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Date: 2025-12-02T11:29:28+00:00

Abstract

In-beam positron emission tomography (In-beam PET) can serve as a non-invasive monitoring technique for heavy-ion tumor therapy. By detecting and identifying coincidence event pairs generated from positron-electron annihilation, it enables rapid and accurate imaging of the incident beam position and dose distribution. In this work, we propose a timestamp-based segmented multi-level pipelined real-time coincidence algorithm. This algorithm integrates the advantages of a merging tree structure and parallel insertion sorting, allowing for complete multi-channel data sorting within five clock cycles (T = 40 ns). Once the sorting is completed, the data are forwarded to the coincidence discrimination module for coincidence event selection and real-time imaging. The proposed scheme achieves an extremely low dead time. After preprocessing, events are first processed through a merging tree structure sorting stage, with the final stage employing parallel comparison. This design significantly reduces hardware resource consumption while maintaining stable operation at high event rates of up to 8.5 Mcps, demonstrating excellent feasibility and scalability. The algorithm was integrated into an In-beam PET prototype and tested using both background irradiation and 22Na radioactive source, while maintaining a disorder rate below 0.5%. In beam experiments using a 190 MeV carbon ion beam to irradiate a PMMA target, real-time Bragg peak imaging with a spatial resolution at the 2 mm was successfully achieved.

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Full Text

Design of a Segmented Multi-Level Real-Time Coincidence Algorithm for In-Beam PET Readout Systems

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In-beam positron emission tomography (In-beam PET) serves as a non-invasive monitoring technique for heavy-ion tumor therapy. By detecting and identifying coincidence event pairs generated from positron-electron annihilation, it enables rapid and accurate imaging of the incident beam position and dose distribution. This work proposes a timestamp-based segmented multi-level pipelined real-time coincidence algorithm that integrates the advantages of a merging tree structure and parallel insertion sorting, allowing complete multi-channel data sorting within five clock cycles (T = 40 ns). Once sorting is completed, data are forwarded to the coincidence discrimination module for coincidence event selection and real-time imaging. The proposed scheme achieves extremely low dead time. After preprocessing, events are first processed through a merging tree structure sorting stage, with the final stage employing parallel comparison. This design significantly reduces hardware resource consumption while maintaining stable operation at high event rates of up to 8.5 Mcps, demonstrating excellent feasibility and scalability. The algorithm was integrated into an In-beam PET prototype and tested using both background irradiation and a ^{22}Na radioactive source, while maintaining a disorder rate below 0.5%. In-beam experiments using a 190 MeV carbon ion beam to irradiate a PMMA target successfully achieved real-time Bragg peak imaging with spatial resolution at the 2 mm level.

Keywords: In-beam monitoring; Positron emission tomography (PET); Heavy-ion therapy; Real-time coincidence algorithms; Field programmable gate array (FPGA)

INTRODUCTION

Heavy ion therapy [?, ?] is considered an ideal radiotherapy method for cancer treatment due to its unique physical and biological characteristics [?]. In heavy ion therapy, the dose increases sharply to a maximum value (the Bragg peak [?]) as penetration depth increases, then rapidly decreases to a lower value within a few millimeters after reaching the peak [?, ?]. By adjusting the beam energy, the depth at which the maximum dose occurs within the target can be altered, enabling heavy ion therapy to precisely treat tumors at millimeter-level depths while significantly reducing irradiation dose to surrounding healthy tissues. Monitoring the range and dose distribution of incident ions within a patient' s body provides radiological reference data for precise radiotherapy, ensures treatment effectiveness, guides effective utilization of the Bragg peak dose, and enables analysis of biological effects near the Bragg peak [?]. To achieve non-invasive monitoring of in-body dose distribution during treatment and verification of beam position and dose, the Institute of Modern Physics, Chinese Academy of Sciences, has developed a Positron Emission Tomography (PET) system installed at the beam and treatment site, known as the in-beam PET system, for dose monitoring in heavy-ion cancer treatment devices (Heavy-Ion Medical Machine, HIMM) [?].

