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Monte Carlo Modeling of Cascade Gamma Rays in ^{86}Y PET imaging: Preliminary results

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Abstract

^{86}Y is a PET agent that could be used as an ideal surrogate to allow personalized dosimetry in ^{90}Y radionuclide therapy. However, ^{86}Y also emits cascade gamma rays. We have developed a Monte Carlo program based on SimSET to model cascade gamma rays in PET imaging. The new simulation was validated with the GATE simulation package. Agreements within 15% were found in spatial resolution, apparent scatter fraction (ratio of coincidences outside peak regions in line source sinograms), singles and coincidences statistics and detected photons energy distribution within the PET energy window. A 20% discrepancy was observed in the absolute scatter fraction, likely caused by differences in the tracking of higher-energy cascade gamma photons. On average the new simulation is 6 times faster than GATE, and the computing time can be further improved by using variance reduction techniques currently available in SimSET. Comparison with phantom acquisitions showed agreements in spatial resolutions and the general shape of projection profiles; however, the standard scatter correction method on the scanner is not directly applicable for ^{86}Y PET as it leads to incorrect scatter fractions. The new simulation was used to characterize ^{86}Y PET. Compared with conventional ^{18}F PET, in which major contamination at low count rates comes from scattered events, cascade gamma-involved events are more important in ^{86}Y PET. The two types of contaminations have completely different distribution patterns, which should be considered for the corrections of their effects. Our approach will be further improved in the future in the modeling of random coincidences and tracking of high energy photons, and simulation results will be used for the development of correction methods in ^{86}Y PET.

Keywords

Monte Carlo simulation; yttrium-86 PET; cascade gamma photons; SimSET; GATE

1. Introduction

Targeted radionuclide therapy (TRT) and radioimmunotherapy (RIT) are at the forefront of molecular cancer treatment modalities that involve the use of cancer cell targeting radiopharmaceuticals, such as radiolabeled antibodies, which selectively target certain tumor cells (Ghobrial et al 2004). ^{90}Y is a very promising isotope for internal radionuclide therapy, especially TRT where the linking of therapeutic radioligands with cell-specific carriers allows targeting of tumor cells without reaching the toxicity levels of traditional chemotherapy (Podoloff et al 2002). Patient-specific dosimetry based on personalized biodistribution information is essential in ^{90}Y radionuclide therapy for pre-therapeutic treatment planning and accurate absorbed dose estimation in individual patients. However, since ^{90}Y is a pure beta emitter, its biodistribution cannot be readily imaged. A chemically

identical surrogate, such as ^{86}Y , would be very desirable as a molecular imaging surrogate for ^{90}Y therapy.

PET imaging is usually performed with short-lived pure positron emitters, such as ^{18}F , ^{11}C or ^{15}O . Certain other radionuclides, such as ^{86}Y , ^{76}Br , ^{124}I and ^{66}Ga , are being explored for use in PET imaging because of their chemical properties and longer half-lives (Beattie et al 2003). However, in addition to positron emission and electron capture (EC), these radionuclides also emit prompt gamma rays that are in cascades with a positron or other gamma rays, which causes spurious activity in the images. Correction methods of spurious activity have been an area of active research recently (Beattie et al 2003, Walrand et al 2003, Pentlow et al 2000, Lubberink et al 2002, Buchholz et al 2003, Kull et al 2004, Bockisch et al 2006). In addition, cascade gamma rays also yield increased singles rates, which increase detector dead time and random coincidences rates. The relative importance of these factors depends on the decay scheme of each radionuclide.

A Monte-Carlo approach is very useful for characterizing the effects of cascade gamma rays in PET imaging for different radionuclides, and developing correction algorithms. GATE (the GEANT4 Application for Tomographic Emission) is a well validated simulation tool (Santin et al 2003) and has been used to characterize the impact of cascade gamma rays in ^{124}I and ^{86}Y imaging (Vandenberghe 2006). However, the simulation of complex phantoms with GATE is time consuming.

We have developed a Monte Carlo simulation program to model cascade gamma rays in PET imaging, based on the SimSET simulation package (University of Washington). SimSET (Simulation System for Emission Tomography) is a public-domain software package dedicated to performing flexible and efficient simulation of PET and SPECT imaging systems. We have modified the SimSET program to allow the modeling of PET imaging of radionuclides whose decay scheme involves cascade events. We validated the new simulation with GATE in terms of spatial resolution, sensitivity, scatter fractions, photon statistics and detected photon energy spectrum, and used the new simulation to characterize the effects of cascade events in ^{86}Y PET imaging.

