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Optimization of the Energy Window for PETbox4, a Preclinical PET Tomograph With a Small Inner Diameter

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Abstract

Small animal positron emission tomography (PET) systems are often designed by employing close geometry configurations. Due to the different characteristics caused by geometrical factors, these tomographs require data acquisition protocols that differ from those optimized for conventional large diameter ring systems. In this work we optimized the energy window for data acquisitions with PETbox4, a 50 mm detector separation (box-like geometry) pre-clinical PET scanner, using the Geant4 Application for Tomographic Emission (GATE). The fractions of different types of events were estimated using a voxelized phantom including a mouse as well as its supporting chamber, mimicking a realistic mouse imaging environment. Separate code was developed to extract additional information about the gamma interactions for more accurate event type classification. Three types of detector backscatter events were identified in addition to the trues, phantom scatters and randoms. The energy window was optimized based on the noise equivalent

count rate (NECR) and scatter fraction (SF) with lower-level discriminators (LLD) corresponding to energies from 150 keV to 450 keV. The results were validated based on the calculated image uniformity, spillover ratio (SOR) and recovery coefficient (RC) from physical measurements using the National Electrical Manufacturers Association (NEMA) NU-4 image quality phantom. These results indicate that when PETbox4 is operated with a more narrow energy window (350-650 keV), detector backscatter rejection is unnecessary. For the NEMA NU-4 image quality phantom, the SOR for the water chamber decreases by about 45% from 15.1% to 8.3%, and the SOR for the air chamber decreases by 31% from 12.0% to 8.3% at the LLDs of 150 and 350 keV, without obvious change in uniformity, further supporting the simulation based optimization. The optimization described in this work is not limited to PETbox4, but also applicable or helpful to other small inner diameter geometry scanners.

Index Terms

Backscatter; energy window; GATE; NECR; optimization; PET; PETbox4; SF

I. Introduction

Small animal positron emission tomography (PET) is a widely used imaging modality for non-invasive, in vivo studies of biochemical and metabolic process [1], [2]. High imaging performance is desired for good lesion localization and quantification for applications in pharmacology, genetics, pathology and oncology [3], [4]. For a specific scanner, the imaging protocol including energy window, multiple event acceptance policy, and timing window, need to be optimized to achieve an overall optimized imaging quality.

In recent years several systems have been built or designed by employing close geometry configurations, with the diameters ranging from 35 mm to 65 mm [5]–[10]. Close geometry has many benefits such as high sensitivity provided by the larger detection solid angle, lower cost and reduced complexity [5]. On the other hand, the system characteristics related to the geometries of those scanners are very different from those of the conventional large diameter preclinical PET scanners [11], [12].

Scatter events degrade image contrast in PET by misplacing events during reconstruction and cause errors in the reconstructed radioactivity concentration [13]. There has been extensive research to investigate the scatter fraction (SF) and optimal energy window for conventional small animal PET systems with large inner diameters, for which the object SF originating from a mouse does not change significantly as the lower-level discriminator (LLD) increases [13], [14]. This is because events that scatter through a small angle result in lines of response that still intersect the FOV of mouse imaging, and most of these photons do not lose enough energy and thus are less sensitive to the increase of LLD. A wide open energy window has been suggested or implemented to increase the sensitivity without significantly increasing the scatter and degrading the spillover ratio (SOR) for mouse imaging [14]–[16].

For a scanner employing a close geometry and wide open energy window, scatter events with a larger angle can now intersect the object. This effect increases the fraction of detected

scattered events and leads to degradation of the noise equivalent count rate (NECR) [17], despite the small size of typical imaged subjects. Moreover, due to the large detection solid angle, the 511 keV gamma photons have a higher probability of undergoing a Compton scatter interaction in one detector and then being detected in a second detector, resulting in backscatter coincidence events [18]. Therefore, the optimization of energy window for conventional large inner diameter ring systems cannot be directly applied to close geometry systems.

PETBox4 is a PET system optimized specifically for imaging mice [5]. The system consists of four bismuth germanate (BGO) detector panels, with the opposite panels placed at a spacing of 50 mm. Such close geometry provides a useful field of view (FOV) that can accommodate the vast majority of mice (18–40 g) and therefore presents a compromise in the target subject size in exchange for low cost and high sensitivity.

