Sensitivity recovery for the AX-PET prototype using inter-crystal scattering events

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Abstract
The development of novel detection devices and systems such as the AX-positron emission tomography (PET) demonstrator often introduce or increase the measurement of atypical coincidence events such as inter-crystal scattering (ICS). In more standard systems, ICS events often go undetected and the small measured fraction may be ignored. As the measured quantity of such events in the data increases, so too does the importance of considering them during image reconstruction. Generally, treatment of ICS events will attempt to determine which of the possible candidate lines of response (LoRs) correctly determine the annihilation photon trajectory. However, methods of assessment often have low success rates or are computationally demanding. In this investigation alternative approaches are considered. Experimental data was taken using the AX-PET prototype and a NEMA phantom. Three methods of ICS treatment were assessed—each of which considered all possible candidate LoRs during image reconstruction. Maximum likelihood expectation maximization was used in conjunction with both standard (line-like) and novel (V-like in this investigation) detection responses modeled within the system matrix.

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The investigation assumed that no information other than interaction locations was available to distinguish between candidates, yet the methods assessed all provided means by which such information could be included. In all cases it was shown that the signal to noise ratio is increased using ICS events. However, only one method, which used full modeling of the ICS response in the system matrix—the V-like model—provided enhancement in all figures of merit assessed in this investigation. Finally, the optimal method of ICS incorporation was demonstrated using data from two small animals measured using the AX-PET demonstrator.

Keywords: positron emission tomography (PET), inter-crystal scattering, sensitivity

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(Some figures may appear in colour only in the online journal)

1. Introduction

Enhancement of spatial resolution can be of primary importance for emerging detection devices and imaging systems used in positron emission tomography (PET) (Pichler et al 2008). However, due to the Compton scattering cross-section at 511 keV for standard detection materials, in combination with photo-peak discrimination, there is often a trade-off between detector (and hence reconstructed image) resolution and system sensitivity.

It is common in PET to use a light-sharing detector-block approach (Cherry et al 2003). While multiplexing facilitates a reduction in electronic channels it can also obscure multiple interactions occurring over shared channels. Interactions arising from scattering between multiplexed elements are particularly problematic as the energy measurement is indistinguishable from a single photo-electric interaction. For a single electronic channel a photo-peak window is commonly used for discrimination of single measurements. As spatial resolution is increased (or light-sharing channels reduced) it is possible that the number of single measurements recorded will decrease. Events may be lost as photons interacting multiple times (terminating in photo-electric absorption) are less likely to be contained in small detection volumes (Shao et al 1996). Reducing the low-energy threshold regains these events—often single-Compton-scattering sequences—yet object scatter is no longer rejected by the acquisition system and image quality is reduced. However, measurements of multiple interactions of a single photon may have an energy sum that is within the standard photo-peak gate. Multiple interaction photon events (MIPE), or single-photon events consisting of two or more photon interactions (at least one Compton scattering and termination in photo-electric absorption) occur in all emission imaging systems (Gu et al 2010). When both interactions are measured in different scintillation crystals such events are termed inter crystal scattering (ICS) events. While for systems with low spatial resolution, or a high degree of light-sharing, MIPE may be indistinguishable from standard photo-electric absorption, in this investigation only measured ICS events will be considered. It is possible to reduce the number of ICS events which occur in a given system by increasing crystal size or spatially distancing small detection elements. Such ICS reduction techniques can lead to degraded resolution or sensitivity respectively. It is more common to simply discard ICS from measurement data before image reconstruction. Without the incorporation of ICS events, resolution enhancement may come at an expense to system sensitivity. In this investigation, the enhancement to PET image quality is investigated through the incorporation, during image reconstruction, of...
measured ICS events that would otherwise be discarded. The use of such ICS events provides a source of extra information without the need for extended scan time or increased activity.

Attempts have been made to regain those measurements that are generally lost to multiple interactions (Comanor et al 1996, Rafecas et al 2003, Pratx and Levin 2009, Miceli et al 2012, Clerk-Lamalice et al 2012). So far most approaches address the problem by attempting to choose the primary interactions from a probable ICS sequence. The first interaction for each annihilation photon will still accurately determine the end-points of the line of response (LoR). The LoR can then be used during image reconstruction in a standard algorithm—often, and in this investigation, maximum likelihood expectation maximization (MLEM). Unfortunately, approaches that attempt to identify the primary interaction do poorly with identification rates generally lower than 70% (Comanor et al 1996, Rafecas et al 2003). Increases in success rates require computationally expensive approaches (Michaud et al 2007, Pratx and Levin 2009, Champley et al 2011). However, in this investigation an alternative that instead attempts to more accurately model the system matrix is explored. List-mode MLEM reconstruction algorithms that calculate the elements of the system matrix on-the-fly allow modeling of more complicated detection probabilities, such as ICS, during image reconstruction. Matrix elements that represent ICS measurements can be composed from possible LoR candidates to more accurately represent the underlying detection response. An approach that attempts such enhanced system modeling was first proposed by us in Gillam et al (2012), where a preliminary study was conducted.