2. Methods

2.1 Modeling cascade gamma rays in PET imaging

The SimSET program was modified to simulate cascade events in PET imaging. For each radionuclide, a decay scheme input file was built. The new simulation samples the decay scheme of the radionuclide, and generates then tracks all the cascade and/or annihilation gamma photons in a cascade. Once generated, a photon is tracked through the attenuation distribution, septa and detector crystal using original SimSET functions. The tracked photons can be binned separately according to the number of cascade photons involved in the coincidences.

In a decay event involving cascade gamma rays, the emission of two or more gamma rays in cascade, or the emission of one or more cascade gamma rays following a positron and its subsequent annihilation, all occur within a time interval much smaller than the coincidence window of a PET scanner. Therefore, it is possible that three or more photons from the same decay event reach the detector at the same time, while in conventional PET with pure positron emitters multiple coincidences are always a result of two separate decays. While multiple events are discarded in many scanners, a lossless strategy has been adopted in recent scanners to use information contained in such events. In our simulations, each multiple event with n accepted photons was decomposed into $n(n-1)/2$ sub-pairs, and all valid sub-pairs were binned.

2.2 Yttrium-86

The radionuclide ^{86}Y has a half-life of 14.74 hours, and decays by positron emission or electron capture (EC). The positron abundance of ^{86}Y is 32%. ^{86}Y has a very complex decay scheme. It has 20 β^+ decay lines and 28 EC decay lines, resulting in a large quantity of cascade gamma emissions. ^{86}Y has 104 gamma emissions, the total gamma abundance between 350 and 2000 keV (not including annihilation gamma emissions) is 305%. The complete decay scheme can be found in the on-line database of National Nuclear Data Center (Brookhaven National Laboratory) or ICRP Publication #38 (1983). The energy distribution of ^{86}Y gamma emissions is summarized in Table 1. In our study we modeled major gamma lines with energy between 350 and 2000 keV. Gamma lines with energy higher than 2000 keV were not modeled because of low interaction cross sections and low abundances. Pair production becomes possible for photons with energy higher than 1.02 MeV; however, its cross section is very small for photon energies lower than 2 MeV. Therefore, pair productions were not modeled in our simulations. A total of 38 cascade gamma lines were modeled in our simulations, the total gamma abundance modeled was 299.6%.

2.3 Validation with GATE

GATE, a well-validated simulation tool, was used to validate the newly developed SimSET-based program. Simulations with identical geometry and activity distributions were performed with GATE (version 4.0.0, Geant4 version 9.1) and SimSET. The results were compared in terms of spatial resolution, photon (singles and coincidences) statistics, scatter fraction, energy spectrum of detected photons, and computing time. A GE Discovery ST-E (DST-E) PET/CT scanner operated in 2-D mode was modeled in all the simulations. The DST-E scanner is composed of four block rings of BGO crystals. The total number of crystal rings is 24. Since block detectors are not modeled in the distributed SimSET package currently, the detectors were modeled as 4 continuous BGO crystal rings in both GATE and SimSET. In addition, block detectors were also modeled in GATE to evaluate the discrepancy caused by modeling block detectors as continuous rings. The energy window was 425 ~ 650 keV. In SimSET, simulations are performed in 3D. To simulate 2D PET, one needs to extract the required 2D dataset from the 3D output. To be consistent with the technical specifications of the DST-E scanner, 2D sinograms of 47 axial slices were extracted from 3D output dataset and re-binned with a maximum ring difference of 5 crystal rings. The numbers of transaxial and angular bins were 128 and 140, respectively. A very low activity level was simulated in GATE and random coincidences were not considered.

2.3.1 Spatial resolution—An ideal ^{86}Y line source was placed on the central axis of the scanner. Simulations with 3 million decays were performed. For each simulation, all the slices in the sinograms were summed first, and then all the angular bins were averaged, to generate a line-source response profile. The profiles were fitted with a Gaussian function and the full width at half maximum (FWHM) and full width at tenth maximum (FWTM) were compared (Vandenberghe 2006).