In this study, different types of possible events in PETbox4 were investigated using the Geant4 application for tomographic emission (GATE) Monte Carlo simulation [19]. GATE, with the well validated Geant4 libraries [20], [21], allows highly realistic modeling of scanner geometries, and provides detailed information about transport and energy deposition of each particle. The fraction, energy and spatial distribution of different types of events which cannot be directly retrieved from physical measurements, can be studied with the help of this simulation on an event-by-event basis. Based on the simulation results, the multiple event acceptance policy and the need for backscatter rejection were investigated for PETbox4. A new optimized energy window was proposed and validated with physical measurements of the National Electrical Manufacturers Association (NEMA) NU-4 [22] image quality phantom data acquired in PETbox4.

II. Methods

A. Modeling the System with GATE

The PETbox4 detector module and system configuration are shown in Fig. 1. The basic specifications of the PETbox4 system are summarized in Table I. The GATE Monte Carlo simulation software was used to simulate the data acquired with the PETbox4.

The scanner geometry and associated event handling of the PETbox4 were modeled, with the timing window set to 20 ns. Unless explicitly stated otherwise, all simulations were acquired with an energy resolution of 18%, which is the average measured energy resolution of the PETbox4. The notable exception to this was in one of the NECR and SF simulations described in Section II-D (5), for which the energy resolution was set to 30% as a worst case scenario to evaluate the effect of the poorer energy resolution in a more realistic system on NECR and SF. An energy window of 50–650 keV was applied to the singles processing chain at the stage of initial simulation. The *takeAllGoods* criterion (all the good sub-pairs in multiple coincidences are accepted) was chosen to manage multiple coincidences and the *minSectorDifference* parameter was set to 1, mimicking the system firmware of allowing coincidences in the PETbox4 scanner. Dead time was not modeled, and pile-up events caused by different annihilation events were not considered in this study. Annihilation events were modeled with the emission of opposing pairs of 511 keV photons to speed up

the simulation time. The *Root* format output from GATE [23] stores information of particle transportation and interactions on an event-by-event basis, allowing event history to be retrieved. This model has been validated in [5] against the system sensitivity measurement, showing an agreement within 10% of the measured value.

B. Voxelized Phantom

One of the most important applications of preclinical PET imaging is the measurement of the whole body biodistribution of a radiolabeled probe. For optimization of realistic mouse imaging, simulations were performed with a voxelized phantom including a mouse as well as its supporting chamber to provide the most accurate scatter estimation in heterogeneous media and complex geometry. Among the mouse data we have, a data set from an 18.2 g mouse was chosen, representing the lower limit of object SF that can be introduced from a mouse subject among the vast majority of mice (18-40 g) [24]. The geometry of the mouse and the chamber was measured using a MicroCAT II tomograph (Siemens Preclinical Solutions, Knoxville, TN). A sample FDG-PET mouse emission image was used to represent realistic radionuclide distribution in the mouse model. The total activity in the mouse was set to be 1.85 MBq (50 μ Ci), which is the recommended injected dose for this scanner [5]. The phantom, including the mouse and the imaging chamber were implemented in a voxelized phantom with a matrix size of $200 \times 182 \times 496$ and voxel size of $0.25 \times 0.25 \times 0.25$ mm³. As an example, three different views from overlaid anatomy and emission slices of the voxelized phantom are shown in Fig. 2.

C. Event Classification

Coincidence events in PETbox4 can be classified into six primary categories (as shown in Fig. 3):

1) True Coincidences (T)—Both detected photons are emitted from one annihilation event without Compton interaction in the object. Both photons are detected in the detector panel of first interaction, with the energy deposited in each detector contributed by only one annihilation photon (Fig. 3(1)). A fraction of these events will undergo Compton scatter in the detector. In conventional Anger logic detectors, such as those used in the PETbox4, the center of mass of the primary and scatter photon interactions fall inside the width of the primary events, as defined in the NEMA NU-4 protocol [22]. In line with previous work, these events are categorized as trues [9].

2) Phantom Scatter (PS)—At least one annihilation photon is detected after encountering a Compton interaction in the object (Fig. 3(2)).

3) Single Photon Backscatters (SPB)—One annihilation photon is not detected by any detector, while the other is detected by two detectors through backscattering ((Fig. 3(3)).