The system-matrix models studied in this investigation are fully described in section 2 as is the experimental apparatus, data discrimination, normalization protocols and quantitative measures used in this investigation. In section 3 experimental data taken using the AX-PET detector (Beltrame et al 2011) are quantified using measures based on the NEMA protocol. Finally, data obtained from small animal experiments are used in demonstration. Results are summarized and discussed in the final section.

2. Materials and methods
2.1. Inclusion of triple interaction measurements

While the methods outlined in this investigation may be applied to data of any multiplicity, here only triple measurements are considered for incorporation into the reconstructed image. Higher order measurements are expected to provide diminishing returns in terms of detection sensitivity (Solevi et al 2013). The measurement of each interaction provides a possible endpoint location for an LoR. For three time-coincident measurements—a triple interaction—there are three possible LoRs. However, interactions were further grouped into those that were expected to have been generated by a single incident photon—an ICS group. Grouping was defined by interactions occurring in a single head with an energy sum within the photo-peak. As the AX-PET prototype is a two head system triple interaction measurements with multiplicity [1, 2] or [2, 1] will provide only two candidate LoRs—the product of the multiplicity in each head.

For triple interaction measurements conforming to photo-peak discrimination, ambiguity exists as to which of the interactions in the ICS sequence is the initial interaction and hence represents the true LoR. Should it be possible to determine the initial interaction, triple measurements can be reduced to standard coincidence and included into a regular list-mode data set. Image reconstruction can then be conducted using the standard list-mode MLEM algorithm:

\[ n_{k+1}^j = \frac{n_k^j}{s_j} \sum_{i \in M} \frac{\alpha_{ij}}{\sum_{j'=0}^{M} \alpha_{ij'} n_{j'}^j} \]
Here $n^k_j$ is the value of voxel $j \in \{0 \ldots J\}$ at iteration $k$ and, for list-mode, the sum is over the full set of measurements $M$. The system-matrix elements given by $a_{ij}$ represent the probability that an emission from voxel $j$ is detected in measurement $i$ and $s_j$ is the sensitivity matrix (or simply normalization when the system matrix is not exact) given by $\sum_{j=0}^J a_{ij}$ for all possible measurements $I$. Generally, inclusion of ICS events into the MLEM algorithm requires an initial attempt to determine which of the two possible LoRs of the ICS pair is correct. While attempts to select the best candidate are never entirely successful two approaches are more common (Clerk-Lamalice et al 2012). For ICS measurement $i'$:

- **Separation** and incorporation (with weighting where appropriate) of each possible LoR into the data set

\[
\frac{a_{ij}'}{\sum_{j=0}^J a_{ij} n^k_j} = \frac{\eta_1 a_{ij}'}{\sum_{j=0}^J a_{ij} n^k_j} + \frac{\eta_2 a_{ij}'}{\sum_{j=0}^J a_{ij} n^k_j},
\]

and

- **Selection** and incorporation of only the most probable LoR,

\[
\frac{a_{ij}'}{\sum_{j=0}^J a_{ij} n^k_j} = \frac{a_{ij}'}{\sum_{j=0}^J a_{ij} n^k_j},
\]

where

\[t = \begin{cases} 1 & \text{if } \eta_1 > \eta_2 \\ 2 & \text{if } \eta_1 < \eta_2 \\ 1 \text{ or } 2 & \text{selected randomly otherwise.} \end{cases}\]

Here, $\eta_i$ is the probability that each possible LoR, $i_i$, is the correct alternative (in this investigation $t$ is either 1 or 2 as only two possible LoRs exist). In order to correctly calculate $\eta_i$, extensive simulations or analytically complicated models may be required (as found in Pratx and Levin (2009) or Champley et al (2011)). As selection is based only on a binary comparison, the exact value of $\eta_i$ is unimportant. Instead a simple discrimination metric may be used to select the single most likely alternative between the possible LoR candidates.