2.3.2 Scatter fraction—A cylindrical water-filled phantom with an ideal ^{86}Y line source 4.5 cm from the central axis was placed in the scanner. The phantom was 20 cm in diameter and 18 cm in height. Simulations with 3 million decays were performed. Valid coincidence events with or without scattered photons were scored separately. The scatter fraction was calculated by taking the ratio of coincidences involving at least one scattered photons over total coincidences. Apparent scatter fraction was also calculated from the sinograms. For each simulation, the 47 slices in the sinograms were summed first. For each projection angle within the summed sinogram, the location of the center of line source was determined by finding the pixel with the highest counts. Total counts in 4 pixels centered at the line source

position (2 pixels on each side, total 1.875 cm) were considered as true coincidences, while the remaining counts in the projection were considered as apparent scattered coincidences (which also include true coincidences involving cascade gamma rays). The scattered events contribution in the center area was relatively small and therefore ignored. The apparent scatter fraction was calculated by taking the ratio of apparent scattered coincidences and total events.

2.3.3 Photon statistics—A cylindrical water-filled flood phantom was placed on the central axis of the scanner. The phantom was 20 cm in diameter and 18 cm in height. Simulations with 3 million decays were performed and repeated for 3 times with different random seeds. Total valid coincidences, accepted singles and multiple coincidence events were scored in each simulation and averaged for repeated runs.

2.3.4 Energy spectrum of detected photons—The energy spectrum of all detected photons with energy between 200 keV and 2 MeV were scored for each simulation result from the above photon statistics evaluations. The general shape of the spectrum, as well as the total counts within the DST-E energy window and in two higher-energy regions, were compared.

2.3.5 Computing time—All the simulations were performed on a 32-core Beowulf computer cluster running Fedora Linux operating system and OSCAR cluster software. The computing (CPU) times of above simulations were compared between SimSET and GATE.

2.4 Characterization of ^{86}Y PET imaging

The newly developed simulation program was used to characterize PET imaging with ^{86}Y . Spatial resolution, scatter fraction and photon statistics were compared between ^{86}Y and ^{18}F PET, using the same methods as in the validations. One million decays were simulated in each run with ^{18}F so that the number of positron emissions was similar to that of ^{86}Y simulations. In addition, the line-source-in-water phantom used in scatter fraction evaluations was simulated again using the newly developed program with 300 million decays for ^{86}Y and 100 million decays for ^{18}F . Contributions from coincidences involving scattered and/or cascade photons were tallied for two energy windows: 425~650 keV (the default DST-E energy window) and 450~600 keV. The same phantom was simulated again in 3-D mode, with septa removed, and tallied for energy window 425~650 keV. The results were compared to that of 2-D mode in terms of percentages of coincidence events involving scattered and/or cascade gamma photons.

For the 2-D ^{86}Y simulations, sinogram components involving cascade and/or scattered photons were binned for energy window 425~650 keV and summed for all 47 slices. Projection profiles of 15 adjacent angular bins were averaged for 3 angular positions to observe the behavior of coincidences involving scattered and/or cascade photons.

2.5 Phantom acquisitions on GE DST-E scanner

A fillable cylindrical phantom with ports for line source inserts was used for physical acquisitions on the GE DST-E PET/CT scanner. The phantom was 20 cm in diameter, 16 cm in height, with line source ports parallel to the axis of the cylinder at radii of 0, 3, 5, 7 and 9 cm. A 16-cm long plastic tube with an inner diameter of 0.3 cm was filled with ^{18}F or ^{86}Y activity and used as the line source insert. Two acquisitions were taken at 2-D mode with each radionuclide: an empty (air-filled) phantom with line source at the center (hereby referred to as Air-0), or a water-filled phantom with the line source at the radius of 5 cm (hereby referred to as Water-5). The acquisition parameters are listed in Table 2. Raw sinogram files in the dimensions of 329 by 280 were obtained from the scanner.

The Air-0 acquisitions were used to evaluate the spatial resolution performance. For each radionuclide, after correcting for random coincidences, all 47 slices of sinograms were summed, and profiles of 5 adjacent angular bins were averaged to generate a line-source response profile. The profiles were fitted with a Gaussian function and the full width at half maximum (FWHM) and full width at tenth maximum (FWTM) were compared. The Water-5 acquisitions were used to evaluate apparent scatter fractions. The sinograms were corrected for random coincidences first, and then the apparent scatter fractions were evaluated with the same method as in the simulations (Section 2.3.2). To accommodate for the size of the actual line source and finer pixel grids in acquisitions, total counts in 6 pixels (1.36 cm) centered at the line source position were considered as true coincidences. In both simulations and acquisitions the central regions were inspected visually to ensure the widths of central regions were set appropriately. The evaluated apparent scatter fractions were compared with scanner reported scatter fractions. All four acquisitions were simulated using the newly developed program with 300 million decays for ^{86}Y and 100 million decays for ^{18}F . Spatial resolutions and apparent scatter fractions were evaluated in the same manner and compared with acquisition results. Coincidences and singles rates and block unit dead times were compared between the two radionuclides for both acquisitions.

