Practical reconstruction protocol for quantitative ^{90}Y bremsstrahlung SPECT/CT

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Purpose: To develop a practical background compensation (BC) technique to improve quantitative ^{90}Y -bremsstrahlung single-photon emission computed tomography (SPECT)/computed tomography (CT) using a commercially available imaging system.

Methods: All images were acquired using medium-energy collimation in six energy windows (EWs), ranging from 70 to 410 keV. The EWs were determined based on the signal-to-background ratio in planar images of an acrylic phantom of different thicknesses (2–16 cm) positioned below a ^{90}Y source and set at different distances (15–35 cm) from a gamma camera. The authors adapted the widely used EW-based scatter-correction technique by modeling the BC as scaled images. The BC EW was determined empirically in SPECT/CT studies using an IEC phantom based on the sphere activity recovery and residual activity in the cold lung insert. The scaling factor was calculated from 20 clinical planar ^{90}Y images. Reconstruction parameters were optimized in the same SPECT images for improved image quantification and contrast. A count-to-activity calibration factor was calculated from 30 clinical ^{90}Y images.

Results: The authors found that the most appropriate imaging EW range was 90–125 keV. BC was modeled as $0.53\times$ images in the EW of 310–410 keV. The background-compensated clinical images had higher image contrast than uncompensated images. The maximum deviation of their SPECT calibration in clinical studies was lowest ($<10\%$) for SPECT with attenuation correction (AC) and SPECT with AC + BC. Using the proposed SPECT-with-AC + BC reconstruction protocol, the authors found that the recovery coefficient of a 37-mm sphere (in a 10-mm volume of interest) increased from 39% to 90% and that the residual activity in the lung insert decreased from 44% to 14% over that of SPECT images with AC alone.

Conclusions: The proposed EW-based BC model was developed for ^{90}Y bremsstrahlung imaging. SPECT with AC + BC gave improved lesion detectability and activity quantification compared to SPECT with AC only. The proposed methodology can readily be used to tailor ^{90}Y SPECT/CT acquisition and reconstruction protocols with different SPECT/CT systems for quantification and improved image quality in clinical settings. © 2016 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4960629>]

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1. INTRODUCTION

Yttrium-90 microsphere therapies are used in the management of unresectable primary and metastatic liver cancers.^{1,2} In treatment planning, the radiopharmaceutical macroaggregated albumin ($^{99\text{m}}\text{Tc}$ -MAA) is used as a surrogate for ^{90}Y microspheres. First, planar imaging is used to determine the lung shunt fraction, which is incorporated into the dosimetry calculation to prevent radiation pneumonitis from ^{90}Y therapy. Next, single-photon emission computed tomography (SPECT)/computed tomography (CT) imaging is used to determine whether there is extrahepatic uptake of the $^{99\text{m}}\text{Tc}$ -MAA and adequate perfusion of the target lesions. However, several studies have shown that the distribution of $^{99\text{m}}\text{Tc}$ -MAA prior to treatment may not be a consistent and reliable indicator of the post-treatment distribution of the ^{90}Y -microspheres.^{3,4} These potential discrepancies in distribution between planning $^{99\text{m}}\text{Tc}$ -MAA and treatment ^{90}Y -microspheres support the need

for post-treatment ^{90}Y imaging to assess treatment delivery. However, bremsstrahlung ^{90}Y imaging is challenging.

In contrast with the majority of the radionuclides used in nuclear medicine imaging, ^{90}Y is effectively a pure beta emitter, i.e., it lacks discrete-energy photon emissions, such as gamma rays and/or characteristic fluorescence x-rays. The x-ray photons emitted by ^{90}Y are very low in both yield ($\ll 1$ ppm) and energy ($\ll 18$ keV), and the gamma photons emitted by ^{90}Y have an insignificant yield ($\ll 1$ ppm) and very high energy (~ 2 MeV). Yttrium-90 activity distribution *in vivo* is traditionally assessed by imaging the bremsstrahlung photon, which is produced from interactions of energetic beta particles with soft tissue, using planar and/or SPECT/CT imaging.

Yttrium-90's lack of photopeaks has stunted standardization of ^{90}Y bremsstrahlung imaging procedures; consequently, image quality varies widely amongst different facilities. The ^{90}Y decay process also has a very small branching to the excited state of stable ^{90}Zr , which is followed by an internal

pair production (32 ppm/ β^- decay).⁵ The positrons generate a pair of 511-keV annihilation photons that can be imaged using ^{90}Y positron emission tomography (PET)/CT. Recent studies have suggested that ^{90}Y PET/CT imaging provides better image quality (contrast and resolution) and quantification than bremsstrahlung SPECT/CT.^{6,7} Preliminary results of studies of tumor dosimetry, treatment response, and toxicity based on quantitative ^{90}Y PET/CT and ^{90}Y SPECT/CT post-therapy imaging have been presented.^{8–10} However, at present, there is no well-established standardized imaging protocol for ^{90}Y imaging *in vivo* with either SPECT/CT or PET/CT.