Selection using such a discrimination metric is the most common approach for incorporation of triple measurements into standard PET data streams (Rafecas et al 2003). Possible metrics used for discrimination in selection include simplistic values such as LoR length to more complicated measures that introduce extra information such as the measured energy (Pratx and Levin 2009, Rafecas et al 2003). Each approach has different levels of success dependent on detection geometry and resolution. In order that the selection criteria be kept simple yet without introducing extra measurement information, when conducted in this investigation the most probable LoR alternative was selected using the differential Klein–Nishina cross-section. The cross section was calculated using the geometrical scattering angle taken from interaction locations (Rafecas et al 2003). In the absence of extra information, $\eta_i$ may be taken to be 0.5 for both LoR candidates (an uninformativ—uniform or constant—distribution of $\eta_i$ values).

In all cases other than selection using the Klein–Nishina cross-section, an uninformative $\eta_i$ was assumed.

In the case of distributions of $\eta_i$ values with no discriminatory power selection is random. Separation has been shown to reduce system resolution (Solevi et al 2011). Here, where on-the-fly list-mode calculation of the system matrix is considered, two alternatives are proposed.

- **Randomized selection** for which selection is performed randomly at each iteration based on the $\eta_i$ distribution, and

- **Inclusion** of the full probability function relating to the measurement:

\[
\frac{a_{ij}'}{\sum_{j=0}^J a_{ij} n^k_j}, \quad \text{where } a_{ij} = \eta_1 a_{ij} + \eta_2 a_{ij},
\]
Neither separation nor selection attempt to determine the underlying detection response function of an ICS measurement. Each approach instead aims to enhance statistics by approximate binning or reassignment (separation and selection respectively) of triple measurement data into standard-data forms. Randomized selection attempts to rectify incorrect LoR identification by using different data at each iteration. While randomized selection is computationally less expensive than inclusion, each projection operation still only considers one LoR possibility. An ICS event is a different type of measurement which should be modeled as such. Inclusion composes a new row of the system matrix to represent the full ICS measurement—termed a V-projection due to its shape. The V-projection is composed from standard LoR elements but is considered separately from the constituent components. While more complicated approaches may be considered, the inclusion-based detection response attempts to model each triple measurement as a V-shaped projection and so generalizes the notion of an LoR to more accurately reflect the system-matrix probabilities.

2.1.1. Image reconstruction. Data were reconstructed using simulated one pass list-mode (SOPL) (Gillam et al 2013). SOPL is essentially a multi-ray algorithm, based on Siddon ray-tracing (Siddon 1985), using bootstrap Monte-Carlo sampling of detection uncertainty functions to generate new rays at each iteration. For all data each measurement is modeled using five rays per LoR candidate. With this approach to image reconstruction, the treatment of ICS measurements interacts with the computational burden as both separation and inclusion incur a computational penalty. Computational considerations are discussed in further depth with reference to obtained results in section 3.4.2.

2.2. Experimental

2.2.1. The AX-PET demonstrator. The AX-PET demonstrator (Beltrame et al 2011, Solevi et al 2013) is a system composed of two detection modules based on the AX-PET concept (Beltrame et al 2011, Bolle et al 2012) a schematic is shown in figure 1. Each module, or head, is composed of 48 axially oriented LYSO scintillation crystals of dimension $3 \times 3 \times 100$ mm$^3$ (six layers with eight crystals per layer). The crystal layers are interleaved with orthogonal wavelength shifting (WLS) plastic strips of dimension $0.9 \times 3 \times 40$ mm$^3$ with 26 strips per layer. For all elements light output was measured using Geiger-mode avalanche photo-diodes, also referred to as silicon photo multipliers (SiPMs). Signal measured from scintillation crystals provide a unique location in the trans-axial plane, while the axial depth is determined using the centroid taken from contiguous WLS signals (or clusters). Simultaneous measurement from one LYSO crystal and a cluster of WLS signals from the corresponding layer result in unambiguous three-dimensional localization of a photon interaction. While ambiguous measurements (multiple single-layer LYSO or WLS cluster signals) exist and are potentially useful (Hueso 2012) they are not considered in this investigation.

Each module provides continuous measurement along the axial coordinate and precise discretized measurement in the trans-axial plane (including radial depth of interaction). The staggered radial layers of the AX-PET are leveraged to increase both sensitivity and angular sampling, while long crystal dimensions provide high angular coverage, sensitivity and resolution in the axial domain. The two modules are located at a radius of 75 mm. For data acquisition—constituting one scan—the phantom stage was rotated in 20° steps—first over 180° with the modules face-to-face. Subsequently, one of the modules was offset by 20° in order to expand the imaging Field of View (FoV) and the phantom again rotated in 20° steps, this time over 360°. For each scan step the phantom stage was stationary for two minutes.
while acquiring data, and multiple scans—as many as were feasible—were conducted for each object.