4) Backscattered Multiples (BM)—Both photons emitted from one annihilation event are detected and at least one photon is detected by two detectors through backscattering, leading to multiple coincidence events (Fig. 3(4)). The mis-positioned line of response (LOR) in the multiples will be classified into backscatter multiples (For example, two

coincidences in a triple event or four coincidences in a quadruple event are mis-positioned and identified as backscatter multiples, corresponding to the coincidence between the backscattered photon with its originating Compton scatter, or with other annihilation photons).

5) Randoms (R)—Two photons detected are emitted from different annihilation events (Fig. 3(5)).

6) Pile-Ups (PU)—The energy deposited in one detector panel is contributed by both annihilation photons through backscattering (Fig. 3(6)).

To retrieve the characteristics of coincidence events for appropriate event classification, customized software was developed in C++ to analyze the *Root* output file from GATE. The interaction history of each particle in each coincidence event was investigated by the algorithm at eight steps, as shown in Fig. 4. The detailed instructions for each step are included in the Appendix section.

The energy spectrum for different types of events was plotted with an open energy window of 150-650 keV. Then the counts for each event type were sorted with the LLD increasing from 150 keV to 450 keV at 50 keV steps and an upper-level threshold (ULD) fixed at 650 keV. The numbers of counts as a function of event type and LLD were extracted.

D. Energy Window Optimization Based on NECR and SF

1) NECR and SF Calculation—The count rates of different event types were extracted from the voxelized mouse phantom simulation, and the corresponding NECR and SF were calculated as below:

$$NECR = T^2 / (P + R) \quad (1)$$

$$SF = S_{tot} / (S_{tot} + T) \quad (2)$$

$$P = T + PU + BM + SPB + PS + R \quad (3)$$

$$S_{tot} = PU + BM + SPB + PS \quad (4)$$

T , PU , BM , SPB , PS and R are the count rates for different types of events as defined in Section II-C. S_{tot} is the count rate of the total scatter events and P is the count rate of the prompt events. NECR and SF are plotted as a function of the energy window, with the LLD increasing from 150 keV to 450 keV at 50 keV increments.

2) Identification of Backscatter Events—For event classification in previous studies performed by other groups [9], [14], [25], events were most commonly categorized into trues, phantom scatters and randoms. To illustrate the importance of appropriate classification of the backscatter events (including backscatter multiples, single photon

backscatters and pile-ups) for our study, the NECR and SF were calculated without identifying backscatter events (excluding steps 5, 6 and 7 in Fig. 4). In that case, all the backscatter events were wrongly identified as trues.

3) Backscatter Rejection—Although backscatter events cannot be rejected by traditional energy discrimination if a wide open energy window is used via the lower level discriminator, other methods might be applicable for eliminating or suppressing backscatters. For example, the sum of energy deposited from a backscattered photon and its original Compton scatter will have a high probability of falling into a 511 keV peak, making it possible to eliminate a large fraction of single photon backscatters by applying energy discrimination on the sum of the energies from the two detections in a coincidence event. Backscatter multiple events can be suppressed by employing a multiple event policy based on *takeWinnerOfGoods* (only the sub-pair with the highest energy in multiple coincidences is accepted), or *killAll* (no multiple coincidences are accepted, no matter how many sub-pairs are present) as defined in GATE. Alternatively, one could use geometry criteria to extract true LORs and reject mis-positioned LORs from multiple coincidences as reported in [26]. To investigate the necessity of implementing backscatter rejection, the NECR and SF were derived assuming a perfect backscatter rejection by arbitrarily setting the backscatter events to zero, representing the upper limit of what can be achieved with the rejection methods described above.

4) Effect of the Imaging Chamber—To examine the contribution from the attenuation and scatter introduced by the imaging chamber to the total SF, a simulation without the imaging chamber was performed, from which NECR and SF were derived.

5) Effect of the Energy Resolution—In the previous simulations, an 18% energy resolution was used based on the measured average energy resolution of PETBox4. However in a realistic system, the energy resolution ranges from 13.5% to 48.3% due to the poorer light collection efficiency for edge crystals or crystals at the junction of the two position-sensitive photomultiplier tubes (PSPMT). About 21% of the crystals have energy resolution worse than 20%. To evaluate the effect of the poorer energy resolution on imaging performance in a more realistic system, a simulation with an energy resolution of 30% was performed as a worst case scenario, from which NECR and SF were derived.

