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Abstract. Using analytical and Monte Carlo modeling, we explored performance of a lightweight wearable helmet-shaped brain positron emission tomography (PET), or BET camera, based on thin-film digital Geiger avalanche photodiode arrays with Lutetium-yttrium oxyorthosilicate (LYSO) or LaBr₃ scintillators for imaging *in vivo* human brain function of freely moving and acting subjects. We investigated a spherical cap BET and cylindrical brain PET (CYL) geometries with 250-mm diameter. We also considered a clinical whole-body (WB) LYSO PET/CT scanner. The simulated energy resolutions were 10.8% (LYSO) and 3.3% (LaBr₃), and the coincidence window was set at 2 ns. The brain was simulated as a water sphere of uniform F-18 activity with a radius of 100 mm. We found that BET achieved >40% better noise equivalent count (NEC) performance relative to the CYL and >800% than WB. For 10-mm-thick LaBr₃ equivalent mass systems, LYSO (7-mm thick) had ~40% higher NEC than LaBr₃. We found that 1 × 1 × 3 mm scintillator crystals achieved ~1.1 mm full-width-half-maximum spatial resolution without parallax errors. Additionally, our simulations showed that LYSO generally outperformed LaBr₃ for NEC unless the timing resolution for LaBr₃ was considerably smaller than that presently used for LYSO, i.e., well below 300 ps. © 2016 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JMI.4.1.011003]

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1 Introduction

The ability to observe neurological, pharmacological, and metabolic processes in a live brain, while performing active tasks in a naturalistic environment and in response to realistic challenges, is critical for understanding brain function. In particular, positron emission tomography (PET) represents a promising means of imaging the live brain.^{1–6} In this paper, we describe the initial stages in the performance evaluation and design of two dedicated brain PET (BET) imaging systems that are lightweight, portable (or even wearable), and specifically tailored toward imaging the human brain while performing active tasks.⁷

Because the biological and physiological processes in the brain are multiscale in nature, running from large coordinated dynamics across the whole brain, down to the cellular and molecular level, there is effectively no bound on the useful performance range of such a system. As a result, the key questions we are addressing are: (i) what is the best performance achievable with current technology? (ii) How do we design a system that can achieve this performance? The answers to these

questions begin with identifying key performance metrics and a means of optimizing them via the various design parameters, and to evaluate them in the context of a detector array we refer to hereafter as an autonomous detector array (ADA), which can be layered or tiled into autonomous detector block (ADB)⁸ and assembled into a full BET imaging system.

PET central nervous system imaging has a long and rich history.⁹ In the modern era of three-dimensional (3-D) imaging, a number of groups has developed and evaluated dedicated systems to improve brain imaging. The ECAT high-resolution research tomograph from CTI PET Systems Inc. was an early dedicated brain 3-D PET/CT.¹⁰ Since this scanner's introduction in 2000, the field of PET/CT has been largely dominated by whole-body (WB) imaging for oncologic applications due to reimbursement for ¹⁸F-FDG PET/CT examinations. However, recently, there is a renewed interest in building dedicated brain imaging systems that utilize more conformal geometries and more advanced detector designs.^{11–17} The paper by Gong et al.¹⁵ is particularly interesting as they use the Cramer–Rao lower bound on image variance to optimize their design choices. This

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implies the evaluation is for a maximum-likelihood image estimate,¹⁸ which is an appropriate design criterion; however, it requires the detailed knowledge of a system matrix relating detected counts to PET radiotracer activity distribution.

The focus of this paper is on modeling the performance of an innovative wearable PET brain imaging system that we are designing; however, the development of such a system requires an appropriate low-power, low-volume, high 3-D spatial, and coincidence timing resolution (CTR) detector module, which we briefly describe here. It has long been realized that using small scintillator volumes enables the best possible imaging spatial and timing resolution,¹⁹ while layering of these small scintillators can be used to provide both depth-of-interaction (DOI) and improved efficiency of gamma ray capture. Early attempts to explore these concepts by Bieniosek et al.,²⁰ Vandenbroucke et al.,²¹ and Omura et al.,²² achieved success in improving resolution and DOI estimation but created detectors that were bulky, power hungry, and achieved relatively poor CRT. Recently, it has been recognized that monolithic integration of complementary metal–oxide–semiconductor (CMOS) readout circuits with digital silicon photomultipliers (dSiPMs) provides an excellent path to decreasing power, reducing system size/complexity, and improving CTR. Today, the best CTR in commercial PET scanners is achieved by the Philips Vereos systems²³ using the Philips dSiPM devices,²⁴ achieving a CTR of about 325 ps. Other examples using a multichannel dSiPM approach with large integrated foundry CMOS dSiPMs^{25,26} show promising timing resolution performance, however, they still lag behind discrete implementations that use optimized, discrete amplification, and timing electronics.²⁷ The success of discrete implementations indicates that CTR = 100 ps is feasible for monolithically integrated arrays SiPMs 1:1 optically coupled to suitably small scintillators.

Our design exploits scaling advantages offered by reduced single photon avalanche diodes element size (increasing dynamic range) and decreased SiPM area (resulting in a higher speed response), enabling the use of smaller scintillator segments and leading to a substantial boost in timing resolution. Our present design envisions integrating the analog processing, digital control, and communication directly with SiPMs in a hierarchical architecture. At the lowest architectural level, two-dimensional SiPM arrays with local analog processing form a thin, fast, and high functionality ADA. The arrays are then integrated via thin-film 3-D packaging and interconnect to facilitate creation of small tightly integrated ADBs (patent pending⁸). In contrast, BET systems built or proposed to date are based upon existing conventional detector block designs, which limit the number of signal channels that could be incorporated into a system. This limitation necessitates the use of larger scintillator and/or light sharing strategies for event localization within the crystal, which generally degrades timing resolution. The ADBs, in contrast, allow a finer granularity in the design resulting in improved timing resolution and leading to a more conformal and ultimately lower mass system. This will allow for markedly unconventional PET system designs. We believe that these reductions in weight and system complexity, coupled with independent local event processing, will enable fabrication of lightweight PET systems capable of patient imaging in ways currently unavailable. In this paper, we consider and analyze a BET system based on ADAs combined into ADBs.