Events are classed according to the number of distinguishable interactions that are measured in each of the two detector heads. A lower level trigger of 50 keV was applied at crystal level (Beltrame et al. 2011) and single crystal energy resolution was 11.8% (FWHM) at 511 keV (Bolle et al. 2012). The discrimination based on measured energy was applied to the sum of all 48 crystal measurements in each AX-PET head—the module level energy resolution was 12.8% (FWHM) at 511 keV (Bolle et al. 2012). Separate contributing measurements were recorded such that the multiplicity in each head was at least one and for which the energy sum was within the range 400–600 keV. Those interactions that produce only one unambiguous measurement in each head are considered ‘Golden’ events: the most informative PET measurements. Triple interactions are those for which there are three measurements in total (at least one measurement per head) with no event ambiguity. In order to ensure that interactions are distinguishable, multiple events in the same LYSO layer (likely to be ambiguous) were disallowed so that in this investigation ICS measurements have a minimum separation of 7 mm (between LYSO layers). Coincident spectra are shown in figure 2 as well as a histogram of interaction separation for ICS events taken from experimental data.

2.2.2. Sensitivity correction. The AX-PET prototype requires one and a half full rotations at 20° increments of the phantom stage for complete data acquisition—9 face-to-face and 18 head-offset steps. Data acquisition times are multiplied by the number of steps required, so

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Figure 1. The AX-PET prototype geometry. (a) shows a layout of a single AX-PET head with information regarding dimensions. (b) shows the rotational geometry used for the two head-positions (face-to-face and offset) and object rotation used to acquire data. (c) shows the two (face-to-face and oblique) sensitivity estimates to be weighted before addition. (d) shows the measurement geometry of a triple-event with multiplicity [1,2] and the incorrect LoR as a dotted line.

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6 One full scan required 70 min. Data were not acquired during phantom motion: 11 s between each 2 min step and 4–5 min when changing between face-to-face and oblique geometries.
that even for relatively short acquisition times (per head orientation) 70 min are required for a single scan and a number of hours may be needed to acquire a full data set. Long acquisition times lead to count differences at each step not solely due to phantom geometry—such as radio-isotope decay. The requirement for long acquisition times necessitated a large starting activity to ensure sufficient counts were still available for measurement in the final scans. Often the AX-PET paralysis-curve was traversed during measurement of a single data set. While such acquisition-based count-rate changes can be factored into the sensitivity or normalization correction, determination of the correct factors can still be difficult and without such correction, quantification can be problematic. A correction scheme based on the scanning protocol was developed for the prototype.

While radioactive decay can be corrected for in an analytical manner (given the half life of the isotope and the acquisition time at each orientation), dead-time effects are more problematic. For the AX-PET, the exact dead-time curve contains a mixture of both paralyzable and non-paralyzable effects and was observed to vary as a function of word-count (SiPM measurements) per head. Because the dead-time was difficult to analytically model—except in cases of simple known objects (Bolle et al 2012)—the count-rate curve was instead modeled empirically. The count-rate model was based on the acquisition of multiple scans that composed the full observation of each object. As each orientation was visited multiple times (separated by the full-scan period), multiple measurements at the same orientation allowed a time-count-curve to be independently fitted to each position.

After data acquisition the logarithm of the time-count curve for each position was corrected for radioactive decay and fitted using a least squares model to a second order polynomial. In the absence of extra information, the count-estimate at the final time-point (least affected by scanner dead-time) was then used as a base-line to determine correction coefficients. The correction coefficients for each position were averaged when multiple scans were used together. As this approach provides only approximate sensitivity correction, a subsequent empirical optimization was performed specifically for the NEMA phantom data under investigation. The estimation-points were regularly altered around the final time point to enhance uniformity in the known-uniform region.

In order to calculate the system sensitivity swiftly, an estimate is calculated for both the face-to-face and oblique detector geometry only at an object rotation of 0°, see figure 1(b). Subsequent rotation and weighting, based on phantom position and correction coefficients respectively, was applied to the single-position normalization arrays. Summation yielded an
Figure 3. The NEMA phantom used in this study was composed of three regions: a feature region with both hot (black) and cold water (white) features, a uniform region and a region composed of hot-rods of different diameter in a cold background. Rod features d1–d5 have diameter 1–5 mm, respectively.

estimate of the full system sensitivity. The single-position sensitivity estimates were calculated using the multiplication of two-dimensional trans-axial (see figure 1(c)) and axial (parallel to the long axis of the LYSO crystals) sensitivity matrices calculated independently (Gillam et al 2013). To account for finite detector size Gaussian filtering with a crystal-size kernel was applied to the resultant estimate.