In contrast to the imaging of gamma or x-ray emitters where the spatial information of the object is carried by photons with a discrete energy, bremsstrahlung imaging's object spatial information is carried by photons with a continuous energy distribution. In discrete energy photopeak imaging, the imaging energy window (EW) is defined such that it accepts most of the primary photon emission while rejecting most of the scatter. The EW is usually centered on the photopeak and its extend (width) is governed by the energy resolution of the gamma camera; however, the continuous nature of ^{90}Y photon emissions prohibit such straightforward approach. Simulation work^{11,12} has shown that a typical ^{90}Y bremsstrahlung emission spectrum from ^{90}Y activity in the liver can be expressed as the sum of five spectral components: primary bremsstrahlung, object scatter, camera backscatter, collimator scatter and penetration, and lead x-rays produced in the collimator. At any given EW, the ratio of primary bremsstrahlung to the total number of photons detected is <15%, with the highest primary fraction around 80–180 keV.^{11–13}

Research on improving ^{90}Y bremsstrahlung imaging both qualitatively and quantitatively is ongoing, but most of the published solutions require some sort of Monte Carlo simulation. Rong *et al.* used Monte Carlo simulations to accurately model the energy dependent object attenuation, scatter, and the collimator-detector response to obtain quantitatively accurate images.¹⁴ The net percent errors in activity estimates from physical geometrical phantom experiments and simulated patient data were shown to be 5%–10%. Elschot *et al.* directly incorporated into the reconstruction algorithm the energy dependent photon scatter and attenuation estimated from Monte Carlo simulations.¹⁵ Their approach demonstrated higher tumor contrast and lower mean residual count in lung insert albeit at the cost of higher image noise. These advanced Monte Carlo based approaches are not commercially available and cannot be easily implemented in the routine clinical practice. The lack of their widespread use is further exacerbated by the fact that many ^{90}Y procedures, at least in the United States, are performed in interventional radiology clinics that are often not associated with academic hospitals.

The objective of this study was to develop a practical imaging protocol to improve ^{90}Y bremsstrahlung SPECT/CT image quality and quantification that could be readily implemented on commercially available imaging systems. To accomplish our objective, we developed a simple method for determining an appropriate imaging EW, its EW-based

background compensation (BC), and CT-based attenuation correction (AC). Furthermore, we present approaches for the optimization of SPECT reconstruction parameters for both detection and quantification. Finally, we address the implementation and accuracy of self-calibration that lead to total activity quantification from ^{90}Y SPECT/CT images.

2. MATERIALS AND METHODS

All data acquisition and analysis were performed on Symbia TruePoint SPECT/CT systems (Siemens Medical Solutions, Hoffman Estates, IL, USA).

2.A. Defining energy windows for CT attenuation correction

Six preliminary EWs (the maximum allowed on the SymbiaTruePoint SPECT/CT systems) were defined in order to separate the total ^{90}Y bremsstrahlung spectrum into regions dominated by different spectral components: 70–100 keV (object scatter and lead x-rays), 100–125 keV (object scatter), 125–175 keV (backscatter), 175–225 keV (backscatter), 225–300 keV (backscatter, collimator scatter and septal penetration), and 300–400 keV (collimator scatter and septal penetration). The maximum widths of the EWs were constrained by the ability to accurately represent photon attenuation at the mean energy of each window to facilitate SPECT AC, such that, if $\Delta\mu$ is the difference in linear attenuation, μ , between the extreme energies of a window, we required $\Delta\mu/\mu_{\text{mean}} < 10\%$. The 10% limit on $\Delta\mu$ was based on earlier work that showed that SPECT images were accurate to within 1% when $\Delta\mu/\mu_{\text{mean}} < 6\%$.¹⁶

The electron density phantom we used (model 062, CIRS, Norfolk, VA) enables precise correlation of CT data in Hounsfield units (HU) to the linear attenuation coefficient, μ (cm^{-1}). It includes eight different reference tissues with CT values ranging from –790 HU (lung inhale) to 235 HU (trabecular bone). An axial CT scan of the electron density phantom was performed at a high tube current to minimize CT noise (130 kVp, 200 mAs). The CT image was converted into μ -maps using proprietary software (e.Soft, Siemens Medical Solutions) that converted each CT image into a μ -map at a user-defined emission energy at 5 keV intervals from 70 to 511 keV (the range is limited by the software). Circular regions of interest (ROIs) were drawn within the inserts to calculate their μ as a function of photon energy.

Starting with the above-defined 6 EWs, we iterated on the EW widths so that the $\Delta\mu/\mu_{\text{mean}}$ was <10% in each EW for the adipose, soft tissue, muscle, and liver inserts. Considerations were also made to isolate the various scatter components in different EWs.

