Spectrometric properties of timepix pixel detector for x-ray color and phase sensitive radiography. *2007 IEEE Nucl. Sci. Symposium Conf. Rec. (IEEE)* 3, 2323–2326. doi:10.1109/nssmic.2007.4436610

Llopart, X., Alozy, J., Ballabriga, R., Campbell, M., Casanova, R., Gromov, V., et al. (2022). Timepix4, a large area pixel detector readout chip which can be tiled on 4 sides providing sub-200 ps timestamp binning. *J. Instrum.* 17, C01044. doi:10.1088/1748-0221/17/01/c01044

Longo, R., Arfelli, F., Bonazza, D., Bottigli, U., Brombal, L., Contillo, A., et al. (2019). Advancements towards the implementation of clinical phase-contrast breast computed tomography at elettra. *J. Synchrotron Radiat.* 26, 1343–1353. doi:10.1107/S1600577519005502

Mazzini, V., Velardita, S., Biesuz, N., Bolzonella, R., Cavallini, V., Cimmino, L., et al. (2025). Characterization of a hybrid photon-counting detector based on timepix4 with a quasi-monochromatic source for spectral x-ray imaging applications. *Il Nuovo Cimento* 48, 244. doi:10.1393/ncc/i2025-25244-5

Meißner, T., Cerbone, L. A., Russo, P., Nahm, W., and Hesser, J. (2024a). 3d-localization of single point-like gamma sources with a coded aperture camera. *Phys. Med. and Biol.* 69, 165004. doi:10.1088/1361-6560/ad6370

Meißner, T., Cerbone, L. A., Russo, P., Nahm, W., and Hesser, J. (2024b). Assessment of the axial resolution of a compact gamma camera with coded aperture collimator. *EJNMMI Phys.* 11, 30. doi:10.1186/s40658-024-00631-5

Russo, P., Curion, A. S., Mettivier, G., Esposito, M., Aurilio, M., Caracò, C., et al. (2011). Evaluation of a cdte semiconductor based compact gamma camera for sentinel lymph node imaging. *Med. Phys.* 38, 1547–1560. doi:10.1118/1.3555034

Russo, P., Di Lillo, F., Corvino, V., Frallicciardi, P. M., Sarno, A., and Mettivier, G. (2020). CdTe compact gamma camera for coded aperture imaging in radioguided surgery. *Phys. Medica* 69, 223–232. doi:10.1016/j.ejmp.2019.12.024

Sriskaran, V., Alozy, J., Ballabriga, R., Campbell, M., Christodoulou, P., Heijne, E., et al. (2024). High-rate, high-resolution single photon x-ray imaging: medipix4, a large 4-side buttable pixel readout chip with high granularity and spectroscopic capabilities. *J. Instrum.* 19, P02024. doi:10.1088/1748-0221/19/02/p02024

Velardita, S., Mazzini, V., Cardarelli, P., Biesuz, N., Bolzonella, R., Cavallini, V., et al. (2025). Energy calibration of a Timepix4 detector assembly with a compact quasi-monochromatic X-ray system. *J. Instrum.* 20, T05003. doi:10.1088/1748-0221/20/05/t05003