Identification of positron-electron annihilation events [?] within the irradiated treatment area represents a key technology for monitoring. Annihilation reactions produce a pair of oppositely directed 511 keV γ photons, known as coincidence events (CE). Identified coincidence events provide valuable information about particle energy, time, and position [?]. In the current system consisting of 16 detection modules, the coincidence event rate processed by the PET system is approximately 230 kcps [?]. These events originate from the large number of positrons generated within the patient' s body during treatment. The critical aspect of coincidence processing involves detecting these photons, confirming they belong to a pair annihilation event, and reconstructing the event distribution within the subject' s body [?]. However, during detection, the detector may also capture other types of coincidence events, such as scatter coincidences and random coincidences. These false coincidence events cause image noise and generate artifacts, compromising the accuracy of dose monitoring during treatment. Therefore, a coincidence processing module capable of handling high event rate data is essential for the in-beam PET system.

There are three main methods for coincidence determination. The first method is AND gate [?, ?] coincidence based on analog circuits, which performs a logical "AND" operation between detector signals and their symmetric counterparts. This method is cost-effective and efficient but suffers from poor scalability and high dependence on hardware customization. The second method is timestamped coincidence based on digital circuits [?], where a timestamp is assigned to each signal and coincidence events are determined based on temporal order. This method offers good flexibility and scalability, making it suitable for multi-channel systems, though algorithm design and resource consumption significantly impact performance. With proper optimization, this method is more suitable for multi-channel, high-count rate PET systems, and on-chip programming significantly enhances system scalability and operational stability. The third method is coincidence determination based on programmable delay chains, which utilizes FPGA to configure adjustable delays for each signal, allowing simultaneous events to be processed by a centralized unit for coincidence determination. This method offers low latency and fast response but has limited flexibility in the time window, making it typically suitable for customized systems with fewer channels. Given that our system has a large number of channels and high event rates, we have chosen the timestamp-based coincidence method as the solution for the in-beam PET system.

This work proposes a segmented multi-level real-time coincidence algorithm based on the timestamp coincidence method, which completes coincidence event determination through energy discrimination, time discrimination, and position discrimination. The most critical component is a multi-level pipeline sorting approach that distributes data serialization and sorting across multiple stages. This segmented sorting algorithm effectively reorders all out-of-sequence events in chronological order, making real-time coincidence event determination within an effective time window more efficient. The entire sorting process takes only five clock cycles, which is significant for analyzing noise events caused by scatter coincidences, random coincidences, and other factors, as well as for improving imaging efficiency and accuracy. Preliminary experimental validation indicates that the sorting algorithm can effectively and real-time execute event sorting and coincidence event identification in the in-beam PET of the HIMM system, ensuring excellent performance even at extremely high event rates.

The structure of this paper is organized as follows: First, we introduce the hardware structure of the detector and readout electronics for the in-beam PET system. Next, we present the segmented multi-level real-time coincidence algorithm, followed by a detailed discussion of the multi-level sorting algorithm design. Finally, we provide electronic performance test results from laboratory and beam testing.

IN-BEAM PET READOUT SYSTEM

As shown in [Figure 1: see original paper], the in-beam PET system consists of two components: the detector array and a high-performance electronics system.

DETECTOR

In the current beam-based PET system, the detection module consists of a detector array composed of 16 detector units designed to detect γ-rays emitted from positron annihilation events [**?**]. The detector arrays are distributed symmetrically on both sides of the system, with eight modules on each side arranged in a 2 × 4 panel configuration. During operation, the distance between the two opposing panels is 50 cm. Compared with the previous system [**?**, **?**], the total number of detector modules has increased from 8 to 16, and the active detection area has expanded from 10.4 cm × 10.4 cm to 20.8 cm × 10.4 cm. Each detection module [**?**] is encapsulated with an LYSO crystal array [**?**], a photomultiplier tube (PMT) [**?**], and a discrete position circuit (DPC) board.

The LYSO crystal array consists of 22 × 22 crystals, each with dimensions of 2 mm × 2 mm × 15 mm, as shown in [Figure 2: see original paper] (left). The overall size of the detection module is 52 mm × 52 mm. Each crystal block is optically read out by an 8 × 8 multi-anode position-sensitive PMT (HAMAMATSU H8500C), as shown in [Figure 2: see original paper] (center). In addition, a discrete position circuit (DPC) ([Figure 2: see original paper], right) is integrated with the PMT, converting its 64 output signals into four readout channels.