2.2.3. Object measurements and quantification. For quantification, a Fluorine-18 filled NEMA (2008) phantom was employed. However, the standard air-filled cold void was replaced with a hot feature (with activity three times that of the uniform region) so that different contrast measures might be assessed. Using the NEMA phantom, seven full scans were measured in data acquisition. For analysis either all scans together or each of the short-time scans separately were used so that performance over statistics might be gauged. For qualitative demonstration using realistic tracer distributions two small animals, juvenile rats, were imaged using the same system—one using Fluorodeoxyglucose (FDG—six scans) and one Fluorine-18 (F18—nine scans). Both Golden and ICS events were drawn from the same initial data set so any enhancement provided by ICS is gained at a static activity level.

From measurements made using the NEMA phantom (see figure 3), images were reconstructed for 100 iterations of the SOPL LM-MLEM algorithm using an image space with voxel size 0.5 × 0.5 × 0.5 mm³. At each iteration a number of different measures from the NEMA 2008 protocol were calculated.

- The mean (μ_U) and standard deviation (σ_U) of the uniform region and the associated signal to noise ratio:
  \[ \text{SNR} = \frac{\mu_U}{\sigma_U}. \]
- The recovery coefficient of line profiles (LPs):
  \[ \text{RC} = \frac{\mu_{LP}}{\mu_U}. \]
- The fractional standard deviation of the RC
  \[ \sigma_{RC} = \sqrt{\left(\frac{\sigma_{LP}}{\mu_{LP}}\right)^2 + \left(\frac{\sigma_U}{\mu_U}\right)^2}, \] and
● The Spill Over Ratio using the water filled cold (C) void:

\[ SOR = \frac{\mu_C}{\mu_U} \]

where LP is the line profile along the maximum projected pixel in a rod-feature and \( U \) designates the uniform region. The standard deviation of the SOR is also used and was determined via summation in quadrature (as for the RC). In addition, two non-protocol measures were used in assessment.

● The contrast to noise ratio (CNR) between the hot feature or a background region and the uniform-region intensity where \( CNR = \frac{\mu_U - \mu_X}{\sigma_X} \), for which \( X \) is either of the cold (\( C \)), hot (\( H \)) or background (\( B \)) regions. The background region (\( B \)) was taken as a cylindrical annulus around, but not including the rod-features (which should contain zero activity).

● An estimate relating to the spatial resolution of the reconstructed image. The uniform region of the reconstructed image was summed axially and the radial average, from the center of the phantom, was taken using four fold pixel oversampling. The resulting profile represents the edge-spread function of the image at the full radius of the phantom. A Gaussian derivative of the edge-spread was subsequently calculated. As the line spread function may be estimated through differentiation of the edge-spread function (Cunningham and Fenster 1987), which here was radially averaged, the FWHM of the resulting distribution was considered as an estimate of the average spatial resolution.

For all measures except the estimate of spatial resolution standard errors were calculated for both \( \mu \) and \( \sigma \) values (Ahn and Fessler 2003) and propagated to estimate measurement uncertainty. For the spatial resolution the uncertainty was based upon the sample-width of the radial average.

3. Results and analysis

3.1. The NEMA phantom

In order to confirm that those events detected as ICS do indeed convey information, the triple events were initially reconstructed independently from Golden events using separation, selection and inclusion. All seven scans acquired were used for image reconstruction—results are shown in figure 4. For each case the phantom was reconstructed with varying degrees of success. As the ICS data alone produce reasonable images each approach should enhance the information provided by Golden data. For ICS-only data, non-uniform intensity was observed over the uniform region (see figure 4 central row) of the reconstructed image. The non-uniformity was understood to be due to sensitivity estimates, based on Golden events alone, when reconstruction was conducted with only ICS measurements. The effect is drastically reduced when Golden events are used in conjunction with ICS events (see figure 5), yet this initial result did indicate that the sensitivity estimation must be improved in future. Visually it was observed that the inclusion method provided estimates with lower noise properties than the other triples methods.

The RC and its error were measured at each fifth iteration over 100 iterations for each method of reconstruction using data from both ICS and Golden events. Line profiles taken from reconstructed images are shown in figure 5. The percentage uncertainty for the RC is shown plotted against the RC itself over all iterations in figure 6. Except for the 1 mm feature, at 100 iterations the RC has converged to a constant value in all cases (at around iteration 75), and further iterations simply increase noise. The inclusion approach closely matches the
Figure 4. Slices from reconstructed images using either Golden or ICS events. Three trans-axial slices through the NEMA phantom are shown illustrating the rod-features, uniform region and void-region. Three methods of ICS calculation are shown: separation, selection and inclusion. All images are normalized such that the sum is unity and axes show voxel-number (0.5 mm).