2.B. Choosing appropriate imaging energy windows

In this work, the primary signal was assumed to be spatially registered within the object, while the background

FIG. 1. The experimental setup used to acquire ^{90}Y planar images under different imaging conditions. Both the acrylic thickness and the distance between the collimator and the phantom were varied.

signal was considered to be more widely distributed across the image. It is important to note that this primary signal definition may contain object scatter in addition to the primary bremsstrahlung and perhaps even some smaller contributions from collimator scatter, septal penetration, and backscatter. We defined the imaging EW as the EW that had the highest fraction of primary signal to background signal.

Figure 1 shows the phantom experiment setup, which was acquired using a gamma camera with 1.6-cm (5/8-in.) crystal. Yttrium-90 (III) chloride solution was placed in a vial ($8.5 \times 3.3 \times 1 \text{ cm}^3$). The ^{90}Y phantom was positioned at 30 cm above the gamma camera with a medium-energy low-penetration (MELP) collimator.³¹ Acrylic slabs of various thicknesses (2, 5, 9, 12, and 16 cm) were placed right below the phantom to introduce attenuation and scatter. For the 5 cm-thick acrylic slab, the distance between the collimator and the phantom was varied to 15, 20, 25, 30, and 35 cm. Planar static images were acquired for each imaging condition. Each static image was acquired in the 6 EWs determined in Sec. 2.A. For each imaging condition, planar images with 2×10^6 counts were acquired in the 90–125 keV EW.

To calculate the signal-to-background ratio, we drew two ROIs on each of the static images (Fig. 2): a small ROI at the center, enclosing the image of the object, and a larger ROI that enclosed the entire field of view (FOV). The total counts in the small ROI represented the numbers of photons carrying more object spatial information. This was designated as the primary signal. The total counts in the periphery, calculated by subtracting the total counts in the smaller ROI from those in the larger ROI, represented the number of scattered

FIG. 2. The larger ROI (periphery), indicated in red, encloses the entire FOV of the gamma camera. The smaller ROI (center), indicated in blue, encloses the projected image of the phantom. The background counts in the periphery region were calculated by subtracting the counts for the small ROI from those of the large ROI. The small ROI contains both the primary signal counts, which carry more object spatial information, and unwanted background counts. (See color online version.)

photons that had already lost their spatial information. This was designated as the background signal.

For each EW, the mean pixel count/keV was calculated by dividing the total counts from the ROIs by the EW width and the number of pixels in the ROI. Signal-to-background ratio was calculated as the mean pixel count/keV in the center divided by the mean pixel counts/keV in the periphery. The signal-to-background ratios were calculated for all static phantom images (all six EWs for all imaging conditions). The EW with the highest signal-to-background ratio was used as the imaging EW.

2.C. Developing empirical energy window-based background compensation for ^{90}Y bremsstrahlung imaging

Our empirical EW-based BC model adapted the EW-based scatter correction model, in which the scatter in the imaging EW is estimated as a scaled image of the scatter-estimate EW.^{18–20} In this work, we used scaled images of the BC EW as a model to compensate for the background signal in the imaging EW. The BC EW was selected empirically from our phantom study and based on the errors in the activity recovery coefficient and the amount of residual background count in the cold lung insert. The scaling coefficients were calculated from clinical images. The use of a single scaling coefficient for BC can be justified if low variation in the scaling coefficients is observed under clinical imaging conditions. We used clinical planar images (anterior and posterior views) of 10 post- ^{90}Y -microsphere therapy patients with inherent random geometries (patient thicknesses and distance to collimator). The images were acquired using a Symbia T gamma camera with a crystal thickness of 1.6 cm. For each potential BC EW (5 EWs: A, C, D, E, and F), the scaling coefficients were derived by averaging the scaling coefficients calculated for each clinical planar image of the 10 patient scans, for 20 images in total. The scaling coefficients were calculated as the ratio of the periphery ROI total counts in the imaging to the potential BC EWs (Fig. 3). The variations in the scaling coefficients for each potential BC EW in the clinical scans were reported as 1 standard deviation.

The most appropriate BC EW was determined empirically according to two criteria: (1) the maximum recovery coefficient of the 37-mm sphere and (2) the minimum residual activity concentration in the cold lung insert of a NEMA

FIG. 3. Clinical planar images in imaging (A) and potential background compensation (B) energy windows showing the positioning of regions of interest (outside but adjacent to the liver) from which the total counts were extracted to calculate the scaling coefficient for the empirical background compensation model. The area superior to the liver was excluded to avoid including any signal contamination from the lung shunt.

IEC body phantom (Biodex, Shirley, NY). The phantom was filled with 2.8 GBq (75.4 mCi) $^{90}\text{YCl}_3$ with the sphere-to-background ratio of 7.8. SPECT/CT images of the phantom were acquired for 28 s/view for 2×64 views over 360° using Symbia T6 SPECT/CT systems with 1.6 cm NaI(Tl) detectors and MELP collimators. The acquisition EWs were chosen based on the results reported in Sec. 3.B.