The optimized energy window was proposed based on the NECR and SF results. The event fraction within the open energy window of 150-650 keV utilized in [5] and the proposed optimized energy window were plotted to show the improvement on data quality.

E. NEMA NU-4 Image Quality Phantom

A physical measurement was performed using the image quality phantom described in the NEMA NU-4 protocol [22] to validate the simulation based optimization. Since the PETbox4 is intended to be used with a low injected dose, the image-quality phantom (Data Spectrum Corporation, Hillsborough, NC) was filled with 1.85 MBq (50 μ Ci) ^{18}F solution measured with a dose calibrator (Atomlab 300; Biodex Medical Systems, Shirley, NY). The phantom was placed on a mouse imaging chamber to simulate actual mouse imaging and

was scanned for 20 min, following the NEMA NU-4 recommendations. For this acquisition, specialized software was utilized on the system electronics, recording the energy of each event into the list-mode data. After the acquisition, energy discrimination with the LLD increasing from 150 keV to 350 keV at 50 keV steps and a ULD fixed at 650 keV was applied to the list mode data in MATLAB (MathWorks, Natick, MA) before data histogramming. Energy window specific normalizations were applied to compensate for the differences in individual detector efficiencies, estimated from measurements of a cylindrical source filled with ^{18}F . Random event correction was applied using a delayed coincidence window method, but no scatter correction was applied. For attenuation correction, a CT transmission scan of the object and its supporting chamber was obtained using a MicroCAT II tomograph (Siemens Preclinical Solutions, Knoxville, TN). The reconstructed CT image was registered with the PET emission image and forward projected through the system response matrix to create an attenuation sinogram. The image was reconstructed by a maximum likelihood and expectation maximization (ML-EM) algorithm with 60 iterations [27]. The uniformity, SOR and recovery coefficient (RC) were calculated from the reconstructed images following the NEMA NU-4 protocol.

III. Results

A. Event Classification

Fig. 5 shows the contributions of different types of events to the coincidence energy spectrum. Between 400 and 650 keV, trues from photoelectric interactions dominate. Between 150 and 400 keV, scatter events including phantom scatter and crystal backscatter are higher than true events.

The energy spectrum for each event type was magnified in the inset in Fig. 5, with the y axis rescaled respectively for better visualization of the distribution characteristics. The phantom scatter spectrum (PS in Fig. 5) occupies the second largest fraction of the total prompt events, from which a larger fraction below the photopeak can be observed compared to the energy spectrum of the trues. This is because at least one annihilation photon from each coincidence lost part of its energy through Compton interaction in the object.

For the single photon backscatter energy spectrum (SPB in Fig. 5), two peaks can be clearly observed. The first corresponds to the energy deposited due to Compton scatter of annihilation photons in the detector of first interaction (around 340 keV), while the second (around 170 keV) corresponds to the energy deposited from the backscattered photons in a different detector.

For the backscatter multiples energy spectrum (BM in Fig. 5), besides a similar energy distribution contributed from the annihilation photon encountering crystal backscatter as described in the single photon backscatters (SPB in Fig. 5), coincidence events can also be formed between the backscattered photon and the other annihilation photon. As a result, a 511 keV peak is obtained.

For the pile-up energy spectrum (PU in Fig. 5), a peak around 340 keV can be clearly observed, corresponding to the energy deposited by the Compton interaction from one of the

two annihilation photons. The backscattered photon escapes from the detector that it first interacts and deposits its energy in a second detector, together with the other annihilation photon. The energy deposited by pile-up events will form a peak around 680 keV corresponding to the full energy deposited from the backscattered photon and the other annihilation photon, part of which is cut off by the ULD of 650 keV.

The shape of the energy spectrum for random events (R in Fig. 5) is similar to that of the total prompt events. With a total radioactivity of 1.85 MBq (50 μ Ci) recommended as the default activity level for mouse imaging using the PETbox4, the fraction of random events is around 8%.