Table 1. SNR, SOR and STD_{SOR} shown at iteration 75.

| Measure       | Golden | Golden + sep. | Golden + sel.(KN) | Golden + sel.(Rand) | Golden + inc. |
|---------------|--------|---------------|-------------------|---------------------|---------------|
| SNR (uniform) | 12.7   | 13.1          | 12.6              | 13.1                | 13.3          |
|               | (0.3)  | (0.3)         | (0.3)             | (0.3)               | (0.3)         |
| SOR (cold)/10^{-3} | 89.8  | 114.8         | 114.0             | 114.6               | 82.9          |
|               | (0.6)  | (0.8)         | (0.7)             | (0.8)               | (0.5)         |
| STD_{SOR}/(%) | 21.5   | 20.1          | 19.3              | 20.2                | 19.3          |

RC results gained when using only Golden events. This would indicate that, as opposed to separation and selection, inclusion does not impact the rod recovery of the Golden only events.

The method of selection using the Klein–Nishina cross-section was shown to have no advantage over either separation or random selection using a uniform $\eta_t$ distribution and so was not considered further in this investigation. It was suspected that the performance of the Klein–Nishina measure used here was degraded by AX-PET measurement conditions and so offered little advantage in this application. The FWHM measure was found to be optimal at iteration 75 (approximately), while the SOR was continually decreasing over all 100 iterations, as seen in figure 6. The FWHM measure was observed to correlate to rod-feature recovery providing confidence in the approach as an approximate measure of image resolution. In table 1 the SOR and SNR are summarized at iteration 75. The SNR of the uniform region was improved for all ICS incorporation strategies, yet only the inclusion approach reduced
the SOR. For these measurements only ICS inclusion improved or retained image quality, compared to Golden-only reconstruction, for all figures of merit assessed.

3.2. Data separated by scan

Quantification of the NEMA phantom showed the enhancement provided by incorporation of ICS events during image reconstruction. Yet this enhancement may change as a function of data statistics. The data were acquired as a group of seven scans, so it was possible to reconstruct images from each scan separately. In doing so the inclusion of ICS measurements was assessed over multiple images, each using fewer events. The measured counts (both Golden and ICS) are shown as a function of scan number (time) in figure 7. The percentage of triples in the acquired data changes slightly (varying between 21.4% and 23.2%) as a function of scan number due to activity and dead-time effects. While increased statistics provided by ICS events may slow convergence, in this investigation reconstructed images were compared at the same iteration. Iteration 75 was selected for comparison because the images reconstructed using both Golden only and inclusion (using Golden and ICS data) had similar FWHM resolution values across all scans, as shown in figure 7.
Of all methods of ICS incorporation, only the method of inclusion enhanced the SOR without impact to image resolution (figure 7). The SNR was increased in the uniform region and the hot-feature CNR was enhanced for all ICS approaches compared to Golden-only images (figure 8). The measurement of SNR in the uniform region considers only voxels within that region. Should an incorrect LoR from an ICS pair be used in image reconstruction it will

Figure 6. Recovery Coefficient and standard deviation (%) over iteration—proceeding from left to right for all RC cases. Bottom-right: FWHM resolution as a function of SOR over iterations—proceeding from right to left. For all images iterations 5–100 are plotted at every fifth iteration. Images are reconstructed using both Golden and ICS events from all scans.

Figure 7. Counts per scan (~70 min per scan) are shown for both Golden and measured triple events, with the corresponding ICS fraction. The SOR and FWHM, measured at the 75th iteration are shown for each data scan using the NEMA phantom. Data were reconstructed using both Golden and ICS events. Uncertainties are based on the standard error.
effectively raise the image background and the resulting SNR measure would be artificially enhanced. However, this effect should not be observed in contrast measures that consider the background level of the reconstructed image. The greatest enhancement to SNR in the uniform region was obtained using selection or separation (figure 8). However, only inclusion provided enhancement to the background CNR while for both selection and separation this measure was degraded. While the approximate sensitivity estimate will effect the SNR of the uniform region more acutely than other measures it was not believed to be a dominant effect in these results (see supplementary data, available at stacks.iop.org/PMB/59/4065/mmedia).