For the Water-5 acquisitions, sinogram files were corrected for random coincidences only, or partially processed with randoms/deadtime/normalization/geometry corrections using standard methods on the scanner. All the 47 slices were then summed, and projection profiles of 15 adjacent angular bins were averaged for 2 angular positions to observe the behavior of coincidences involving scattered and/or cascade photons.

3. Results

3.1 Validation of new simulation program with GATE

In the results presented below, the following denotations were used:

GATE – ring: GATE simulations, ^{86}Y source, detectors modeled as 4 continuous rings.

GATE – block: GATE simulations, ^{86}Y source, block detectors modeled.

GATE – ring- ^{18}F : GATE simulations, ^{18}F source, detectors modeled as 4 continuous rings.

SimSET – ring: newly developed SimSET-based simulations, ^{86}Y source, detectors modeled as 4 continuous rings.

SimSET – ring- ^{18}F : newly developed SimSET-based simulations, ^{18}F source, detectors modeled as 4 continuous rings.

3.1.1 Spatial resolution—The FWHM and FWTM of the line source profile from GATE and SimSET simulations are listed in Table 3. When the detectors are modeled as continuous rings, the FWHM and FWTM of SimSET simulations are approximately 10% smaller than that in GATE simulations. A similar difference (~7%) exists for ^{18}F (i.e. the difference between original SimSET and GATE). When block detectors are modeled in GATE, the spatial resolution is slightly worse.

3.1.2 Scatter fractions—The simulated scatter fractions and apparent scatter fractions are shown in Table 4. For ^{86}Y , the scatter fraction from the new simulation is ~6% higher than in GATE simulations. The apparent scatter fraction estimated from sinograms, on the other hand, is 3% lower. In both simulations the scatter fraction in ^{86}Y PET is higher than in ^{18}F PET. The scatter fraction in GATE is slightly higher when block detectors are modeled.

3.1.3 Photon statistics—The scores of total coincidences, total singles and total multiple coincidences in the simulations of a flood phantom are shown in Table 5. The two simulations agree well with each other on the total number of singles. The new simulation scored for a higher number of total coincidences and a lower number of multiple coincidences. In GATE, when block detectors are modeled, a lower number of total coincidences and higher number of multiple coincidences were scored. The SimSET simulation agrees well with GATE on ^{18}F PET.

3.1.4 Energy spectra—The energy spectra of detected photons are plotted in Figure 1. The total counts in three energy windows are shown in Table 6, one is the GE DST-E energy window, and the other two are higher-energy windows around two gamma lines with relatively high abundances in the ^{86}Y decay scheme. When the detectors are simulated as continuous rings, the difference between SimSET and GATE simulated spectra is very small within the PET energy window of GE DST-E scanner (425 to 650 keV). The counts in higher-energy windows are 7% higher in the new simulation than in GATE. In GATE simulations, when block detectors are modeled, the counts are similar to GATE-ring within the DST-E energy window, but 14% lower in higher-energy windows.

3.1.5 Computing times—The computing times for the simulations of the three phantoms above are listed in Table 7. On average the new simulation is 5.7 times faster than GATE when the detectors are modeled as continuous crystal rings. The computing time can be further reduced if variance reduction options in SimSET are used.

3.2 Characterization of ^{86}Y PET imaging

As shown in Tables 3, 4 and 5, compared with conventional PET imaging with ^{18}F , ^{86}Y PET features similar spatial resolution, significantly higher scatter fraction and singles rates for the same number of positron emission events. Percentages of coincidences involving scattered and/or cascade photons of the line-source-in-water phantom are listed in Table 8. In ^{86}Y PET, approximately one third of all scattered coincidences involve annihilation photons only, and two thirds of scattered events involve cascade gamma photon(s). Approximately 80% cascade gamma-involving coincidences also involve at least one scattered photons. The overall contamination events fraction (38.7%) is significantly higher than in conventional ^{18}F PET (15%). Both scatter and cascade fractions are higher in 3-D mode. The contamination events fractions can be partially reduced by using a narrower energy window.