The ultimate goal of using this detector concept in a PET system is to produce a high fidelity image of the radionuclide

distribution within the patient using the PET detector concept. All the scientific or clinical questions that PET images can answer are either explicitly or implicitly dependent on image fidelity. There are three fundamental mechanisms that contribute to the quality of PET images: system sensitivity, noise, and spatio-temporal localization.²⁸ The first two quantities are well accounted for in the data via the noise equivalent counts (NECs).²⁹ All other things being equal, the system with the better NEC will produce better images.

Spatio-temporal localization is the system's basic ability to identify the spatio-temporal coordinates of the detected gamma photons (counts) and the necessary sampling to map them into the spatial domain (i.e., image reconstruction space). It should be emphasized that this act of projecting the detected gamma photons into the spatial domain, the image reconstruction, is critical for achieving high-quality images and should be considered a part of the design process, even if not explicitly required. We also note that improved localization, e.g., via time-of-flight (TOF) information, improves the effective NEC.³⁰

In this paper, we expand our results from a study described in a short conference paper.⁷ In the current study, we first arrive at some initial performance estimates for several brain imaging systems assembled from distributed ADAs of digital Geiger Avalanche Photodiodes (dGAPDs) integrated into ADBs. We begin with analytical estimates of the geometric efficiency of the proposed three basic detector geometries investigated: spherical cap, dedicated brain cylinder, and WB cylinder.

We follow this with estimates of NEC as a function of the various design parameters. We also estimate the spatial resolution and discuss selected design choices and their effect on count collection and timing. We then compare these estimates to Monte Carlo (MC) predictions that we obtained using the GEANT4 Application for Tomographic Emission (GATE) program.³¹

2 Design Considerations

2.1 System Geometry

We divided the description of system geometry into descriptions of the ADBs and their subsequent arrangement as a brain imaging scanner.

2.1.1 Detector geometry

In our design, the BET system is assembled from distributed ADAs integrated into ADBs. The ADA is comprised of an array of small scintillator segments (voxels with base $a \times a$: $0.5 \leq a \leq 3.0$ mm, length d : $1.0 \leq d \leq 10$ mm), each coated with a thin (5 to 10 μm) reflective layer on five sides. The sixth side is optically coupled to a matched array of dGAPDs with integrated signal electronics using a small portion of the array space. This ADA scintillator assembly will be formed on a single “chip” with control and communication logic integrating the readouts from the local SiPM arrays. To minimize mass and gamma ray attenuation, the total thickness of the silicon substrate will be thinned to ~ 50 μm . Several of these ADA blocks will be stacked together to form the ADB with a total detector thickness of 5 to 25 mm, determined primarily by the required scintillator mass. Figure 1(a) shows the proposed ADA and ADB geometries.

2.1.2 Scanner geometry

We evaluated three basic detector arrangements: spherical cap, dedicated brain cylinder, and WB cylinder [see Fig. 1(b)]. The

Fig. 1 (a) From top to bottom: an ADA with one-to-one scintillator coupling to an SiPM array with an exploded view of an area of the array replaced with an integrated electronic package. (b) From top to bottom: the BET, CYL, and WB geometries are shown with a spherical positron source simulating human head. ADB's will be tiled into a shape similar to the spherical cap in the final design.

spherical cap BET device extended 120 deg from the vertical axis and had a radius of 125 mm. The cylindrical brain PET (CYL) device had a 250-mm diameter and the same total volume of scintillator for a 10-mm-thick scintillator, resulting in a height of 220 mm. The WB PET system had ring geometry with a 410-mm radius, a 158-mm axial field of view (FOV) and, because this configuration represented a real PET/CT scanner (GE D690/710), a fixed scintillator thickness of 25 mm. Assuming a 10- and 25-mm-thick scintillator for BET and CYL geometry, and 25 mm for the WB system, the total scintillator segments volumes were ~ 1800 and $\sim 10,500$ ml, respectively.

2.2 Effective Count Considerations

Image quality is directly related to the effective NEC collected during an acquisition, which includes improved noise rejection from TOF information.³⁰ It is defined by the relation

$$\begin{aligned} \text{NEC}_{\text{eff}} &= \left[\frac{D}{\min(c\Delta t/2, D)} \right] \left[\frac{T + S + (D/D_{\text{FOV}})R}{T + S + (D/D_{\text{FOV}})^2 R} \right] \text{NEC} \\ &= \left[\frac{D}{\min(c\Delta t/2, D)} \right] \left[\frac{T + S + (D/D_{\text{FOV}})R}{T + S + (D/D_{\text{FOV}})^2 R} \right] \\ &\quad \times \frac{T^2}{T + S + R}, \end{aligned} \quad (1)$$

where T , R , and S are true, random, and scatter counts, respectively, and $c\Delta t/2$ represents the TOF photon localization with Δt being the timing resolution for the arrival time difference between the two coincidence photons, D is the head diameter (~ 170 to 200 mm³²), and D_{FOV} is the diameter of the FOV. Clearly, improved TOF for a given source geometry always improves the NEC.

To maximize the NEC for a particular activity distribution within the FOV, a number of issues must be considered. These include geometric sensitivity, detector attenuation efficiency, detector dead-time, source attenuation, and additive noise from random and scatter counts (and cascade counts with some isotopes). The geometric sensitivity and detector attenuation efficiency are defined by the device geometry, and the scintillator attenuation and thickness. In general, because the source's attenuation loss is patient dependent, scatter counts cannot easily be

included in the design considerations. However, in the case of brain imaging, where patient head size variability is smaller than that of body habitus, the effects of patient variability can be more easily considered in the system's design. On the other hand, random counts and dead-time are dependent on the incident photon flux and the detector electronics, which in this study are not fully known. As a result, we use scatter equivalent counts [$\text{SEC} = T^2/(T + S)$, ignoring TOF effects] in lieu of NEC for the initial calculations and simulations but will include random counts and dead-time as correction factors to estimate NEC_{eff} with these effects present.