3.3. Small animal images

Data acquired from small animals was reconstructed using both Golden-only and ICS-inclusion methods. In order to reduce errors arising from sensitivity estimation, only the last three scans of each animal were used and only radioactive decay accounted for in weighting (no dead-time fit was performed). Results are presented in figure 9 for the FDG study and figure 10 for that conducted using F18. In both studies, the relative proportions of ICS events to Golden events was similar to that observed in the phantom study (∼22.5%). Results from sections 3.1 and 3.2 indicate that with the inclusion of ICS events, statistical enhancement is expected to be around 5–10%. Such improvement is unlikely to be visually distinguishable in a single study. Visual observation of the reconstructed images indicated that image resolution was not degraded by inclusion of ICS data and a small noise reduction was perceptible in zero intensity regions of the image. For the F18 study, regions outside the animal (where zero intensity was expected) were used to measure the signal to noise ratio over axially oriented voxel-columns. An improvement in the signal to noise ratio of approximately 10% was observed in these regions when ICS events were incorporated (see figure 10 (right)), which agrees with previous results gained using phantom-data.

3.4. Application and computational considerations

3.4.1. Application to dose reduction. Minimizing scan time or dose can be of great importance in many imaging tasks. ICS represents enhanced sensitivity with minimal loss to resolution
Figure 9. Slices through images from the rat imaged using FDG (displaying the heart), reconstructed images are calculated for iteration 75 and volumes are normalized such that the sum is unity.

Table 2. NEMA figures of merit at iteration 75.

| Data set         | SNR  | SOR/(10^{-3}) (STD/%) | RC 1 mm (STD/%) | RC 3 mm (STD/%) | RC 5 mm (STD/%) |
|------------------|------|------------------------|-----------------|-----------------|-----------------|
| Golden           | 12.7 | 89.8                   | 0.28            | 1.03            | 1.00            |
| Golden+ inclusion (90%) | 12.9 | 83.5                   | 0.26            | 1.05            | 1.00            |
| Golden+ inclusion (19.3) | 13.3 | 82.9                   | 0.26            | 1.05            | 0.99            |
| Golden+ inclusion (17.2) | 13.3 | 82.9                   | 0.26            | 1.05            | 0.99            |
when using the inclusion approach. Rather than enhanced quantitative precision, it is possible to use ICS events to reduce either object activity or scan time whilst retaining the same image quality. As an approximation of reduced scan time the Golden+ICS data was re-sampled excluding every tenth measurement (31,583,937 Golden and 9177,364 ICS events were re-sampled to 28,424,884 Golden and 8260,287 ICS events). The re-sampled data was reconstructed and figures of merit (FoMs) calculated. Results are presented in Table 2. Inclusion of ICS data allow either enhanced FoMs or alternatively similar image quality to be achieved using fewer counts, simulating reduced scan time or activity.

3.4.2. Computational considerations. In list-mode where calculation of the system-matrix elements is conducted on-the-fly, both the separation and the inclusion method incur a penalty.
Selection (both standard and randomized) still only calculate the system-matrix elements for one LoR per measurement per iteration. Non-informative $\eta$ distributions did not require expensive calculations so that the selection approach did not increase the computational burden any more than an extra Golden event in the data stream. However, computation of both LoR possibilities, as is required in separation or inclusion, will consume twice the number of computations as that required by a Golden event alone. Clearly, selection of the correct LoR is preferable to separation as quantitative results are similar in both cases, yet selection requires less computing time. Inclusion improves the image quality yet at a computational cost.

Similarly to randomized selection, it is possible to consider randomized inclusion in order to reduce computation time. SOPL (Gillam et al 2013), the method used in this investigation to calculate elements of the system matrix, is a multi-ray algorithm for which rays are sampled randomly based on models of the detection uncertainty. In the inclusion method investigated, twice the number of rays were used for an ICS event because both LoR possibilities were calculated to the same precision. However, it is reasonable to base the Monte-Carlo generator on the full ICS measurement and sample the same number of rays regardless of measurement type. Results using five rays per measurement per iteration are displayed in figure 11.

From figure 11, by reducing the computational cost of calculation of the ICS system-matrix elements to that of Golden events the RC is reduced. At reconstruction time the optimal activity, scan time and approach to image reconstruction should be chosen considering computational resources and image quality requirements.
4. Discussion and future considerations

The triple measurement response estimated via inclusion is approximately twice as long in the image space as a regular LoR. The relative increase in length of the V-projection means that the SNR enhancement is less than expected for an additional Golden event. When using a distribution of $\eta_t$ values without discriminatory power, separation and selection improved the SNR of the uniform region, yet both increased image noise in cold regions or decreased image resolution. Separation and selection treat each ICS event more like an extra Golden event during image reconstruction. However, ICS events treated as Golden-like in this manner will have an increased false fraction with respect to standard events. The result was that both separation and selection saw a degradation of noise and resolution measures. Inclusion encoded both LoR possibilities into the system matrix, so that little degradation in the reconstructed image was observed. For advanced selection methods, $\eta_t$ values might be more sensitive yet this increase in information can as easily be encoded into the system-matrix elements using the inclusion approach.