Hardware Design of the Electronics System

The readout electronics consist of three main modules: the clock synchronization unit (CSU), the data acquisition unit (DAQU) [?], and the central processing module (CPM). A schematic diagram of the beam-based PET electronics system is shown in [Figure 3: see original paper]. The CSU provides a synchronous clock signal to the other modules, ensuring that the readout system calibrates each signal to a unified reference time. The DAQU performs analog-to-digital conversion and data formatting, processing the energy and timing signals from each detector module into event data frames of a fixed format with attached timestamps. By incorporating dedicated timing and energy extraction algorithms, the DAQU converts the raw signals into event data suitable for digital processing. As the central processing module, the CPM receives event data transmitted from all front-end DAQUs and executes real-time sorting algorithms, arranging the detected signals from the array in chronological order according to their timestamps. Sequentially sorted events facilitate coincidence processing within the time window. The coincidence events are then transferred to the host computer via the CPM' s PCIe interface for subsequent image reconstruction and related tasks.

SEGMENTED MULTI-LEVEL REAL-TIME COINCIDENCE ALGORITHM

As shown in [Figure 4: see original paper], considering that coincidence events are both time and position dependent [?, ?], the coincidence discrimination module of the PET system incorporates energy window discrimination, time window discrimination, and position discrimination. The DAQ extracts the energy and timing information of each event and forwards it to the CPM for coincidence determination. First, all events undergo energy discrimination. The energy window is set to 300-600 keV, and events falling outside this range are discarded. After energy discrimination, the data are forwarded to the sorting module, where a multi-level pipelined sorting algorithm is applied. The 16-channel parallel data are then converted into an ordered serial data stream and forwarded into the time discrimination module. The time discrimination mechanism defines a valid event pair as two single-event data occurring within an ultrashort time window, with the window size determined by the time resolution of the in-beam PET system.

Once the sorted serial data stream enters the time window discrimination module, the time difference between the current event and the preceding event is calculated and compared with the time window. Event pairs that satisfy the coincidence condition are subsequently forwarded to the position discrimination module [?]. The line of response (LOR) generated by a coincidence event must fall within the system' s predefined field of view (FOV). In other words, the two photons emitted from a single annihilation event cannot be simultaneously detected by detectors located on the same side of the dual-panel architecture. Consequently, the position discrimination module compares the detector block values in the incoming data frames to exclude events that violate this spatial constraint. Ultimately, true coincidence events—those passing the triple discrimination of energy, time, and position—are selected and transmitted to the host computer for real-time imaging. Within the entire coincidence event selection workflow, the sorting stage is both the most critical and the most error-prone.

Multi-Level Pipelined Sorting Algorithm

In the readout electronics of the in-beam PET system, single-event data should ideally be output in chronological order to enable real-time coincidence processing. However, the energy measurement and time extraction of each event are independently executed by the DAQUs. After signal processing, digitization, data framing, and multiplexed output, the single-event data detected by the detector modules cannot be transmitted from the DAQUs in strict temporal sequence, particularly at high count-rate conditions. In previous system designs, the real-time data throughput had already approached the upper limit of the processing unit' s capacity, and the real-time sorting algorithm exhibited a misordering rate of approximately 13% [**?**], which posed a significant limitation to overall system performance.

In the DAQU design of the system, the data width of a single-event record is 288 bits, which includes packet headers and trailers, module and board identifiers, timestamps, energy and position information, as well as redundant padding data. To reduce resource consumption and latency during subsequent data transmission and comparison, the padding data are removed prior to input into the sorting algorithm, and the timestamp is compressed to 48 bits. After preprocessing, the data width of a single-event record is reduced to 192 bits, resulting in substantial hardware resource savings.

[Figure 5: see original paper] illustrates the multi-level pipelined sorting algorithm implemented in the CPM. The algorithm acquires single-event data from all DAQUs and sorts them according to their timestamps. The sorted event stream is subsequently forwarded to the coincidence processing stage and ultimately to the host computer for image reconstruction.