Fig. 6 shows the count rate as a function of event type and LLD. With a LLD of 150 keV, a large fraction of backscattered multiples, single photon backscatters and phantom scatters are included. As the LLD increases from 150 keV to 350 keV, almost all the backscattered multiples and single photon backscatters events are rejected. The phantom scatter events decrease by 71% and the random events decrease by 44%. As a tradeoff, trues also decrease by 21%. With a LLD of 450 keV, trues decrease significantly due to the exclusion of photopeak events.

B. Energy Window Optimization

1) NECR and SF Calculation—The curve represented by the diamond symbols “ ” in Fig. 7 shows the PETbox4 mouse imaging conditions, including the imaging chamber, with an energy resolution of 18% and with no backscatter rejection implemented. The NECR increases by 13% as the LLD increases from 150 keV to 400 keV, primarily due to the reduced SF. The NECR decreases as the LLD increases from 400 keV to 450 keV due to the exclusion of trues in the photopeak. The SF decreases by 85% as the LLD increases from 150 to 450 keV.

2) Identification of Backscatter Events—The curve represented by the cross sign symbols “×” in Fig. 7 shows the simple event classification as most commonly used [9], [14], [25] based on the same data set, which excludes step 5, 6 and 7 in Fig. 4 and does not identify backscatters.

Without the appropriate classification in the simulation, backscatter events (including backscatter multiples, single photon backscatters and pile-up events) are inaccurately categorized as trues. Although the total count rate of these backscatter events is much lower than the count rate of the trues (for a LLD of 150 keV, the backscatter events are about 14.6% of the trues), the NECR is proportional to the square of the trues count rate. Therefore, a 14.6% overestimation of trues count rate leads to a 31% overestimation of the NECR. As a result, the NECR calculated at 150 keV LLD based on this misclassification is 17% higher than that at a LLD of 400 keV, leading to a different (and inaccurate) optimization. This result highlights the importance of the methodology described in this work regarding the treatment of event interactions in simulations.

3) Backscatter Rejection—The curve represented by the square box symbols “□” in Fig. 7 shows the NECR and SF derived from the same dataset as for the diamond “ ” data based

on a perfect backscatter rejection assumption by arbitrarily setting all the backscatter events to zero. This represents an idealized performance that can be achieved with the rejection. With the perfect backscatter rejection, the NECR and SF are improved for LLDs lower than 300 keV due to suppressed SF. However, object scatter still dominates the degradation of image quality when employing a wide open energy window. At a LLD of 400 keV, the NECR still reaches its maximum value and the SF decreased by 71% from that at a LLD of 150 keV. The result with the perfect backscatter rejection leads to the same optimized LLD of 400 keV as for the result with no backscatter rejection implemented (diamond “ ” data). Moreover, the backscatter rejection shows almost no improvement on NECR and SF at the optimized LLD of 400 keV, as almost all the backscatter events have already been eliminated through the energy discrimination. As a conclusion, the backscatter rejection is not helpful and will not be developed for the PETbox4 system.

We need to point out here that the simulations and experiments performed throughout this work focused on pure positron emitting sources. In situations where high energy gammas are emitted simultaneously with the positrons, this conclusion regarding backscatter rejection will likely need to be revisited.

4) Effect of the Imaging Chamber—The curve represented by the circle symbols “(x025CB)” in Fig. 7 shows the simulation excluding the imaging chamber and with an energy resolution of 18%. Backscatter events were identified and included. Compared to the diamond “ ” data, the NECR increases by 21% and 10%, and the SF decreases by about 17% and 26% respectively for the circle “○” data at the LLDs of 150 and 400 keV. The optimized LLD is still 400 keV. Therefore, future efforts are desired to reduce the attenuation introduced by the imaging chamber if possible. The circle “○” data representing the lower limit for the chamber scatters also indicates that decreasing imaging chamber material will not change our conclusion on optimized energy window.