In addition, because of recent interest in LaBr_3 for PET, we consider its relative performance to LYSO . For equivalent SEC for these two systems, using the relationship $\text{SEC} = T * (1 - \text{SF})$, where SF is the scatter fraction and adding TOF we have

$$\frac{\text{SEC}_{\text{LYSO}}}{\text{SEC}_{\text{LaBr}_3}} = \frac{T_{\text{LYSO}} \Delta t_{\text{LaBr}_3} (1 - \text{SF}_{\text{LYSO}})}{T_{\text{LaBr}_3} \Delta t_{\text{LYSO}} (1 - \text{SF}_{\text{LaBr}_3})}. \quad (2)$$

The number of true counts is proportional to the detector stopping power given by $(1 - e^{-\mu d})^2$, where μ is the detector's linear attenuation coefficient and d is the detector thickness. Using this proportionality, for the same SEC for otherwise identical systems, the equivalent thickness for LaBr_3 is given by

$$\begin{aligned} d_{\text{LaBr}_3} &= \frac{-1}{\mu_{\text{LaBr}_3}} \log \left[1 - \sqrt{\frac{\Delta t_{\text{LaBr}_3}}{\Delta t_{\text{LYSO}}}} \sqrt{\frac{1 - \text{SF}_{\text{LYSO}}}{1 - \text{SF}_{\text{LaBr}_3}}} (1 - e^{-\mu_{\text{LYSO}} d_{\text{LYSO}}}) \right]. \end{aligned} \quad (3)$$

Now, for a particular object where the SFs and timing resolutions were known and assuming a spherical system, if $d_{\text{LaBr}_3} > [1.43(d_{\text{LYSO}} + R_0)^3 + (1 - 1.43R_0^3)]^{1/3} - R_0$, where the factor 1.43 is the ratio of the crystal densities (7.3 and 5.08 g/ml for LYSO to LaBr_3 , respectively), and R_0 is the inside radius of the scanner, then LYSO will have better performance per unit scintillator mass.

2.3 Analytical Sensitivity Estimation

The geometric sensitivity is defined by the effective solid angle of a point in the FOV and the detector scintillator. Because PET is based on coincidence detection, the true count geometric sensitivity is defined as 4π sr minus the solid angle subtended by the point to the nondetector area or opening and its back projection.³³ For systems with multiple openings, care must be taken to avoid double counting any overlap between various solid angles and back projections. It follows that for both spherical caps and cylindrical geometries, the poorest geometric sensitivity in any particular slice is on the system's central axis.

Detector attenuation efficiency is defined by the system geometry, and, for a system with identical detectors, it can be approximated by a constant.

2.4 Additive Contribution and Noise Equivalent Count Estimation

2.4.1 Energy resolution and true count estimation

The true counts are related to the source activity, attenuation, system energy window, and resolution. In terms of energy resolution and window, the relative true counts can be derived by integrating the energy window over the estimated count distribution (Gaussian kernel) normalizing with respect to the reference distribution and accounting for differing geometries in terms of mean solid angle and detector thickness giving

$$\frac{T}{T_{\text{ref}}} = \frac{\left[\text{erf}\left(\frac{E_2 - E'}{\sigma\sqrt{2}}\right) - \text{erf}\left(\frac{E_1 - E'}{\sigma\sqrt{2}}\right) \right]}{\left[\text{erf}\left(\frac{E_{2,\text{ref}} - E'}{\sqrt{2}\sigma_{\text{ref}}}\right) - \text{erf}\left(\frac{E_{1,\text{ref}} - E'}{\sqrt{2}\sigma_{\text{ref}}}\right) \right]} \left(\frac{\bar{\psi}_C}{\bar{\psi}_{C,\text{ref}}} \right) \left(\frac{1 - e^{-\mu d}}{1 - e^{-\mu d_{\text{ref}}}} \right)^2, \quad (4)$$

where E_1 and E_2 are the energy window thresholds, E' is 511 keV, σ is the energy resolution (typical values of 10.8% and 3.3% at 511 keV were used for LYSO and LaBr₃, respectively), $\bar{\psi}_C$ is the mean solid angle for coincidence counts, μ is the detector's linear attenuation coefficient, d is the detector thickness, and the ref subscript refers to the values used in the reference system, where the original measurements were made.

2.4.2 Random count estimation

The random count distribution can often be approximated by a uniform distribution in projection space. The random counts for a detector pair can be computed from the singles rates via $2\tau \int \rho_i(t)\rho_j(t)dt$, where τ is the coincidence window and $\rho_i(t)$ is the singles rate for a particular detector, i .³⁴ Given this, the total random counts for the system are then just a summation over all detector pairs. Here, the mean singles rate is given by

$$\rho(t) = 2 Ac(t)\bar{\psi}_S\bar{\mu}_{\text{head}}(1 - e^{-\mu d}), \quad (5)$$

where $Ac(t)$ is the activity in the FOV as a function of time, $\bar{\psi}_S$ is the mean solid angle for singles counts, and $\bar{\mu}_{\text{head}}$ is the mean attenuation loss due to the patient. As a result, for a particular geometry and given a reference random count fraction, the change in the random count rate R is proportional to the relative singles mean solid angle, $\bar{\psi}_S/\bar{\psi}_{S,\text{ref}}$, the relative coincidence timing, τ/τ_{ref} , and the singles relative detector attenuation giving

$$\frac{R}{R_{\text{ref}}} = \frac{\left[\text{erf}\left(\frac{E_2 - E'}{\sigma\sqrt{2}}\right) - \text{erf}\left(\frac{E_1 - E'}{\sigma\sqrt{2}}\right) \right]}{\left[\text{erf}\left(\frac{E_{2,\text{ref}} - E'}{\sqrt{2}\sigma_{\text{ref}}}\right) - \text{erf}\left(\frac{E_{1,\text{ref}} - E'}{\sqrt{2}\sigma_{\text{ref}}}\right) \right]} \times \left(\frac{1 - e^{-\mu d}}{1 - e^{-\mu d_{\text{ref}}}} \right)^2 \left(\frac{\bar{\psi}_S}{\bar{\psi}_{S,\text{ref}}} \right)^2 \frac{\tau}{\tau_{\text{ref}}}, \quad (6)$$

where the ref subscript again refers to a reference system, where these values are known.