First-Level Sorting In the first-level sorting stage, potential misordering of the two-channel detector data within each DAQU is addressed. To ensure that data from all eight DAQUs are ordered before entering the global sorting process, intra-DAQU sorting of the two-channel event data is performed at this stage. As shown in [Figure 6: see original paper], once data from each DAQU enter the CPM, they are categorized into three coding modes according to the input sequence: single-channel events, consecutive dual-channel events, and consecutive single-channel events. Among these, the single-channel events and consecutive single-channel events are directly transferred without additional processing, whereas the consecutive dual-channel events are sorted based on timestamp comparison prior to output. Consequently, the event stream originating from the same DAQU is already ordered before entering the second-level sorting stage.

Second-Level Sorting In the second-level sorting stage, a FIFO-based four-to-one (4-to-1) sorting module was developed as the fundamental unit, as shown in [Figure 7: see original paper]. To process the eight-channel data, two identical 4-to-1 sorting modules were instantiated, thereby converting the eight-channel ordered inputs into two-channel ordered outputs. The 4-to-1 sorting module is implemented using a finite state machine, and its primary components include a timestamp comparison unit between DAQUs, an input status encoding unit, and a result output unit. The timestamp comparison unit between DAQUs is implemented with sequential logic. Whenever new data arrive, the comparison results among the four channels are updated on each rising clock edge and transferred to the status encoding unit. The status encoding unit encodes the valid signals from each channel and selects the corresponding sorting strategy based on the encoding results. When only one channel has an active valid signal, the data from that channel are directly output; when multiple channels contain data simultaneously, the event with the smallest timestamp is selected for output. This 4-to-1 sorting module is capable of delivering the earliest event within two clock cycles.

Third-Level Sorting The third-level sorting stage employs a two-to-one (2-to-1) sorting module, as shown in [Figure 8: see original paper], which further processes the two-channel ordered data output from the second-level stage and converts them into a single-channel serial data stream. However, in the third-level sorting, a degree of misordering may occur because the second-level stage consists of two parallel 4-to-1 sorting modules, and the event arrival patterns across the eight channels are not identical. Therefore, when only one channel of the first 4-to-1 sorting module contains data while multiple channels of the second 4-to-1 sorting module contain data simultaneously, the latter incurs a delay in producing its sorted output, leading to a certain degree of minor misordering in the data stream after the third-level sorting stage, and vice versa. To eliminate such misorderings caused by delay, a fourth-level sorting stage is forwarded to complete the final data processing.

Fourth-Level Sorting The fourth-level sorting stage adopts a parallel insertion-sorting method, as shown in [Figure 9: see original paper]. This stage consists of a number of register arrays, each initialized to zero. After the data stream from the third-level stage enters the registers, the timestamps T_1 to T are extracted. For each incoming event, its timestamp is compared in parallel with those stored in the registers. If the new timestamp is greater than the stored value, the comparison result is marked as 1; otherwise, it is marked as 0. Based on these comparison results, the larger timestamp is retained in the register, while the event with the smallest timestamp is output. After passing through such register arrays, the minor misorderings caused by delay are smoothed out, and the final output data stream is kept as sequential as possible.

As shown in [Figure 10: see original paper], the timing diagram of the real-time multi-level pipelined sorting module demonstrates that the design decomposes the processes of parallel-to-serial conversion and sorting for multi-channel data into multiple stages. Each stage performs a relatively simple function, thereby reducing the complexity of verification and maintenance within the module. Moreover, since all stages of the pipeline operate in parallel, the overall dead time of the sorting stage is determined by the maximum dead time among the pipeline stages, which is five clock cycles (T=40 ns). For future designs involving larger numbers of channels, this architecture offers greater flexibility, enabling straightforward system expansion and improvement.

PERFORMANCE TEST

To analyze and evaluate the performance of the proposed sorting algorithm in practical applications, a series of experimental verifications were conducted under detector background, radioactive source conditions, and low trigger threshold configurations, with the test platform shown in [Figure 11: see original paper]. In these conditions—detector background, radioactive source, and low trigger thresholds—the event rates varied from low to high. In particular, when no energy window was applied, the event rate already far exceeded that observed for all energies during heavy-ion therapy. Therefore, successful performance in these test conditions demonstrates that the algorithm has achieved an excellent level of efficiency. With the experimental setup shown above, unsorted data and data processed by the proposed sorting algorithm were collected using the host computer and subsequently analyzed with tools such as ROOT and MATLAB. Through these experiments, results related to the real-time sorting performance were obtained.