5) Effect of the Energy Resolution—The curve represented by the triangle symbols “ ” in Fig. 7 shows the simulation with an energy resolution of 30% as a worst case scenario to evaluate the effect of the poorer energy resolution in a more realistic scanner on imaging performance. Backscatter events were identified and included, and the imaging chamber was simulated. The NECR decreases significantly when the LLD is raised from 350 keV to 450 keV, because in a poorer energy resolution system, a large fraction of true photopeak events is detected between 350 and 450 keV. Under this scenario, these photoelectric events are discarded as falling outside the appropriate energy window when the LLD is raised above 350 keV. As a result, the optimal LLD with the maximum NECR for this poorer energy resolution system decreased to 350 keV, instead of the 400 keV optimal LLD when an 18% energy resolution is available. In the PETbox4 system described in [5], the energy resolution ranges from 13.5% to 48.3%, therefore the implemented threshold needs to provide tolerance for variance of different components such as PMT, scintillation block positioning and coupling. Therefore, 350 keV was proposed as the optimized LLD for the current PETbox4 system. The triangle “ ” data also indicates that a more uniform energy resolution which can improve both NECR and SF is desired for the PETbox4 system in the future if possible.

The fraction occupied by different types of events in prompt coincidences for the open energy window of 150-650 keV (the previous default energy window used in [5]) and the optimized energy window of 350-650 keV are shown in Fig. 8.

C. NEMA NU-4 Image Quality Phantom

Table II summarizes the uniformity and SOR measured from the image quality phantom images with the LLD increasing from 150 keV to 350 keV in 50 keV steps. Fig. 9 shows the profiles across the cold chamber region of the reconstructed NEMA NU-4 image quality phantom images at a LLD of 150 keV and 350 keV. With the ML-EM reconstruction, the percent standard deviation (SD) in the uniform region is 6.0% and 5.8%, the SOR for the water chamber decreases by about 45% from 15.1% to 8.3%, and the SOR for the air chamber decreases by 31% from 12.0% to 8.3% for the LLD of 150 and 350 keV, respectively. Furthermore, the water and air chamber have identical SORs at the optimized LLD of 350 keV. The RCs for five different rod sizes from 1 to 5 mm diameter at a LLD of 150 keV and 350 keV are shown in Fig. 10. The overall RC at the LLD of 350 keV is better than that at the LLD of 150 keV. Results from the physical measurement further support the simulation based optimization. No scatter correction was applied for the image quality phantom images.

IV. Discussion

Decreasing the inner diameter and increasing the axial FOV of the scanner provides larger detectable solid angle and higher sensitivity for PET systems. The compromise of the spatial resolution due to depth of interaction (DOI) effects introduced by crystal penetration when employing close geometry has been significantly improved with DOI detector techniques [28]–[32] and iterative image reconstruction with more accurate system response modeling [33], [34]. This has led to an increased popularity of systems with close geometry and large solid detection angle [5]–[10], [35]. Even for clinical systems, longer axial FOV scanners are currently in the design stage [36]. Therefore, accurate investigation and understanding of the system characteristics introduced by the close geometry are of great importance to guide system design and optimize data acquisition protocols.

In this work, a system that utilizes BGO as a scintillator is described. The choice of scintillator material is beyond the scope of this effort, but it has been shown previously [5], [37] that this high effective atomic number scintillator offers some advantages in system sensitivity and reduced intercrystal scatter. Nevertheless, the results of this work are applicable to other closed geometry imaging systems made from different scintillator materials.

In this study, an 18.2 g mouse was selected to generate the voxelized phantom in GATE, representing the lower limit of the object scatter originated from the mouse. The simulation which excludes the imaging chamber (shown by the circle “○” data in Fig. 7) thus represents the lower limit of the overall object scatter in PETbox4. Even in such an extreme case, the NECR and SF degrade as the LLD decreases mainly due to the large fraction of object scatter events included. Therefore, the proposed optimized energy window of 350-650 keV should be applicable for imaging any mouse with a larger size or using

different imaging chambers in PETbox4. As only attenuation material inside the FOV was modeled in this study, and the detector material employed by the PETbox4 is BGO, a non-intrinsic radioactive scintillator, the studies in this paper represent the lower limit of the influence from environment scatter and intrinsic activity. The more narrow optimized energy window will also be valid if surrounding gantry material is included or detectors with intrinsic activity such as lutetium oxyorthosilicate (LSO) are used, both of which further degrade the NECR and SF [13]. The NEMA NU-4 count rate phantom and its associated methodology are not used in this study, because traditional sinograms are not generated from the PETbox4 that employs an unconventional system geometry [27].