SPECT/CT images of the IEC phantom were reconstructed using the Ordered Subset Expectation Maximization (OSEM) (Flash 3D, Siemens Medical Solutions) algorithm with CT attenuation (See Sec. 2.A) and 5 different BC models. The number of equivalent iterations (subset $\times$ iteration) was 8×16 (based on results reported in Sec. 3.E). The reconstructed images had a matrix size of 128×128 and a voxel size of 4.8 mm. No postreconstruction filter was applied to the images to avoid further image resolution degradation on inherently poor-resolution bremsstrahlung ^{90}Y images.

For each reconstructed image set, a spherical volume of interest (VOI) with a diameter of 10 mm was placed inside the 37-mm sphere, and cylindrical VOIs with diameters and lengths of 25 mm were placed in the adjacent background and in the lung insert. A VOI of 10 mm in diameter for the 37-mm sphere was chosen to decrease the partial volume effect. Observed sphere-to-background ratio recovery was calculated from the mean counts inside these VOIs, i.e., $\text{mean}_{\text{sphere}}/\text{mean}_{\text{background}}$. Residual activity concentration in the lung insert was calculated as a fraction of mean count in the background, i.e., $\text{mean}_{\text{insert}}/\text{mean}_{\text{background}}$. The most suitable BC model was determined based on the recovery of the true sphere-to-background ratio (measured/true) and the residual mean count in the lung insert.

The improvement in image contrast after BC was evaluated visually and semi-quantitatively by comparing the contrast-to-noise ratio (CNR) of the lesions before and after the BC was applied. The CNRs of the lesions were calculated as $\text{CNR} = (\text{mean}_{\text{lesion}} - \text{mean}_{\text{background}}) / \sqrt{\text{mean}_{\text{background}}}$, where $\text{mean}_{\text{lesion}}$ and $\text{mean}_{\text{background}}$ are mean ROI counts in the hot lesions and warm liver, respectively.

2.D. SPECT/CT activity calibration for quantification

The SPECT calibration factor was defined as the ratio of the total activity in the FOV to the total counts in the FOV. For ideal image reconstruction (with accurate corrections for scatter, attenuation, and collimator-detector response), calibration with a point source in air suffices. In practice, however, the image reconstruction is not ideal, so the calibration factor is usually derived from phantom images with all the necessary corrections applied. It is imperative that the calibration of the SPECT/CT imaging system remains valid under clinically relevant conditions to minimize the variations in activity quantification that may result from a mismatch between the calibration and clinical imaging conditions.

Post-therapy ^{90}Y SPECT/CT scanning presents a unique condition in which the total ^{90}Y activity inside the liver (and hence inside the SPECT FOV) can be determined with uncertainty $<10\%$. Clinical images acquired under

such conditions can be used to calibrate the SPECT/CT imaging system. In this study, the calibration factors were calculated from 30 post- ^{90}Y -microsphere therapy SPECT/CT studies with a wide range of abdomen sizes, from 19 to 40 cm (measured in the anterior–posterior direction from the transaxial CT images). The patient scans were chosen such that the net administered activity could be determined with high accuracy. Activity uncertainty in the FOV was maintained at $<7\%$ by selecting patient scans with a lung shunt fraction $<5\%$ and administered activity residuals $\leq 2\%$ and by assuming the error in dose calibrator assay $\leq 3\%$.

All clinical images were acquired using gamma cameras with a crystal thickness of 1.6 cm in the EWs described in Secs. 2.A and 2.B. The planar images were acquired for 10 min with a matrix size of 256×256 and pixel size of 2.4 mm. The SPECT projection images were acquired for 28 s/view for 2×64 views over 360° . The SPECT images were reconstructed using the OSEM algorithm with number of equivalent iterations of 128 (optimized in Sec. 2.E), matrix size of 128×128 , voxel size of 4.8 mm, and postreconstruction Gaussian filter of 4.8 mm.

The calibration factors were calculated for the following image types: planar images, SPECT images with no correction (SPECT only), SPECT images with CT-based AC (Sec. 2.A) (SPECT with AC), and SPECT images with both CT-AC (Sec. 2.A) and BC (Sec. 2.C) (SPECT with AC + BC). For each image type, we used linear regression analysis to derive the relationship between the total injected activity in the FOV and the corresponding total count rates (total counts/frame duration) in the same image FOV. The global calibration factor and its uncertainty were calculated from the regression equation as the gradient and its standard error. The validity of using a single global calibration factor under various clinical imaging conditions was evaluated based on the standard deviation of the residuals (the difference between the actual activities with the predicted injected activities with respect to the actual values) in the linear regression analysis.