Detector Background Test

The intrinsic background irradiation of the detector originates from the scintillation crystal itself, with an event rate of approximately 115 kcps, and was used as a test condition during algorithm debugging. As shown in [Figure 12: see original paper], under this condition, 45.9k single events in the unsorted data were found to be out of sequence. After applying the sorting algorithm, the number of misordered events was reduced to 0.3%, which is nearly negligible.

^{22}Na Radioactive Source Test

The experimental setup with a radioactive source simulated the scenario of beam irradiation on a PMMA target using a point source, serving as a preliminary test before actual beam experiments. To evaluate the performance of the real-time coincidence algorithm in this setup, a ^{22}Na source was used for analysis, with an event rate of approximately 209 kcps. This rate is comparable to that encountered in practical in-beam PET treatments, making the results highly relevant for assessing the algorithm' s performance in clinical scenarios. As shown in [Figure 13: see original paper], without sorting, the aggregated data contained 55.2k misordered events, corresponding to a misordering rate of 42.1%. After applying the sorting algorithm, the misordering rate was reduced to 0.5%.

We also compared imaging results with and without the coincidence algorithm. As shown in [Figure 14: see original paper], unprocessed data exhibit significant background noise in the reconstructed image, resulting in poor contrast that makes it difficult to identify the point source location. Such image quality would lead to inaccurate Bragg peak localization during treatment monitoring, failing to provide reliable real-time feedback on therapeutic effects. In contrast, after coincidence processing ([Figure 15: see original paper]), background signals are effectively suppressed, yielding high image contrast and a clearly distinguishable point source position, demonstrating excellent spatial resolution. This performance meets the requirements for in-beam PET applications. [Figure 16: see original paper] further shows the image generated with coincidence processing after relocating the point source, where the source remains clearly visible with complete background suppression.

Low Trigger Threshold Test

When the leading-edge discriminator is configured with a low trigger threshold, a large number of spurious triggers are introduced into the data stream. In the present system, intrinsic background irradiation alone can generate event rates of up to 8.5 Mcps, which far exceed those encountered during actual treatment. Evaluating the algorithm under these conditions is therefore critical for determining whether the current design can continue to operate reliably and sustain high performance in extreme conditions. As shown in [Figure 17: see original paper], the left bar group (Unsorted) presents the analysis results of data acquired by the CPM without the sorting algorithm. The test results indicate that, out of a total of 131.1k events, as many as 65.4k events exhibited timestamp misordering, corresponding to a misordering rate of 49.8%. The right bar group shows the analysis results of data acquired by the CPM with the sorting algorithm applied, where the number of misordered events decreased to 2725, yielding a misordering rate of only 2%.

Beam Experiment

To validate the system' s capability for real-time monitoring during actual treatment procedures, a beam experiment was conducted at the Fujian Matsu Heavy Ion Hospital in China, in which multiple tests were performed. In the experiment, a ^{12}C beam with an energy of 190 MeV was directed onto a PMMA target. Positrons produced by annihilation decays within the carbon beam were detected by PET in both spatial and temporal dimensions, allowing analysis of the Bragg peak distribution deposited in the PMMA. The system' s host computer was located in the control room, where it remotely controlled data acquisition via cables. A photograph of the on-site beam test setup is shown in [Figure 18: see original paper].

Beam Track Imaging Experiment

Using a 190 MeV carbon beam to irradiate the PMMA target, the transverse central cross-sectional distribution of the resulting Bragg peak is shown in [Figure 19: see original paper]. The beam incident direction is defined as the X-axis, and the perpendicular spatial direction as the Y-axis. Different color scales represent the magnitude of particle counts in the corresponding regions. The figure clearly reveals the spatial distribution of positron-emitting nuclides generated during irradiation. The region centered at the Bragg peak corresponds to the location where the beam energy is most intensely deposited and where nuclide accumulation is greatest, while fewer nuclides are distributed in the plateau region. This observation is consistent with the principles of beam diagnostics. The Bragg effect corresponds to a depth of approximately 57 mm within the PMMA target, where the majority of the beam' s energy is released. This result is in strong agreement with the peak depth of 57 mm obtained from GATE simulations of 190 MeV carbon ion beam pulses [**?**]. The deviation falls within the detector' s spatial resolution of approximately 2 mm, demonstrating superior performance compared to the INSIDE system [**?**].