2.4.3 Scatter count estimation

Scatter counts arise from Compton scattering of photons within the patient and camera. Because of finite energy resolution in the scintillator, the apparent energy of the true and scattered count distributions overlap and become indistinguishable. The scatter count rate depends on the attenuation and activity distribution of the object, the energy window, and the scintillator energy resolution. The actual estimation of the scatter distribution is difficult and requires solving a transport equation. However, using Klein–Nishina cross sections, the single scatter energy distribution can be more easily estimated for a line or point source. Thus, given an estimate of the SF for a particular energy window of a representative geometry, a relative improvement can be approximated. Using these references, we estimate the reference scatter counts as $S_{\text{ref}} = T_{\text{ref}}\text{SF}_{\text{ref}}/(1 - \text{SF}_{\text{ref}})$, and then we approximate scatter as a function of energy, via the Compton scatter and Klein–Nishina relations, where the scatter angle θ is a function of originating photon ($E' = 511$ keV) and scattered photon energies given by

$$\theta(E, E') = \text{acos}(2 - E'/E). \quad (7)$$

Substituting this into the Klein–Nishina relation for scattering angle likelihood, p_{511} , we get

$$p_{511} = \frac{\left[\frac{1 + (2 - E'/E)^2}{(E'/E)^2} \right] \left\{ 1 + \frac{(E'/E - 1)^2}{[1 + (2 - E'/E)](E'/E)} \right\}}{\int_{E'_1}^{E'_2} \left[\frac{1 + (2 - E'/E)^2}{(E'/E)^2} \right] \left\{ 1 + \frac{(E'/E - 1)^2}{[1 + (2 - E'/E)](E'/E)} \right\} dE'}, \quad (8)$$

which gives the energy probability distribution of a single Compton scatter for 511-keV photons. Again, using the idea that relative scatter counts are proportional to the solid angle and detector attenuation ratios, this gives an estimate of the relative scatter ratio with respect to a reference amount of scatter

$$\frac{S}{S_{\text{ref}}} = \frac{\int_{E_{1,\text{ref}}}^{E_{2,\text{ref}}} \frac{p_{511}(E)}{\sigma\sqrt{2\pi}} \exp\left[\frac{-(E - E')^2}{2\sigma^2}\right] dE}{\int_{E_{1,\text{ref}}}^{E_{2,\text{ref}}} \frac{p_{511}(E)}{\sigma_{\text{ref}}\sqrt{2\pi}} \exp\left[\frac{-(E - E')^2}{2\sigma_{\text{ref}}^2}\right] dE} \left(\frac{\bar{\psi}_C}{\bar{\psi}_{C,\text{ref}}} \right) \left(\frac{1 - e^{-\mu d}}{1 - e^{-\mu d_{\text{ref}}}} \right), \quad (9)$$

where σ is again the system's energy resolution. This result was obtained under assumptions that the two systems compared have an identical source and an equivalent number of detected counts, prior to energy window discrimination and blurring effects. Based on these results and using the definition of the SF for the estimated system and source geometry, we can model the scatter distribution as a function of energy resolution. Further, given a particular true counts and singles rate, the SEC or NEC can be estimated for a number of different configurations.

2.4.4 Dead-time estimation

System dead-time results from a number of effects, most notably the detector pulse integration time and downstream signal processing. In older designs, with light sharing between scintillator crystals, dead-time is sensitive to counts within the whole block. In this case, the dead-time is a function of the solid angle of the source to a scintillator block. Hence, smaller blocks exhibit less total dead-time. In some newer systems, including the one proposed in this paper, small scintillation elements are individually coupled to dedicated SiPM arrays to further reduce the effective dead-time. In the ADA and ADBs proposed in this paper, we further integrate signal processing into each SiPM array, which we anticipate will both improve timing resolution and reduce dead-time. The majority of the dead-time improvement is simply a function of the ratio of the block to single crystal areas, where smaller elements will see less dead-time. Given this, and because detector dead-time is generally parallelizable, the dead-time detriment can be written as

$$\frac{\rho_{DT}}{\rho} = e^{-\tau_{DT} \left(\frac{\bar{\psi}_{S,DT}}{\bar{\psi}_{S,\rho}} \right) \rho}, \quad (10)$$

where τ_{DT} is the dead-time time constant (the same for both systems), ρ is the incident singles rate in the absence of dead-time, and $\bar{\psi}_{S,DT}/\bar{\psi}_{S,\rho}$ is the ratio of the mean solid angles for the singles to a detector element to that of the system. We do not take the lutetium decay contribution into account. Because the dead-time represents a probability for a single event the dead-time loss for coincidence counts is $(\rho_{DT}/\rho)^2$. As a result, the dead-time loss is the same for true, random, and scatter counts, and similarly for NEC. In this paper, we assume a dead-time of 600 ns, measured from a General Electric Discovery 690 via fitting the singles data, again ignoring lutetium decay. This number is consistent with measurements on past PET/CT.³⁵ Finally, we add that because downstream signal processing is a separate engineering issue and can be effectively reduced using parallel readouts, we do not include its effects in this paper.

2.4.5 Optimal energy window estimation

Using the derived analytical estimate for true and scatter counts, the optimal energy windows can be estimated by finding the lower energy threshold that maximizes the SEC. The upper window estimate is made by finding the energy threshold at which additional counts' contribution to improved SEC is negligible (~1% to 3%). An energy resolution of 10.8% and 3.3% at 511 keV was used for LYSO and LaBr₃, respectively. A more detailed model, which could include the effects of cascade photons from isotopes such as ¹²⁴I or pulse pileup effects, is necessary for a more accurate estimate.