2.E. Reconstruction-parameter optimization for qualitative and quantitative SPECT/CT images

The IEC phantom data acquired in Sec. 2.C were also used for this section. The SPECT/CT images were reconstructed using the 3D-OSEM (Flash 3D) algorithm with CT attenuation (Sec. 2.A) and a final empirical BC model (Sec. 3.C). We varied the number of equivalent iterations²¹ from 8 to 256: 8 subsets with 1–16 iterations and 16 subsets with 12–16 iterations. The reconstructed images had a matrix size of 128×128 and a voxel size of 4.8 mm. No postreconstruction filter was applied to the images. For each total number of iterations, the SPECT/CT count-to-activity calibration factor was calculated as the total injected ^{90}Y activity divided by the total counts in the entire reconstructed volume. Self-calibration of the respective SPECT/CT images was performed for absolute image quantification, i.e., voxel unit in Bq/ml.

Spatial resolution (partial volume effect) and convergence of iterative reconstruction both affect the SPECT quantitative accuracy. For each reconstructed image, a spherical VOI

with a diameter of 10 mm was placed inside the 37-mm sphere, and cylindrical VOIs with a diameter and length of 25 mm were placed in the adjacent background and in the lung insert. VOI of 10 mm in diameter for 37-mm sphere was used to minimize the partial volume effect. Measured sphere-to-background ratios were calculated from the mean counts inside these VOIs ($\text{mean}_{\text{sphere}}/\text{mean}_{\text{background}}$). The total number of iterations was optimized based on the recovery of the true SBR, i.e., $\text{SBR}_{\text{measured}}/\text{SBR}_{\text{true}}$. The activity quantification accuracy was measured as the activity recoveries in the 37-mm sphere and in the background, i.e., measured activity/true activity. The efficacy of the EW BC was also evaluated by measuring the relative activity in the lung insert with respect to the background activity. In addition, the activity quantifications in the 37-mm sphere and in the background using SPECT with CT AC + BC were also compared with the activity quantification in SPECT with AC.

3. RESULTS

3.A. Defining energy windows for CT attenuation correction

Table I shows the six energy windows (EW A–B) that maintained $\Delta\mu/\mu_{\text{mean}} < 10\%$ for each of the four materials considered. The E_{low} and E_{high} limits were very similar for all four materials. The average E_{low} and E_{high} values are shown in the column of Table I labeled “Average_{CT-AC}.” When considering BC, it is best to define the EWs such that the various spectral components are isolated in different EWs (e.g., the dual-EW technique uses 1 window for photopeak + scatter and a second window for scatter only). Since individual separation of 5 spectral components of bremsstrahlung is not possible because of its continuous nature, we adjusted the Average_{CT-AC} windows to maximize separation between the various spectral components. These EW definitions are labeled “Nominal_{AC,SC}” and were selected as the acquisition EWs in this experiment. Based on the energy and spatial distribution analyses, EW B (90–125 keV) was determined to be the primary imaging window.

3.B. Choosing an appropriate imaging energy window

The calculated SBRs from the images acquired under different imaging conditions (scattering material thickness

of 2–16 cm at 30 cm away from the MELP collimator and scattering material thickness of 4.8 cm at 15–35 cm away from the MELP collimator) exhibited similar patterns, i.e., the sphere-to-background ratio was the highest in EW B (~ 8.53), as shown in Fig. 4.

3.C. Developing empirical energy window-based background compensation for ^{90}Y bremsstrahlung imaging

The mean scaling coefficients ± 1 standard deviation for each BC model were 0.92 ± 0.04 , 0.91 ± 0.05 , 0.55 ± 0.05 , 0.75 ± 0.09 , 0.53 ± 0.07 for EWs A, C, D, E, and F, respectively. The coefficient of variance of the scaling coefficients was $\sim 10\%$, which suggests that a fixed scaling coefficient factor may be implemented for BC in clinical images.

Using EW F for BC in SPECT/CT image reconstruction of the IEC phantom fulfilled both criteria: maximum SBR recovery and minimum lung insert residual activity; therefore, the EW-based BC for imaging EW B can be modeled as $\text{EW B} - 0.53 \times \text{EW F}$. Using this model, the SBR recovery coefficient for the 37-mm sphere of the IEC phantom was the highest at 87%, and the lung insert residual activity was the lowest at 14%, as shown in Fig. 5.

Figure 6 shows clinical examples of background-compensated planar images from four different patients. The BC improved the image contrast of the planar images. The tumors’ detectability as measured by CNRs (shown beside selected tumors in Fig. 6) increased after the application of the proposed BC. While the edges of the images still look fuzzy because of the inherently poor resolution of ^{90}Y , whose maximum beta range is 11 mm in water, improved delineation of the liver and liver lobes is apparent.