The component sinogram profiles of the line-source-in-water phantom of summed slices are shown in Figure 2. In the plots, the scattered events include coincidences between two annihilation photons, at least one of which has been scattered before reaching the detector. These are equivalent to scattered events distributions in conventional ^{18}F PET. The cascade events include coincidences involving at least one cascade photon, regardless of the scattering history of both photons. These are the additional contaminations caused by cascade gamma rays. Since GATE does not label the origin of detected photons, the cascade gamma-involved events cannot be readily distinguished from others. Therefore, only the overall profiles were plotted to be compared with that of the new simulations. The scales were adjusted to optimally display the shapes of profiles outside the peak regions. The results showed that the overall sinogram profiles of the new simulation agreed well with that of GATE. While the distribution of scattered events was centered toward the peak, as in conventional ^{18}F PET (Bergstrom et al 1983), the distribution of cascade gamma-involving events suggested a shallow, slow-changing parabolic shape with higher counts toward the edge of the field of view (FOV).

3.3 Phantom acquisitions with GE DST-E PET/CT scanner

The FWHM and FWTM of Air-0 line source profiles are listed in Table 9. The acquisition and simulation results agree within 10%. The difference between ^{18}F and ^{86}Y resolutions is slightly larger in acquisitions than in simulations. The scatter fractions and apparent scatter fractions are shown in Table 10. For ^{18}F , where simulations were performed using the original SimSET program, simulated scatter fraction was lower than scanner reported scatter fraction, which is because some features of the scanner, such as patient couch, detector/collimator casings, etc, were not modeled in the simulations. The scanner reported scatter fraction for ^{86}Y , however, was significantly lower than in simulations, and even lower than that of ^{18}F , which is obviously incorrect. This indicated that conventional scatter correction methods cannot be directly applied when cascade gamma photons exist. In both simulations and acquisitions, the apparent scatter fraction of ^{86}Y was approximately 3 times that of ^{18}F .

The singles and coincidences counts of the four acquisitions are shown in Table 11. Although the positron emission fraction of ^{86}Y is only 32% that of ^{18}F , the total gamma emission rate is ~ 3.5 times higher, therefore the singles rates (per mCi per minute) is 3.76 and 4.81 times higher for Air-0 and Water-5, respectively. The high singles rates in ^{86}Y PET will result in larger detector dead time and higher random coincidence rates. The coincidence rates for ^{86}Y were also higher than ^{18}F , caused by high random rates (29.3% for Air-0- ^{86}Y and 39.8% for Water-5- ^{86}Y) and contamination coincidences involving cascade gamma rays. When a scattering medium such as water is present, higher energy gamma photons of ^{86}Y have a better chance to be down scattered into the PET energy window, therefore both the singles and coincidences rates are less reduced compared to ^{18}F .

The sinogram profiles of Water-5 acquisitions are shown in Figure 3. The scales were adjusted to optimally display the shapes of profiles outside the peak regions. The general shapes of overall ^{86}Y projection profiles agree with simulated profiles shown in Figure 2. The partially processed profiles were processed for all the standard corrections available on the scanner except for scatter and attenuation corrections. Random coincidences were corrected with delayed events subtraction method. Similar results (not shown here) were obtained when the randoms were corrected by singles. We can see that coincidences involving cascade gamma rays in ^{86}Y PET cannot be corrected by conventional randoms correction. Furthermore, its distributions toward the edges of FOV were magnified by subsequent deadtime/normalization/geometry corrections, which will greatly affect the accuracy of conventional model-based scatter corrections and image quantitations thereafter.

4. Discussions

Characterizing the effects of cascade γ rays in ^{86}Y PET imaging is crucial for images quantitation and potential radiation dosimetry with ^{90}Y . In this work, we developed a simulation program based on SimSET to model cascade gamma rays in PET imaging. The simulation samples the decay scheme of the radionuclide, and generates and tracks all the cascade and/or annihilation gamma photons in a cascade. The generated photons are tracked using original SimSET functions. This work is an extension of the SimSET simulation package without modifications of the photon tracking and physics implementations in the original program. The program can be easily extended to the PET imaging of other cascade gamma-emitting radionuclides by providing different decay scheme input files.

We compared our simulations with the well-validated GATE simulation package. We have found that in general, the new program agrees well with GATE (mostly within 15%) in terms of spatial resolution, apparent scatter fraction, singles and coincidences statistics and detected photons energy distribution within the PET energy window. A larger discrepancy ($\sim 20\%$) was observed in the absolute scatter fraction. Since the simulated scatter fractions

of ^{18}F agreed with each other, this discrepancy was likely caused by differences in the tracking of higher-energy cascade gamma photons. A comparison of detected photons energy spectra revealed that for identical simulation parameters, the SimSET counts are lower than GATE counts at low photon energies and higher at high photon energies, indicating in the new simulations less high-energy photons are down-scattered toward lower energies compared with in GATE simulations. In the simulations of a ^{86}Y line in a water cylinder, the overall shape of sinogram profiles agreed well between the two simulations. On average the new simulation is 5.7 times faster than GATE, and the computing time can be further improved by using variance reduction techniques currently available in SimSET.