2.5 System Resolution Estimation

The intrinsic resolution is largely a function of detection localization and source uncertainty. One aspect of detection localization is the system geometry, which is essentially determined by the solid angle coverage of the FOV and provides the available oversampling. It also provides the overall detector framework and the subdivision of the detector elements into groups or blocks. Within this framework, the light sharing and interdetector Compton scatter define the ability of the detector to localize a particular detection event.³⁶ These phenomena provide the detector's contribution to the overall system point spread function (PSF).³⁷ In addition,

DOI for off-center events can result in resolution loss for the system. The intrinsic source uncertainty is isotope dependent and arises from positron transport (positron range)^{38–40} and residual momentum in the annihilation process (annihilation location uncertainty, noncollinearity).²⁸ These sources of resolution uncertainty are independent and can be added in quadrature giving

$$\sigma_{\text{total}} = \sqrt{\sigma_{\text{det}}^2 + \sigma_{\text{pos},AX}^2 + \sigma_{\theta}^2 + \sigma_{\parallel}^2}, \quad (11)$$

where σ_{det} , $\sigma_{\text{pos},AX}$, σ_{θ} , and $\sigma_{\parallel}$ are full-width-half-maximum (FWHM) detector, positron range, noncollinearity, and DOI uncertainties, respectively.^{28,39} We note that the positron range uncertainty is tissue and isotope dependent (density dependence provides a good approximation). The source location uncertainty can be found in the literature or estimated via MC.

The detector's position uncertainty can be broken down further into detections via photoelectric (PE) and Compton interactions. The number of detected events for each type of interaction depends on their respective cross-section ratios for the particular interaction. In the case of the ADA system described here, where there is no light sharing, the uncertainty of detection via PE effect (and correctly identified points of first interaction for Compton interactions) can be well approximated by the detector sampling distance because the range of the photoelectrons is very small (compared to the size of the scintillator crystals). The position uncertainty is limited by sampling and is $\sigma_{\text{PE}}^2 = (a/2)^2$, where a is the scintillator crystal width.

The effect of Compton scatter on resolution is more difficult to estimate and it cannot simply be added in quadrature to the sampling uncertainty because it affects only mispositioned events. Nonetheless, it does contribute to the system PSF. The uncertainty induced by Compton scatter is approximated by $\sigma_C = \sqrt{\bar{x}_C^2 + a^2}/2$, where the 1/2 term results from sampling and $\bar{x}_C$ is the mean-free-path of a 511-keV photon in the scintillator. The mean Compton path length can be derived and calculated via the integral

$$\bar{x}_C = \int_0^{\pi} p_{511}(\theta) \frac{\sin \theta}{\mu(E)} d\theta, \quad (12)$$

where $p_{511}(\theta)$ is the probability of a particular scattering angle for incident 511-keV photons as given by Eq. (8), the sine term is a forward scattering correction, and $\mu(E)$ is the density and mass attenuation coefficient product at energy E , which in this case is given by the Compton energy loss [Eq. (4)], $E = 0.511/(2 - \cos \theta)$ MeV.

The combined effect of using the spatial resolution estimates for PE and Compton scattered detection events can be estimated if the relative fractions of these events are known via convolution of their distributions. The spatial blurring kernel, $h(x)$, in sinogram space can be estimated via

$$h(x) = h_{\text{pos},AX}(x) * h_{\theta}(x) * h_{\parallel}(x) * h_{\text{det}}(x) * [\eta \delta_{\text{PE}} + (1 - \eta) h_C(x)], \quad (13)$$

where the subscripts indicate the blurring source, (pos: positron range, θ : noncollinearity, $\parallel$: depth of interaction, det: detector size) x is the count displacement distance, η is the PE fraction, $*$ represents convolution, and δ_{PE} is the delta function. However, the PE fraction is a function of the event binning strategy and

may be difficult to estimate without MC. We note that correctly identifying the point-of-first interaction implies $\eta = 1$ and $\sigma_{\text{det}} = \sigma_{\text{PE}}$.

In a multilayered detector design, where individual detector elements cannot localize events, some DOI resolution loss will occur. The uncompensated loss for scintillators within blocks can be described by $\sigma_{\parallel} = (\bar{x}_{mfp}/2) \times (r\sqrt{R^2 - r^2}/R^2)$, where r and R are the radial offset and system radius, respectively, and $\bar{x}_{mfp} = 1/\mu(E)$ is the mean-free-path for a photon at a particular energy. The factor of 1/2 is due to detector penetration likelihood at both ends of the line-of-response.

DOI correction can be accomplished by a number of means, including position sensitive detectors and stacked detectors. In either case, reducing the penetration depth effect mitigates the resolution loss. In the case of the stacked detector block, ignoring detector Compton scatter, the best achievable FWHM resolution as a function of thickness from Eq. (11) results in the following relationship:

$$\sigma_{\text{total}}(d) = \sqrt{\sigma_{\text{det}}^2 + \sigma_{\text{pos}, \text{AX}}^2 + \sigma_{\theta}^2 + \left[\frac{\min(d, \bar{x}_{mfp}) r \sqrt{R^2 - r^2}}{2R^2} \right]^2}. \quad (14)$$

Note that the scintillator segment thickness must be less than the mean-free-path length of the photon in the scintillator.

In this study, for the various distribution functions, we used a dual-exponential fit for positron range for ^{18}F in water, a normal distribution for noncollinearity, and a triangle distribution for detector size (center of the FOV) using the values from Ref. 39. In Eqs. (11) and (14), we used 0.54 mm for the effective FWHM of positron range taken from Ref. 28.

2.6 Monte Carlo Estimation

The GATE v7.1 software³¹ has been shown to successfully model PET systems. In the present case, we modeled each system using a monolithic shell for easy evaluation of any subset of detected events. Because of this detector configuration, individual blocks were not modeled, but instead, all event digitization was performed by in-house software using the “hits” data, subsequently binning them into singles and coincidences. Random background counts from the naturally occurring isotope ^{176}Lu in LYSO were not modeled. Further, we initially used a 300- to 700-keV energy window in our events processing to remove events that would not contribute to the overall analysis. In each geometry/scintillator combination, 10^7 decays were simulated at a very low count rate to avoid activity dependence.

Both system and attenuation sensitivities for a particular point can be computed via MC. As a first-order approximation, a human head can be represented by a sphere with a volume of 4400 ml or a radius of 100 mm (200-mm thickness through the center). We used both back-to-back photon and positron sources. The back-to-back source, along with point-of-first-interaction, provides an improved means to identify scattered photons and differentiate between PE and Compton interactions in the detectors. This is done by measuring the distance between the source location and the line-of-response and avoids using GATE’s Compton counter, which is more susceptible to misidentifying sensitive segments in the model.