3.D. SPECT/CT activity calibration for quantification

For various reconstructed SPECT and planar images, the global calibration factors (gradients), their uncertainties (standard errors of the gradients), and the coefficients of determination (R^2) of the regression lines are presented in Table II. In all cases, the total counts observed were proportional to the ^{90}Y activity in the FOV with $R^2 > 0.9$. As expected, the variations in the calibration factors exhibited the lowest variation in SPECT with AC + SC and the highest in SPECT-only and planar images.

TABLE I. The low and high photon energy limits of the 6 energy windows for $<10\%$ change in the attenuation coefficient (Average_{CT-AC}) for adipose, soft tissue, muscle, and liver, and modified for energy window-based background compensation (Nominal_{AC,BC}). CT numbers are in HU units and energy windows A–F are in keV.

	Adipose	Soft tissue	Muscle	Liver	Average _{CT-AC}	Nominal _{AC,BC}
CT#	–63.6	–4.4	40.1	48.7	n/a	n/a
A	70–90	70–90	70–90	70–90	70–90	70–90
B	90–130	90–125	90–125	90–125	90–126	90–125
C	130–175	125–180	125–170	125–170	126–174	125–160
D	175–235	180–245	170–230	170–230	174–235	160–215
E	235–310	245–320	230–305	230–300	235–309	250–310
F	310–400	320–420	305–410	300–400	309–408	310–410

FIG. 4. (A) The signal-to-background ratios (SBR) of 6 energy windows (EWs) for the tested attenuating material thicknesses and source-to-collimator distance combinations, indicated by different bar colors. EWs A, B, and C had high signal-to-background ratios, i.e., they contained relatively high spatial information, whereas EWs E and F had low signal-to-background ratios, i.e., they contained relatively low spatial information. (B) The means and standard deviations (stdev) of the SBRs for the EWs.

The activity residual in EW B after linear regression is plotted in Fig. 7; the standard deviations of the activity residuals were 11.3%, 5.6%, 5.2%, and 9.1% for SPECT only, SPECT with AC, SPECT with AC + SC, and planar images, respectively. Activity predictions using SPECT with AC and SPECT with AC + SC had lower variation than did predictions made using SPECT-only or planar images. The predicted activity in an IEC phantom using the global calibration factor derived from clinical scans introduced an error of -25% with respect to the true injected activity.

3.E. Reconstruction-parameter optimization for qualitative and quantitative SPECT/CT images

3.E.1. Quantitative SPECT/CT imaging

The activity concentration and SBR recovery of the 37-mm sphere and the activity recovery in the background region in SPECT/CT images of the IEC phantom with CT AC + BC are shown in Fig. 8. The background activity concentration

converged rapidly (after 16 iterations), while the 37-mm sphere activity converged more slowly (after 128 iterations). The activity concentration in the background was fully recovered ($\sim 100\%$) at convergence, and the activity concentration in the 37-mm sphere was partially recovered (90%) at convergence. The SBR recovery (87%) converged after 128 iterations as well. The measured activity concentration in the cold lung insert was calculated with respect to the background activity. The activity concentration in the cold lung insert vanished slowly as a function of total number of iterations. At 128 iterations, the activity concentration in the lung inserts was 14% of the activity concentration in the background.

As a comparison, at 128 iterations, the SPECT/CT images of the IEC phantom reconstructed using CT AC only had recovery of 39%, 82%, 48%, and 44% for the sphere, background, SBR, and lung insert, respectively.

The proposed BC method increased the activity concentration in the sphere and the SBR recovery by more than twofold (from 39% to 90%). The false-positive activity in the cold lung insert fell from 44% to 14%.

FIG. 5. Recovery coefficients for 37-mm sphere and lung insert residual in the IEC phantom for SPECT/CT images reconstructed without background compensation and with 5 models of background compensation.

3.E.2. Qualitative SPECT/CT images

As the number of equivalent iterations increased, the recovery of the activity in the sphere also increased. For OSEM reconstruction, however, the background noise also increased as a function of the number of equivalent iterations, as demonstrated by the growing error bars in Fig. 8 as a function of the number of equivalent iterations. Figure 9 shows the 37-mm sphere detectability (measured as CNR) as a function of the number of equivalent iterations. The highest CNR, 25, was achieved at 16–24 number of equivalent iterations before the sphere activity concentration converged. At convergence (64 iterations), the CNR had decreased to 18 for SPECT with AC + SC and 13 for SPECT with AC. Visually, more spheres were detectable at lower iterations [Fig. 9(a)] than at higher iterations at convergence [Fig. 9(b)]. SPECT with AC [Fig. 9(c)] had lower detectability than did SPECT with AC + BC.

FIG. 6. The uncorrected and background-compensated clinical images demonstrating that the energy window-based background correction improves the visualization of the liver and lesions. All images are shown using the same window width and level. The background-corrected images show improvement in the contrast-to-noise ratios of the lesions (inset numbers), which corresponds to improved visibility. The corrected images also exhibit improved liver and tumor delineation.