The modeling of block detectors in SimSET was under development (Harrison et al 2006, 2008) but not included in the distributed package at the time this work was conducted; therefore block detectors were not simulated in our new simulation. We compared two scenarios in GATE simulations: the detectors were either modeled as block detectors, or continuous crystal rings. Similar spatial resolution, scatter fraction and photon/coincidence statistics were found between these two scenarios. When the block detectors were modeled, the apparent scatter fraction in ^{86}Y was slightly (~8%) higher. Also, in the detected photons energy spectrum, the counts are lower at high photon energies and higher at low photon energies, indicating more high energy photons are down-scattered when block detectors are modeled. From our comparison, reasonable results within PET energy window can be obtained when block detectors are modeled as continuous crystal rings, but the modeling of higher-energy cascade gamma photons can be improved if block detectors are modeled.

In our simulations of a simple line-source-in-water phantom in 2-D mode and with the default DST-E energy window, the count rate of total cascade-involving events was 2.62 times that of pure scattered events. In addition, the distributions of these two types of contamination events are very different from each other. While the distributions of scattered events were highest around the positions of peak activities and decreasing fast toward the edge of the scattering medium, the distributions of cascade gamma-involving events were more uniform at the center and slightly increased toward the edges of FOV. With the source activity at the center of FOV, the elevation of sinogram tails at the edges is likely a geometric effect. Assuming cascade photons are uniformly detected in all the crystals, pixels near the edges of FOV are facing the crystals at an angle, therefore seeing slightly larger regions of the detector. When the source activity was off-centered, the elevation was higher on the side nearest to the line source, likely caused by higher cascade gamma photon detection rates in crystals closer to the source activity. The elevated sinogram tails of ^{86}Y PET were also observed in phantom acquisitions. The difference in the distribution patterns of scattered and cascade-involving events should be considered for the corrections of their effects.

We also compared some of our simulation results with phantom acquisitions on the GE DST-E scanner. The general shapes of overall projection profiles in our acquisitions agreed with that of simulation. The spatial resolutions also agreed within 10%. In both simulations and acquisitions, the apparent scatter fraction of ^{86}Y was approximately 3 times that of ^{18}F . We also found that coincidences caused by cascade gamma photons cannot be corrected by standard correction methods used on the scanner when directly applied to ^{86}Y PET. Furthermore, contaminations at the edge of FOV were greatly elevated, likely caused by geometry corrections. The model-based scatter correction methods used by many commercial PET scanners use sinogram tails information. With corrupted sinogram tails, the scanner reported an incorrect scatter fraction which was even lower than that of ^{18}F . For accurate image quantitation, cascade gamma-involving events would require normalization different from those for true or scattered events. If the scattered and cascade-involving events are to be corrected separately, preferably the cascade gamma-involving events should

be corrected before scatter corrections and other standard corrections. Both contamination components were reduced when a narrower energy windows was used, indicating energy information could be used for the correction of these events.

5. Future work

We have shown that our new program can reasonably simulate the effects caused by cascade gamma rays in ^{86}Y PET. In the future, we plan to further improve the simulation of high-energy cascade photons by improving the implementation of photon tracking physics and by modeling block detectors. Because of high singles rates, random coincidences are more important in ^{86}Y PET than in conventional ^{18}F PET. On April 22, 2009, a new version of SimSET (Version 2.9) was released which provides three major new features for PET simulations: block detectors, random coincidence modeling, and time-of-flight binning (University of Washington 2009). We will expend our program to include these features in the future. Correction methods for scattered and/or cascade events will be investigated based on simulation results.