Using inclusion, ICS events form a V-projection that can be used to represent the detection response in the system matrix, instead of the more standard LoR. Rather than separating the two possible LoRs represented by an ICS event for use in image reconstruction, the V-projection is a more natural representation which led to enhanced image quality in this investigation. By estimating the detection response using a V-projection SNR enhancement is still obtained (albeit at a lower level), while contrast and SOR values are improved and the recovery coefficient is unchanged. Triple ICS measurements represent, approximately, 20% of the full data set. However, a 5–10% enhancement in non-resolution metrics were observed. The enhancement might be considered in analogy to the extra information offered in time-of-flight...
(ToF) PET systems. In ToF PET the resolution is not expected to improve, yet the SNR should be enhanced in proportion to the square root of the reduction in LoR length achieved via temporal truncation inside the FoV (Budinger 1983). For ICS events with no information as to the correct LoR, the line length within the FoV is effectively doubled. The SNR enhancement provided by such events is expected to be less than if the extra statistics were composed of Golden events (or if \( \eta_t \) allows exact selection) by a factor \( \sim \sqrt{2} \) (following a similar reasoning as Budinger (1983)).

In addition to ICS triples, other sources of extra data also exist that may be addressed using similar techniques as outlined in this investigation. The requirement of distinguishability meant that multiple measurements in the same LYSO crystal or those inducing signals on the same WLS-strips were categorized separately as triples with missing information. Because of the extra ambiguity, triples with missing information and higher order multiplicity events were not considered. Additionally, triple measurements arising from the detection of an extra random photon in coincidence with true pair are possible. While such events will have an energy sum above the discrimination window they still contain a True LoR and so may be modeled using a V-projection. Finally, while the two head AX-PET prototype provided a sensitivity increase of 20% using ICS, this fraction is expected to increase in full-ring systems enhancing the effect of incorporation of these data. The enhancement to image quality may be weighed against computational burden for all additional measurements and each type assessed as an extra reservoir of data in any future investigations.

In studies using the NEMA phantom the normalization estimate of \( s_j \) was enhanced using the uniform region as a guide. The empirical approach was conducted so that all FoMs, which are dependent on the uniform region, were as accurate as possible. However, as a result of inexact sensitivity normalization, enhanced activity was observed at the center of the FoV. In addition, correction estimates used were based on only the Golden events from the system. However, in the AX-PET system paralysis effects are dependent on word-counts per head so that measurements of different multiplicities may involve different dead-time curves. While sensitivity normalization is under constant refinement for this prototype scanner, in this investigation it served to provide robust FoMs for quantification of any enhancement provided using ICS measurements.

Single-animal studies did not show great visual enhancement under incorporation of ICS using inclusion, yet the NEMA results would indicate ICS data will improve the quantitative precision of the reconstructed images. Data separated by scan provided information using multiple independent data sets. However, system-level studies across multiple acquisitions are required in order to assess the true imaging potential of ICS inclusion for image quality enhancement and dose or scan-time reduction.

5. Conclusion

This investigation concentrated on image quality enhancement by incorporation, during image reconstruction, of inter-crystal Scattering (ICS) data acquired simultaneously with standard coincidence measurements. For positron emission tomography (PET) systems capable of measuring multiple interactions of single photons, the measured data can incorporate large fractions of ICS events. While the morphology and abundance of ICS events will depend on system specifics such as geometry and detection material, in the case of the AX-PET prototype the ICS fraction was \( \sim 20\% \). For the AX-PET, the fraction is expected to increase in a full-ring implementation or when considering alternate multiplicities. Lack of consideration of ICS events during image reconstruction contributes to unnecessary sensitivity loss and subsequent
image quality reduction. ICS events were treated using a number of different approaches, separation, selection (using both a selection parameter and randomized) and inclusion were investigated. Each approach to ICS incorporation enhanced the SNR measured in the uniform region of the NEMA phantom. However, only the inclusion approach using V-projections did not measurably degrade the image resolution (compared to Golden only images) and in fact also provided reduction to the SOR. The enhancement offered by inclusion of ICS measurements was also demonstrated on two small animal data sets. Using the inclusion approach with triple interaction measurements the sensitivity enhancement in data was transformed to 5–10% enhancement to image quality measures with no measurable degradation to resolution metrics. Future studies will address multiple phantom/animal scenarios and alternate detection geometries.

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