Our conclusion is different from the results reported for mouse imaging in conventional large diameter systems, in which the optimized NECR can be achieved at a wide open energy window, and the object SF is much less sensitive to the change of the LLD [13], [14]. This difference emphasizes the strong dependence of the SF on scanner geometry: the larger distance between the location for scattering and detection in a scanner with a larger diameter, results in a more significant misplacement of the LOR for the same scattering angle. As a result, a larger fraction of mis-positioned LORs falls out of the FOV and will not contribute to the degradation of the image. For a close geometry system, most of the scatter LORs intersect the FOV leading to a dominant factor of the degradation of NECR and SF when employing an open energy window. Therefore, optimization of the imaging protocol in accordance to the specific scanner is necessary.

This study also highlights that crystal backscatter events cannot be neglected for a large detection solid angle system such as PETbox4. As shown in Fig. 8, the backscatter events occupy about 9% of the total prompts at a LLD of 150 keV, compared with 24% for phantom SF and a random events fraction of 8%. In most of the previous studies involving event classification in GATE [9], [14], [25], only phantom scatter and random events were identified based on *eventID* and *ComptonPhantom* provided by *Root* output from GATE. Ignoring backscatter events results in overestimation of the NECR and underestimation of the SF derived from the simulation (as shown by the cross sign “×” data in Fig. 7), which may bias the conclusion in system design.

In this study, NECR and SF were examined as the criteria for optimization. While correlation between NECR and signal-to-noise ratio (SNR) has been experimentally demonstrated for 3D PET, such work has, to date, been performed only on systems with conventional geometries [38]. Direct correlation between NECR and image SNR has not been validated for longer axial FOV and box like geometry scanners such as PETbox4. Nevertheless, the results from the reconstructed images lead to satisfactory agreement with our simulation based optimization. SF is also an important measure of overall error in PET due to the misplacement of the LORs. A higher SF leads to degradation of SOR, RC and target-to-background ratio (TBR) as the spill-out of counts cannot be compensated by the spill-in of counts, and decrease of the NECR and SNR of the reconstructed images. Contrast-to-noise ratio (CNR), as a more comprehensive figure of merit accounting for the influence from both NECR and SF, is strongly related to the lesion detectability, target localization and quantification accuracy of a system [39]–[41] and could perhaps be considered as part of protocol optimization and system design. While the choice of the LLD

on NECR and SF have been discussed separately in this work, it is essential to understand the simultaneous effects and tradeoff of the changes of NECR and SF on CNR, as future investigation.

V. Conclusion

In this work, the energy window of PETbox4 for whole body mouse scans has been optimized using GATE simulations. The event type classification described in this paper provides a more accurate methodology and is important for imaging protocol optimization and system evaluation. For the pure positron emitting source investigated here, backscatter rejection did not prove useful and therefore was not developed for the PETbox4 system. An LLD of 350 keV was proposed as the optimized energy threshold. Analysis of the NEMA image quality phantom images further support the simulation based optimization. Due to the importance of object scatter and the significant differences of NECR and SF from the simulation with and without imaging chamber, it is concluded that reduction in attenuation introduced by the imaging chamber should be pursued. Furthermore, decreasing imaging chamber material will not change our conclusion on optimized energy window. The optimization in this study is not limited to PETbox4, but should also be applicable or helpful to other close geometry scanners [6]–[10].

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Appendix

The interaction history of each particle in each coincidence event is investigated by the event classification algorithm at eight steps, as shown below:

1) Energy discrimination

The *energy* variable for each detection in a coincidence event is extracted from the coincidence tree of the *Root* output. Events will be rejected if any of the recorded *energies* fall out of the predefined energy window.

2) Check if the LOR intersects the FOV

The distance from projection of the LOR on the transaxial plane to the center of the transaxial FOV is calculated based on the *rsectorID* and *crystalID* of each detection from the coincidence tree. LORs falling out of the FOV will be rejected.

3) Randoms

The *eventID* of the two detections from the coincidence tree are compared. Coincidence events with different *eventID* will be classified into randoms.

4) Phantom scatter

If any of the two detections has a *comptonPhantom* (from the coincidence tree) higher than zero, the coincidence event will be classified into phantom scatter.

5) Single photon backscatter

Based on the *eventID* retrieved from the coincidence tree, all the hits with the same *eventID* in the hits tree of the Root output are examined for *photonID*. If only one *photonID* is recorded, the event will be classified into single photon backscatters.