Given the various sensitivity values from the MC simulations obtained for singles and coincidence counts for both the attenuated and nonattenuated source geometries, the associated sensitivities

can be computed and the performance of the system can be approximated at various count levels.

The system’s optimal energy windows were estimated using MC by maximizing the SEC for the BET, CYL, and WB PET geometries, and using the back-to-back line source in the spherical water phantom. This model was designed to be similar to the National Electrical Manufacturers Association, NEMA NU2, SF, and count rate tests.

3 Results

3.1 Estimation of Optimal Energy Window

We estimated the optimal low-energy threshold for the energy window, via analytical means using Eqs. (1), (4), (6), and (9), to be 467 keV and 495 keV for LYSO and LaBr₃, respectively. These threshold estimates used energy resolutions of 10.8% and 3.3% at 511 keV for LYSO and LaBr₃, respectively, where the reference scatter fraction values were taken from the D690/710 PET/CT. We also determined that beyond 585 and 535 keV for LYSO and LaBr₃, respectively, the upper energy window does not appreciably improve sensitivity.

The MC estimates were used to maximize the SEC to find the optimal energy windows, which for the various configurations were 445 to 620 keV and 485 to 575 keV for Lu₂SiO₅ and LaBr₃, respectively. We note that, as with the analytical estimates, the SEC is relatively insensitive to the upper threshold, which would not be the case for an isotope with cascade photons, such as ^{124}I or pulse pileup effects. Plots of the energy spectra for the various systems using these geometries are shown in Fig. 2. The energy window was insensitive to the system’s geometry and instead depended only on the scintillator material. We used the obtained values for all subsequent calculations.

3.2 Estimation of System Sensitivity

The analytically and MC (GATE) estimated system sensitivity comparisons for the central axis of BET, CYL, and WB PET systems are shown in Fig. 3 and collected in Table 1. We observe that mean sensitivity relative to 4π for BET is 1.5- and 6-times higher, as compared to CYL and WB PET, respectively.

3.3 Estimation of Scatter Equivalent Counts, Noise Equivalent Count, and Scatter Fraction and the Effects of Dead-Time

We computed the scatter, NECs, and SF using the conventional NEMA NU 2-2007 approach via a line source in an attenuating medium (100-mm radius water sphere) and also with a distributed source in an attenuation medium (spherical source in a water sphere). The SEC obtained results are collected in Table 2 and Fig. 4 for both LYSO and LaBr₃. In addition, the estimates for both the BET and CYL geometries are given for 10- and 25-mm-thick LaBr₃ mass equivalent LYSO systems using 7- and 18-mm-thick LYSO crystals, respectively.

Using the analytical approach from Eq. (3), the required thickness of LaBr₃ for an equivalent SEC of a 25-mm LYSO BET system with the same TOF is 35.7 and 37.2 mm for line source and a sphere sources in a spherical phantom, respectively. For WB PET systems, the SF ratios favor LYSO systems even more. For PET systems of same crystal thickness, the TOF improvement must be 30% and 37% to provide better SEC performance for BET and WB systems, respectively. However, for equivalent mass, the MC results show LYSO has superior mass

Fig. 2 (a) LYSO and (b) LaBr₃, and from left to right the MC estimates of the total (black), true (blue), and scatter (red) count spectra for BET, CYL, and WB PET systems, respectively, see text. Dotted lines represent the energy window that maximizes SEC.

Fig. 3 (a) Analytically, estimated intrinsic sensitivity for a line source for the BET, CYL, and WB PET systems, (b) MC estimation of the sensitivity for a line source in air, and (c) MC estimation of the sensitivity for a line source in an attenuating sphere made of water.

Table 1 Analytically and MC (GATE) estimated geometric sensitivities, relative to 4π , for BET (hemisphere radius 125 mm), CYL (cylinder radius 125 mm and axial length 220 mm), and WB PET (ring radius 410.0 mm and axial FOV 158.0 mm) are shown. The ratio of BET to CYL and WB PET mean sensitivities are 1.53 and 6.07, respectively.

	BET	CYL	WB PET
Analytically estimated mean sensitivity	0.577	0.377	0.096
Analytically estimated maximum sensitivity	0.863	0.661	0.187
GATE estimated sensitivity for LYSO 10 mm	105.8 counts/kBq	74.7 counts/kBq	—
Scintillator mass for LYSO 10 mm	13.1 kg	13.1 kg	—
GATE estimated sensitivity for LaBr ₃ 10 mm	40.7 counts/kBq	26.6 counts/kBq	—
Scintillator mass for LaBr ₃ 10 mm	9.1 kg	9.2 kg	—
GATE estimated sensitivity for LYSO 25 mm	226.1 counts/kBq	167.2 counts/kBq	26.3 counts/kBq
Scintillator mass for LYSO 25 mm	36.7 kg	34.7 kg	76.5 kg
GATE estimated sensitivity for LaBr ₃ 25 mm	108.7 counts/kBq	75.7 counts/kBq	11.4 counts/kBq
Scintillator mass for LaBr ₃ 25 mm	25.6 kg	24.2 kg	53.4 kg

Table 2 MC (GATE) estimates of the SEC and SF for the various PET camera configurations with LYSO and LaBr₃ scintillators for line and spherical sources in 100-mm radius water sphere.