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References

- Beattie BJ, Finn RD, Rowland DJ, Pentlow KS. Quantitative imaging of bromine-76 and yttrium-86 with PET: a method for the removal of spurious activity introduced by cascade gamma rays. *Med. Phys.* 2003; 30:2410–2423. [PubMed: 14528963]
- Bergstrom M, Eriksson L, Bohm C, Blomqvist G, Litton J. Correction for scattered radiation in a ring detector positron camera by integral transformation of the projections. *J. Comput. Assist. Tomogr.* 1983; 7:42–50. [PubMed: 6600755]
- Bockisch A, Freudenberg L, Rosenbaum S, Jentzen W. ^{124}I in PET imaging: impact on quantification, radiopharmaceutical development and distribution. *Eur. J. Nucl. Med. Mol. Imaging.* 2006; 33:1247–1248. [PubMed: 16909225]
- Brookhaven National Laboratory. National Nuclear Data Center Nudat2: <http://www.nndc.bnl.gov/nudat2/>.
- Buchholz HG, Herzog H, Foster GJ, Reber H, Nickel O, Rosch F, Bartenstein P. PET imaging with Yttrium-86: comparison of phantom measurements acquired with different PET scanners before and after applying background subtraction. *Eur. J. Nucl. Med. Mol. Imaging.* 2003; 30:716–720. [PubMed: 12605273]
- Ghobrial I, Witzig T. Radioimmunotherapy: a new treatment modality for B-cell non-Hodgkin's lymphoma. *Oncology (Williston Park).* 2004; 18:623–630. [PubMed: 15209190]
- Harrison, RL.; Gillispie, SB.; Lewellen, TK. Design and implementation of a block detector simulation in SimSET; IEEE Nuclear Science Symposium Conf. Record; 2006. p. 3151-3153.
- Harrison RL, Gillispie SB, Schmitz R, Lewellen TK. Modeling block detectors in SimSET. *J. Nucl. Med.* 2008; 49 Supplement 1:410P.
- International Commission on Radiological Protection (ICRP). Radionuclide Transformations: Energy and Intensity of Emissions ICRP Publication #38. New York: Pergamon Press; 1983.
- Kull T, Ruckgaber J, Weller R, Reske S, Glatting G. Quantitative imaging of yttrium-86 PET with the ECAT EXACT HR+ in 2D mode. *Cancer Biother. Radiopharm.* 2004; 19:482–490. [PubMed: 15453963]
- Lubberink M, Schneider H, Bergstrom M, Lundqvist H. Quantitative imaging and correction for cascade gamma radiation of ^{76}Br with 2D and 3D PET. *Phys. Med. Biol.* 2002; 47:3519–3534. [PubMed: 12408479]

- Pentlow KS, Finn RD, Larson SM, Erdi YE, Beattie BJ, Humm JL. Quantitative Imaging of Yttrium-86 with PET: The Occurrence and Correction of Anomalous Apparent Activity in High Density Regions. *Clinical Positron Imaging*. 2000; 3:85–90. [PubMed: 11008097]
- Podoloff DA. Diagnostic and therapeutic applications of radiolabeled Somatostatin analogs: current status in an oncology center. *Current Pharm. Des.* 2002; 8:1809–1814.
- Santin G, Strul D, Lazaro D, Simon L, Krieguer M. GATE: A Geant4-based simulation platform for PET and SPECT integrating movement and time management. *IEEE Trans. Nucl. Sci.* 2003; 50:1516–1521.
- University of Washington. SimSET: http://depts.washington.edu/~simset/html/simset_main.html.
- Vandenberghe S. Three-dimensional positron emission tomography imaging with ^{124}I and ^{86}Y . *Nuclear Medicine Communications*. 2006; 27:237–245. [PubMed: 16479243]
- Walrand S, Jamar F, Mathieu I, Camps J, Lonneux M, Sibomana M, Labar D, Michel C, Pauwels S. Quantitation in PET using isotopes emitting prompt single gammas: application to yttrium-86. *Eur. J. Nucl. Med.* 2003; 30:354–361.

Figure 1.
Energy spectra of detected photons from ^{86}Y flood phantom simulations

Figure 2.

Sinogram projection profiles of a ^{86}Y line source in a water phantom. The scattered events include coincidences between two annihilation photons, at least one of which has been scattered before reaching the detector. These are equivalent to scattered events distributions in conventional ^{18}F PET. The cascade events include coincidences involving at least one cascade photon, regardless of the scattering history of both photons.

Figure 3.

Sinogram projection profiles from line source phantom acquisitions. In the “randoms corrected” profiles, random coincidences were corrected with the delayed events subtraction method. In the “partially processed” profiles, standard methods for randoms/deadtime/normalization/geometry corrections available on the scanner were applied to the sinograms.