6) Backscattered multiples

Based on the *eventID* retrieved from the coincidence tree, all the hits with the same *eventID* in the hits tree of the Root output are examined for *rsectorID* and *photonID* to determine the detector (*rsectorID*) that each of annihilation photon first hits. If the two *rsectorIDs* extracted from the coincidence tree for a coincidence event are different from the *rsectorIDs* of the first hits, the coincidence event will be classified into backscatter multiples.

7) Pile-ups

The *rsectorID* and *eventID* for each of the two detections in the coincidence event can be extracted from the coincidence tree, based on which the *photonID* of all the hits with the same *rsectorID* and *eventID* from the hits tree are examined. If more than one *photonID* are found for certain *rsectorID* and *eventID*, the coincidence event will be classified into pile-up events.

8) Trues

The coincidence events that pass through the previous seven steps will be identified as trues.

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Fig 1.

(a) A photograph of a PETbox4 detector module. The complete detector module employs two H8500 PMTs to detect scintillation light from a 24×50 BGO crystal array. (b) PETbox4 system detector configuration. Four detector modules are arranged in a box-like geometry, with a crystal separation of 5 cm between opposing detector panels.

Fig 2.

Three different views (transverse (a), coronal (b) and sagittal (c)) from the voxelized phantom including the mouse anatomical data and imaging chamber data, with emission (colored) data overlaid. Attenuation coefficient values were assigned for the anatomical and imaging chamber data.

Fig 3. Illustration of different types of coincidence events: (1) Trues, (2) phantom scatters, (3) single photon backscatters, (4) backscattered multiples, (5) randoms, (6) pile-ups.

Fig 4.
Detection scheme for different types of coincidence events.

Fig 5.

Energy spectrums of different event types in a simulated mouse scan (including the imaging chamber). The energy spectrum for each event type was magnified in the inset, with the y axis rescaled respectively for better visualization of the distribution characteristics: trues (T), pile-ups (PU), backscattered multiples (BM), single photon backscatters (SPB), phantom scatters (PS) and randoms (R).

Fig 6. Count rate as a function of event type and LLD: trues (T), backscatters (BS), phantom scatters (PS) and randoms (R). The composition of the backscatters was shown in the inset: pile-ups (PU), backscattered multiples (BM) and single photon backscatters (SPB).

Fig 7.

NECR (a) and SF (b) as a function of LLD for five different configurations: “x”, “□” and “x” data were calculated from the same simulation dataset with different analysis on the backscatter events. “○” represents a different simulation excluding the imaging chamber. “△” represents a different simulation assuming an energy resolution of 30%.

Fig 8.

The fraction occupied by different types of events in prompts for the open energy window of 150-650 keV (a) and the optimized energy window of 350-650 keV (b): trues (T), pile-ups (PU), backscattered multiples (BM), single photon backscatters (SPB), phantom scatters (PS) and randoms (R). Detector backscatter events are virtually eliminated at a LLD of 350 keV.

Fig 9. Profiles across the cold chamber region of the reconstructed NEMA NU-4 image quality phantom images at a LLD of 150 keV and 350 keV.

Fig 10.

RCs and SDs for five rods of different sizes with the open energy window of 150-650 keV and the optimized energy window of 350-650 keV.

Table I
Basic Specifications of the PETBox4 System

Crystal material	BGO
Photodetector	PSPMT (H8500)
Detector separation	50 mm
Crystal size	$1.825 \times 1.825 \times 7 \text{ mm}^3$
Number of crystals	24×50 (per detector panel)
Number of detector panels	4
Transaxial FOV	45 mm
Axial FOV	94 mm
Solid Angle fraction	$\sim 87\%$
Coincidence time window	20 ns
Average energy resolution	18%

Table II
Uniformity and SOR for the Cold Chambers Filled with Air and Water of the NEMA
NU-4 Image Quality Phantom Images Acquired with Different LLDs

LLD (keV)	Uniformity	SOR (air)	SOR (water)
150	6.0%	0.120 ± 0.020	0.151 ± 0.031
200	5.9%	0.105 ± 0.019	0.126 ± 0.028
250	5.9%	0.101 ± 0.018	0.115 ± 0.026
300	5.7%	0.094 ± 0.018	0.101 ± 0.022
350	5.8%	0.083 ± 0.016	0.083 ± 0.019