At the same beam energy and with the same number of incident particles, the transverse central cross-sectional distribution of the Bragg peak without the multi-stage pipeline sorting algorithm is shown in [Figure 20: see original paper]. In contrast to [Figure 19: see original paper], the particle distribution here is markedly more diffuse, the core of the Bragg peak appears blurred, and the spatial distribution of positron-emitting nuclides shows reduced clarity and accuracy. As a result, the concentration of energy deposition is not well resolved. This comparison highlights the capability of the multi-stage pipeline sorting algorithm to enhance data accuracy and spatial resolution, demonstrating that the algorithm provides a more faithful characterization of the beam energy deposition profile and thereby offers a stronger data foundation for subsequent beam diagnostic applications.

Performance Evaluation of Real-Time Monitoring

To evaluate the capability of the proposed algorithm to monitor the Bragg-peak position in real time during heavy-ion therapy, we acquired 30-s in-beam PET data and reconstructed the corresponding images. The reconstruction of each data set was completed within 1 s. According to the real-time monitoring guideline issued by CNAO [**?**], the ability to generate reliable images from 30-s acquisition data is sufficient to demonstrate real-time monitoring performance. The present study employed a dual-panel in-beam PET system whose geometry makes the beam direction (x-axis) the direction of highest spatial resolving power. Along this axis, the system can resolve position shifts as small as approximately 2 mm. By projecting all annihilation events within the selected field of view onto the x-axis, we obtained a one-dimensional activity profile along the beam path.

During the 30-s irradiation, the real-time coincidence-processing algorithm successfully identified approximately valid coincidence events. This event-collection efficiency surpasses that reported for the INSIDE system during 270 s of online acquisition [**?**]. As shown in [Figure 21: see original paper], the image reconstructed from the 30-s data already provides a clear delineation of the Bragg-peak position with a narrow peak shape. This demonstrates that the system can accurately determine the Bragg-peak depth even at early stages of beam delivery, when the number of incident particles is still limited. Overall, these results indicate that the proposed real-time coincidence-event processing approach can provide clinicians with stable and reliable online feedback during treatment, thereby supporting timely adjustments to treatment-planning parameters as irradiation proceeds.

Resource Utilization

Due to the high instantaneous event rate inherent in in-beam PET, FIFO buffers were implemented between each stage of the sorting algorithm. In principle, as long as the event rate does not exceed five cycles of the sorting algorithm' s dead time, i.e., 25 Mcps, no event loss will occur. In the current firmware design with 16 detector modules, as shown in , the real-time sorting algorithm utilizes 2% of the available BRAM, approximately 4% of the lookup tables (LUTs), and 7% of the slices on the FPGA chip (xc7k325tffg900-2). The resource utilization remains at an extremely low level, which demonstrates the rationality of the code design. This indicates that the implemented functions can be achieved within limited hardware resources, while also ensuring lower power consumption, improved maintainability, and enhanced scalability. These findings strongly indicate that the algorithm can be readily adapted to in-beam PET systems with different detector counts and configurations, as well as to other PET system designs.

CONCLUSION

This work presents a timestamp-based real-time multi-level pipeline sorting algorithm that has been successfully developed and implemented on the CPM of an in-beam PET system. The algorithm was tested with background signals, radioactive sources, and low trigger thresholds. The results demonstrate consistently high sorting performance across all scenarios. Even at event rates well beyond those encountered in current clinical treatments, the algorithm maintained stable operation with event loss and misordering rates kept at exceptionally low, practically ideal levels. In the present 16-detector-module PET system, the firmware design shows modest resource utilization, leaving ample headroom for integrating more versatile functions and advanced features, while also ensuring low power consumption during operation. This combination of scalability and energy efficiency is particularly valuable for real-time online coincidence processing.

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Note: Figure translations are in progress. See original paper for figures.

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