Table 1Energy distribution of ^{86}Y gamma emissions

Energy range	<350 keV	350~650 keV	650~1000 keV	1000~2000 keV	>2000 keV	Total
Total abundance	8.784%	79.496%+64.0%	56.35%	168.911%	5.333%	382.9%

Table 2

Acquisition parameters of phantom studies

Acquisition	Air-0- ¹⁸ F	Water-5- ¹⁸ F	Air-0- ⁸⁶ Y	Water-5- ⁸⁶ Y
Nuclide	¹⁸ F	¹⁸ F	⁸⁶ Y	⁸⁶ Y
Starting activity (mCi)	5.93	9.05	1.91	1.99
Acquisition time (min)	3.0	6.0	8.0	15.0

Table 3

Line source spatial resolution results

	GATE-ring	GATE-block	GATE-ring- ¹⁸ F	SimSET-ring	SimSET-ring- ¹⁸ F
FWHM (mm)	5.87	6.06	5.69	5.25	5.28
FWTM (mm)	10.69	11.05	10.38	9.57	9.62

Table 4

Scatter fractions of a line source in a water phantom

	GATE-ring	GATE-block	GATE-ring- ¹⁸ F	SimSET-ring	SimSET-ring- ¹⁸ F
Scatter fraction	26.6%	26.9%	15.2%	32.9%	14.3%
Apparent scatter fraction	40.6%	43.8%	12.5%	36.9%	13.3%

Table 5

Photon statistics of a flood phantom

	GATE-ring	GATE-block	GATE-ring- ¹⁸ F	SimSET-ring	SimSET-ring- ¹⁸ F
Total coincidences	3354 ± 43	2944 ± 26	2694 ± 23	3704 ± 73	2666 ± 24
Total singles	205354 ± 345	201454 ± 294	62967 ± 96	203639 ± 582	63354 ± 128
Total multiples	306 ± 21	387 ± 17		212 ± 12	

Table 6

Coincident counts in 3 energy windows in Figure 1.

Energy window, keV	GATE-ring	GATE-block	SimSET-ring
425–650	213637	209517	211588
955–1265	124898	108758	132944
1755–1985	27028	22547	30850

Table 7

Computing (CPU) times of simulations

	GATE-ring (s)	GATE-block (s)	SimSET-ring (s)	GATE/SimSET
Phantom 1	1849	2047	296	6.25
Phantom 2	1738	1882	328	5.30
Phantom 3	1744	1833	311	5.61
Average				5.72

Table 8

Percentage of coincidences involving scattered and/or cascade photons

Simulation	Energy window (keV)	%scatters	% cascades	%pure scatters	%pure cascades	%scattered cascades	% overall contamination
2D-W- ⁸⁶ Y	425–650	33.0%	28.0%	10.7%	5.7%	22.3%	38.7%
2D-N- ⁸⁶ Y	450–600	24.8%	18.0%	10.4%	3.5%	14.5%	28.4%
3D-W- ⁸⁶ Y	425–650	45.8%	40.6%	16.9%	11.7%	28.9%	57.5%
3D-N- ⁸⁶ Y	450–600	38.0%	28.3%	17.5%	7.7%	20.6%	45.8%
2D-W- ¹⁸ F	425–650	15.0%		15.0%			15.0%

% scatters: events involving scattered photon(s) regardless of photon origins

%cascades: events involving cascade photon(s) regardless of scattering histories

%pure scatters: events between two annihilation photons, one or both being scattered

%pure cascades: events between two un-scattered photons, one or both with a cascade photon origin

%scattered cascades: events involving at least one scattered cascade photon

%overall contamination: events involving at least one scattered or cascade photon

Table 9

Line source spatial resolutions of phantom acquisitions

	Air-0-¹⁸F	Air-0-⁸⁶Y	SimSET Air-0-¹⁸F	SimSET Air-0-⁸⁶Y
FWHM (mm)	5.56	6.06	5.90	5.91
FWTM (mm)	10.34	11.23	10.80	10.82

Table 10

Scatter fractions of phantom acquisitions

	Water-5-¹⁸F	Water-5-⁸⁶Y	SimSET Water-5-¹⁸F	SimSET Water-5-⁸⁶Y
Scanner reported scatter fraction	23.12%	12.96%		
Simulated scatter fraction			13.98%	33.6%
Apparent scatter fraction	21.70%	69.30%	11.38%	36.75%

Table 11

Singles and coincidences counts in phantom acquisitions

Acquisition	Air-0- ¹⁸ F	Air-0- ⁸⁶ Y	Water-5- ¹⁸ F	Water-5- ⁸⁶ Y
Total singles, $\times 10^9$	1.12	3.61	2.05	5.43
Singles/(mCi*min), $\times 10^7$	6.27	23.6	3.78	18.2
Total coincidences, $\times 10^7$	9.21	12.3	7.30	10.5
Coincidences/(mCi*min), $\times 10^6$	5.17	8.04	1.34	3.51