4. DISCUSSION

4.A. Limitation of the proposed background-compensation method

The proposed BC method is an empirical model. Monte Carlo simulation studies are required to accurately correct for specific components of scatter in the imaging EW. For example, Monte Carlo simulation studies^{11,12} suggest that EW F (315–415 keV) may contain little or no object scatter information. Although our proposed BC method was not designed to correct for any specific source of contamination in the imaging EW B (e.g., object scatter, septal penetration, septal scatter, backscatter), we have shown that the proposed method increased both the CNR (detectability) and the accuracy of activity quantification.

The BC factor was derived for a Siemens Symbia T gamma camera with a 1.6-cm crystal and MELP collimator. Since energy window-based scatter correction is dependent on the energy spectrum, other makes and models of cameras with different crystal thicknesses and collimators will likely require different BC parameters, i.e., EW selections and BC scaling factors. The methodology described here, however, could be applied to develop BC models for ^{90}Y bremsstrahlung SPECT/CT imaging using other SPECT/CT systems. The readers are encouraged to use the procedure outlined here to determine the BC factors on their own systems prior to the clinical implementation of this technique.

TABLE II. Results of the linear regression analysis of the relationship between total activity in the field of view and the corresponding total counts in the images. AC: attenuation correction, BC: background compensation, CF: calibration factor.

Image type	R^2	CF (Bq/cps)	Std. error (%)
SPECT	0.901	7.5	6.9
SPECT AC	0.972	2.3	4.0
SPECT AC + BC	0.982	4.0	2.8
Planar	0.917	417.5	5.7

4.B. Energy window selection

The signal-to-background ratio the highest in EWs A and B (and perhaps even C), which means that these EWs provided more spatial information in the image than did the other EWs. This finding is consistent with other studies that found that the optimal EW for qualitative ^{90}Y bremsstrahlung imaging was 80–180 keV.^{13,22} However, EW A was contaminated by the characteristic x-rays (70–90 keV) from the lead collimator and lead housing, so we chose EW B (the EW with the highest SBR) as the imaging EW of the ^{90}Y bremsstrahlung images.

However, the BC EW was chosen empirically based on the SBR recovery, as shown in Fig. 5. Since EWs A and C had signal-to-background ratios comparable to that of EW B—that is, they contained good spatial information—using these EWs to compensate for background yielded a decrease in SBR recovery compared to using no BC.

To further validate our empirical method, two line profiles were extracted from the static images in EW B and EW F (Fig. 10). One line profile was extracted across an image of a liver and the other one was drawn in the background region. The line profiles of the liver images showed that EW B provided much more spatial information of the liver image than did EW F. The line profiles in the background region suggest that the spatial distributions of the background signal were similar in EW B and EW F, supporting the usefulness of the proposed BC mode to compensate for the background signal.

4.C. Partial volume effect and bremsstrahlung ^{90}Y quantitative accuracy

Yttrium-90 bremsstrahlung imaging using current commercially available gamma camera is hardware limited. The collimators used for nuclear medicine imaging are not designed for such high energy (up to 2.3 MeV) bremsstrahlung photon spectra of ^{90}Y . The observed events in the gamma camera have

FIG. 7. The activity residuals, defined as the difference between the true and predicted values relative to the true value, in EW B (90–125 keV) after linear regression. (A) Variations from SPECT/CT images with attenuation correction and background compensation. The mean and the maximum of the *absolute* deviation were 4% and 10%, respectively. The red square indicates the data point from the IEC phantom with a sphere-to-background ratio of 8. (B) Variations from SPECT/CT images with attenuation correction only. The mean and the maximum of the *absolute* deviation were 4.5% and 12%. (C) Variations from uncorrected SPECT images. The mean and the maximum of the *absolute* deviation were 9% and 27%, respectively. (D) Variations from total counts in opposing planar views. The mean and the maximum of the *absolute* deviation were 10% and 23%, respectively. SD: standard deviation.

high contaminations from photons that have undergone septal penetration, septal scatter, and backscatter that contribute to low image contrast. Furthermore, bremsstrahlung imaging has an inherent poor resolution due to electron staggering (up to 11 mm in soft tissue) in the bremsstrahlung production. These limitations may be addressed by optimizing^{17,23} the gamma camera collimator design for ^{90}Y bremsstrahlung imaging and by incorporating the physics model of electron staggering and bremsstrahlung photon generation in ^{90}Y SPECT/CT reconstruction using Monte Carlo simulation.^{14,15,24}