GATE estimates	BET	CYL	WB PET
Line source in sphere phantom			
SEC for LYSO 10 mm	17.1 counts/kBq	10.1 counts/kBq	—
SEC for LaBr ₃ 10 mm	8.1 counts/kBq	4.4 counts/kBq	—
SEC for LYSO 25 mm	35.2 counts/kBq	23.0 counts/kBq	3.2 counts/kBq
SEC for LaBr ₃ 25 mm	20.8 counts/kBq	12.5 counts/kBq	1.6 counts/kBq
SF for LYSO	27.2%	28.1%	24.7%
SF for LaBr ₃	12.1%	13.2%	14.4%
SEC for LYSO w/ equiv. mass 10 mm LaBr ₃	11.1 counts/kBq (7.0-mm crystal)	6.3 counts/kBq (7.0-mm crystal)	—
SEC for LYSO w/ equiv. mass 25 mm LaBr ₃	30.0 counts/kBq (18.0-mm crystal)	18.8 counts/kBq (18.0-mm crystal)	—
SF for LYSO w/ equiv. mass 25 mm LaBr ₃	27.1% (18.0-mm crystal)	28.4% (18.0-mm crystal)	—
Spherical source in sphere phantom			
SEC for LYSO 25 mm	54.4 counts/kBq	39.9 counts/kBq	6.8 counts/kBq
SEC for LaBr ₃ 25 mm	31.8 counts/kBq	22.3 counts/kBq	3.2 counts/kBq
SF for LYSO	23.3%	23.8%	15.4%
SF for LaBr ₃	10.3%	11.0%	9.8%

Fig. 4 The top row shows NEMA NU2-like tests of SEC as a function of axial position using MC (GATE) simulations with a line source in air with (a) LYSO and (b) LaBr₃. The lower row shows similar results with a spherical source in a water sphere, again with (c) LYSO and (d) LaBr₃.

performance of 27%, and 30% for 10-mm LaBr₃ (7-mm LYSO) and 25-mm LaBr₃ (18-mm LYSO), respectively. This differs from the analytical results that show LYSO's advantage as being 22% and 11% better for 7- and 18-mm LYSO, respectively.

The dead-time count loss for singles with a line source embedded in a 200-mm diameter sphere as a function of activity concentration is shown in the left side of Fig. 5. On the right-hand side, this figure shows the relative improvement for each of

Fig. 5 The relative effects of dead-time on NEC for (a) LYSO and (b) LaBr₃. The left plots show dead-time loss as a function of activity concentration. The right plots show the improvement relative to the reference system.

Fig. 6 (a) Shows the effective NECR as a function of count rate. The combined effects of dead-time and TOF dramatically improve the effective performance of the system. (b) Shows the relative performance of LaBr₃ to LYSO for similar volumes of scintillator.

these systems using the ADB detector design. The left-hand side plots are for LYSO and the right-hand side plots are for LaBr₃. LaBr₃ has slightly better dead-time performance due to poorer photon detection.

The NEC rate (NECR) as a function of activity concentration for each of these systems is then estimated using Eqs. (6) and (10) to correct the SEC estimates due to the presence of random counts and dead-time. These results are shown in Fig. 6, where the upper plot shows the expected NECR as a function of

activity concentration in the line embedded in the sphere source geometry. The lower plot shows the relative performance of NECR for LaBr₃ to LYSO. Again, LaBr₃'s poorer photon detection results in reduced NECR relative to LYSO.

3.4 Estimation of Spatial Resolution

We estimated the spatial resolution with DOI information via Eq. (14) with the results given in Table 3. However, these results

Table 3 Analytically estimated spatial resolution of the BET, CYL, and WB PET systems at 75 mm from the central axis for several detector configurations.

	1 × 1 × 3 mm detectors	2 × 2 × 3 mm detectors	2 × 2 × 6 mm detectors
BET/CYL FWHM (mm)	1.07	1.37	1.86
WB PET FWHM (mm)	3.49 (LYSO with 25-mm-thick detectors)		

do not take detector scatter into account. The Compton contribution of spatial resolution loss was estimated via MC simulations and defined the count locations by the centroid of hits location and by the location of the hit with the highest energy. Using these two definitions, we separated the effective Compton counts by removing all lines-of-response, with zero offset from the source, and by using a back-to-back photon source to avoid positron range and noncollinearity effects. Note that while the locations of the hits with the maximum energy events resulted in higher resolution loss, they also had a much larger effective PE fraction indicating that more counts were binned correctly to the point-of-first-interaction. These effects, without DOI, can be seen in Fig. 7 and are listed in Table 4 using Eq. (13). This figure shows that the PE contribution is roughly 10-times the Compton contribution near the point-of-first-interaction. This is consistent with the observation that PSF of PET strongly deviates from normal at the tails of the distribution. This effect is seen in the measurement of the tenth-width at half-maximum (FWTM) when performing NEMA NU2 tests.

Using the convolution approach from Eq. (13), the MC-based detector scatter distribution in Fig. 7, and the percent

of events correctly binned (PE %, also from MC), we estimated the total resolution in terms of FWHM and FWTM. These are shown in Table 4 as two strategies for estimating the point-of-first-interaction: the location of the energy-weighted centroid and the location of the event with the maximum energy. The various count distributions we used in the estimates are shown in Fig. 8. The additional contribution of DOI (from Table 3) can be estimated via quadrature using Eq. (14).

4 Discussion

In the present work, we have shown preliminary results that provide insight into the performance envelopes of dedicated brain imaging PET systems and allow their comparison to equivalently modeled WB PET systems. Further, we compared the relative performance of two candidate scintillators (LYSO and LaBr₃) in these configurations to better understand their role in the performance trade-offs.

Our analytical estimate of the optimal lower energy window threshold for LYSO was within 4.9% of the MC predicted value: 467 keV estimated versus 445 keV obtained with MC. For LaBr₃, the analytical optimal lower energy window threshold estimate was within 2.1% of the MC predicted value: 495 keV estimated versus 485 keV obtained with MC. Our analytical estimates were likely larger than the MC estimates because we used a single scatter model, which would tend to steepen the scatter peak in the energy window due to spectrum hardening from the preferential absorption of the lower energy scatter photons. This would seemingly remove counts, but the analytic model relies on a reference SF that preserves total counts and thus lifts the, now more peaked, spectrum.

In terms of system sensitivity, LYSO has considerably better stopping power than LaBr₃, and hence, requires less scintillator thickness for equivalent detection efficiency. This is partially a

Fig. 7 (a) LYSO and (b) LaBr₃, and from left to right, the MC estimates of the centroid of hit locations (blue) and maximum energy hit locations (red) for BET, CYL, and WB PET system geometries, respectively. The red and blue curves are shifted by ± 5 mm for clarity. Note that the log-scale distorts the relative contribution of Compton scatter.

Table 4 Intradetector Compton scatter correction strategies for determination of interaction point listed with their effective PE fractions (the fraction of events correctly binned) and partial contribution to FWHM.