In order to minimize the interplay of the partial volume effect when assessing SPECT convergence, we used a VOI with 10-mm diameter to assess the recovery of activity

concentration for the 37-mm sphere. As a result, up to 90% of the activity concentration in the 37-mm sphere was recovered at convergence. Qualitatively, as seen in Fig. 9, spheres with diameter below 22 mm were not clearly visible in reconstructed ^{90}Y SPECT/CT images. As shown in Fig. 11, the closer the VOI diameter is to the nominal diameter of the 37-mm sphere, the lower the recovery coefficient. Due to the partial volume effect, when using a VOI that matches the 37-mm sphere size, a recovery coefficient of 55% was realized. However, matched VOIs between CT and SPECT are needed for tumor dosimetry. Therefore, use of various published techniques to compensate for the partial volume effect will need to be employed for tumor dosimetry in clinical

FIG. 8. Recovery coefficients as a function of the total number of iterations. The background activity concentration reached 100% recovery rapidly (after 16 number of equivalent iterations). The activity concentration in the 37-mm spheres (using a 10 mm-diameter VOI to minimize the partial volume effect) reached a plateau after 128 equivalent iterations (90% recovery). After 128 equivalent iterations, the signal-to-background ratio recovery also reached a plateau. The measured activity concentration in the cold lung insert was calculated with respect to the background activity. At 128 iterations, the activity concentration in the lung insert was 14% of the activity concentration in the background. The error bars indicate standard deviations for the volumes of interest. SUB: subset, IT: iteration.

FIG. 9. (Left) Detectability (contrast-to-noise ratio, CNR) of the 37-mm sphere as a function of the number of equivalent iterations in SPECT/CT images with CT attenuation and background compensation (solid blue line). The red square indicates the CNR of the sphere for SPECT/CT images with CT attenuation correction only at convergence. (Right) Transaxial and coronal images of the IEC phantom: (a) attenuation-corrected and background-compensated at the highest CNR (37-mm sphere), (b) attenuation-corrected and background-compensated at convergence (37-mm sphere), and (c) attenuation-corrected at convergence. Attenuation correction and background compensation improved detectability [(b) versus (c)]. The highest detectability was achieved before convergence [(a) versus (b)]. In (b), the SBR was about 7, whereas the SBR in (c) was only about 3. SUB: subset, IT: iteration.

practice.^{25,26} The partial volume effect in ^{90}Y PET/CT is less pronounced. Recent ^{90}Y PET/CT quantitative studies^{27,28} have suggested that a recovery coefficient of 90% is achievable in a 37-mm sphere using a matching VOI size.

4.D. Count-to-activity calibration factor derivation

The unique imaging conditions of ^{90}Y microsphere therapy permit SPECT/CT counts-to-activity calibration for generating quantitative ^{90}Y SPECT/CT images to be performed using clinical ^{90}Y images. SPECT images with CT AC + BC can be used to accurately quantify the activity present in the FOV with a mean absolute deviation $\leq 4\%$. Because the calibration factor determined using the IEC phantom demonstrated a substantial bias, caution is warranted when using an IEC phantom to calibrate SPECT/CT systems, since it may not accurately represent clinical imaging conditions in terms of attenuation and scatter.

4.E. Reconstruction parameter optimization

For OSEM reconstruction, the background noise also increases as a function of the number of equivalent iterations (Fig. 8); therefore, the highest detectability (as measured by CNR) is usually achieved before the convergence (Fig. 9). At convergence, even though the image quantification is more accurate, image detectability may actually be lower.

4.F. Correction for deadtime count loss

Because the yield of bremsstrahlung radiation in adipose and soft tissue (low-Z material) with a high energy spectrum is low, the number of detected photons is low; hence, gamma camera deadtime count loss is not an issue for post-therapy ^{90}Y SPECT/CT imaging. The number of total counts per activity was found to be linear (at least in the activity range of 1–5 GBq), providing further confirmation

FIG. 10. The images on the top are clinical images from Fig. 3 in energy window (EW) B (left) and F (right) showing the locations from which the line profiles were extracted. The graphs at the bottom show line profiles in EWs B and F (scaled) across the liver image (left graph) and line profiles of EWs B and F (scaled) across the background region outside the liver (right graph). In the regions outside the liver (shaded), the background profiles in EWs B and F (scaled) are indistinguishable.

FIG. 11. Graph of signal-to-background ratio recovery as a function of the diameter of the volume of interest (VOI). The SBR recovery decreases as the VOI diameter increases, demonstrating the partial volume effect.

that the gamma camera does not suffer from deadtime count loss. If, however, correction for deadtime count loss is needed, the recently proposed revised monitor source method for practical deadtime count loss compensation can be employed.^{29,30}

5. CONCLUSIONS

We have proposed a practical method to reconstruct quantitative SPECT images with CT attenuation correction and empirical EW-based BC. For Siemens SymbiaT SPECT/CT systems, we found that EW B (90–130 keV) and EW F (310–400 keV) are the most appropriate to be used as the imaging and BC EWs. Despite our empirical correction method's limitations, our phantom study shows that our reconstruction and compensation method improves both image quality and quantification.

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CONFLICT OF INTEREST DISCLOSURE

The authors have no COI to report.

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