	BET			CYL			WB PET		
	FWHM (mm)	FWTM (mm)	PE (%)	FWHM (mm)	FWTM (mm)	PE (%)	FWHM (mm)	FWTM (mm)	PE (%)
LYSO									
Analytical estimate w/o Compton 1.3-mm FWHM									
Interaction via centroid	2.7	8.1	9.9	2.7	8.0	11	4.9	12.0	11
Interaction via max energy	1.6	4.5	52	1.5	4.5	53	3.1	13.4	35
LaBr ₃									
Analytical estimate w/o Compton 2.4-mm FWTM									
Interaction via centroid	3.2	11.9	6.6	3.2	11.1	7.6	6.8	17.4	6.6
Interaction via max energy	1.5	3.5	60	1.5	3.5	60	2.7	13.2	39

function of LYSO's higher density of 7.3 g/ml versus LaBr₃'s of 5.08 g/ml, but also because LYSO has more tightly bound K- and L-shell electrons greatly increasing PE absorption. This is seen in the mean-free-paths of 511-keV photons that are 11.52 and 22.24 mm for LYSO and LaBr₃, respectively. However, as discussed earlier, sensitivity is not sufficient for estimating real system performance as it does not consider the effects of scatter and random count contamination.

In this study, we used both SEC and NEC as our performance metrics as they are more informative of the quality of the collected counts than sensitivity. In particular, the use of SEC/mm for a line source embedded in a sphere shows the basic system performance for activity concentrated along a line, while avoiding the complications introduced by the singles rate and dead-time. This

provides a measurement of relative performance along the line source that can be substituted (in a limited way) for the Cramer–Rao variance lower bound¹⁵ without the need for a system matrix. That is, a uniform SEC/mm would be indicative of uniform image noise. However, unlike SEC, the Cramer–Rao variance lower bound provides an estimate of the variance of the unbiased maximum-likelihood estimate of the images,⁴¹ and if a system matrix is available, it is a better choice.

Using MC, with a spherical source (lower half of Table 2), the initial SEC relative performance of the systems shows that BET is ~1.4 and ~8 times better than CYL and WB, respectively, when TOF, dead-time, and random counts are not considered. The SEC results also provided estimates of the SFs of the various systems along with their singles to coincidence

Fig. 8 The various factors responsible for resolution loss including (a) nonlinearity, (b) positron range, (c) detector discretization, and (d) Compton scatter are shown normalized to one. The far right plots show the total PSF combined through convolution for (e) LYSO and (f) LaBr₃.

ratios. The SF measurements directly provide the correct scaling for the scatter counts in the analytical model and the singles to coincidence ratios provide the singles rate for both dead-time and random count estimation, which in turn allow the analytical estimation of the NECR with dead-time effects included.

In terms of SEC and NECR, LaBr₃'s improved energy resolution (3.3% versus 10.8% for LYSO, as modeled here) lowered the SF and improved the NECR. This allowed for a smaller energy window of 485 to 575 keV for LaBr₃ compared to 445- to 650-keV LYSO and produced smaller SFs, often less than half of LYSO's. In addition, LaBr₃ had slightly less dead-time than LYSO but given the one-to-one coupling of the detector element to the signal processing and SiPMs, this effect was small, and, in general, dead-time effects at typical patient activity concentrations for the ADA's and ADB's are small (<5% loss). Nonetheless, the resulting NEC estimates for LYSO were still almost double that of LaBr₃ for 25-mm-thick scintillators and 30% better equivalent mass LYSO. This is consistent with Eq. (3) that, for LaBr₃ to be a feasible candidate for a wearable PET brain (BET) system on the basis of equivalent volume, it must provide 30% better timing resolution than LYSO. Considering that some commercial PET systems now have 300-ps timing resolution, an LaBr₃ PET system must be at or below 200 ps to offer a useful advantage for a similar volume of crystal. Furthermore, recent results²⁷ show that state-of-the-art LYSO timing is already below 160 ps requiring LaBr₃ timing to be ~110 ps for similar performance given the same volume of crystal. We add that these levels of performance necessitate the use of layered crystals due to the speed of scintillation light transport within the scintillators themselves (e.g., 6 ps/mm).

Last, we modeled the spatial resolution, and in particular the contribution of Compton scatter of the detected events, to estimate the system's spatial resolution. As mentioned earlier, those photons captured via the PE process do not intrinsically contribute to resolution loss (neglecting photoelectron transport). Instead, it is discrete sampling that adds uncertainty to the detected photon's position. As a result, the PE events contribute strongly to the perceived resolution of the system and the FWHM of the measured PSF. Compton scatter, on the other hand, adds to the detection position uncertainty because the point-of-first-interaction information is lost (i.e., point-of-first-interaction requires subpicosecond timing within the detector block). MC allows us to both locate this point and to model feasible strategies for its estimation. The maximum energy deposition approach tended to correctly classify PE interaction position information but produced a slightly broader tail, while the energy-weighted centroid approach did poorly. In either case, these effects contribute to the broadening of the systems PSF as is shown in Table 4 and Fig. 8. From these, it is clear that the Compton events add to the systems FWTM, which is well known to depart from a normal distribution. In addition, Compton scattered photons can carry considerable energy from the point-of-first-interaction and can escape either the system or detector block, thereby reducing counting efficiency. Regardless, they effectively represent an additional mechanism for sensitivity loss. However, this was not modeled in this study.

5 Conclusions

This study is a preliminary investigation of the effects of geometry and scintillator material on the performance of a dedicated spherically shaped BET imaging camera. It shows that a spherical cap provides improved NEC while preserving spatial resolution when

compared to an equivalent dedicated cylindrical PET brain camera, and greatly improved PET performance relative to a conventional WB PET/CT. In addition, our simulations show that LYSO will generally outperform LaBr₃ for NEC unless the timing resolution is considerably smaller than 300 ps. Nonetheless, LaBr₃, despite its larger Compton scatter distribution, which can degrade the system PSF, has slightly better resolution performance relative to LYSO due to the tighter energy window. However, the larger Compton scatter distribution of LaBr₃ will allow more events to escape detector blocks and can contribute to count loss, though this was not evaluated in this study.

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