Optimization of energy window for ^{90}Y bremsstrahlung SPECT imaging for detection tasks using the ideal observer with model-mismatch

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Purpose: In yttrium-90 (^{90}Y) microsphere brachytherapy (radioembolization) of unresectable liver cancer, posttherapy ^{90}Y bremsstrahlung single photon emission computed tomography (SPECT) has been used to document the distribution of microspheres in the patient and to help predict potential side effects. The energy window used during projection acquisition can have a significant effect on image quality. Thus, using an optimal energy window is desirable. However, there has been great variability in the choice of energy window due to the continuous and broad energy distribution of ^{90}Y bremsstrahlung photons. The area under the receiver operating characteristic curve (AUC) for the ideal observer (IO) is a widely used figure of merit (FOM) for optimizing the imaging system for detection tasks. The IO implicitly assumes a perfect model of the image formation process. However, for ^{90}Y bremsstrahlung SPECT there can be substantial model-mismatch (i.e., difference between the actual image formation process and the model of it assumed in reconstruction), and the amount of the model-mismatch depends on the energy window. It is thus important to account for the degradation of the observer performance due to model-mismatch in the optimization of the energy window. The purpose of this paper is to optimize the energy window for ^{90}Y bremsstrahlung SPECT for a detection task while taking into account the effects of the model-mismatch.

Methods: An observer, termed the ideal observer with model-mismatch (IO-MM), has been proposed previously to account for the effects of the model-mismatch on IO performance. In this work, the AUC for the IO-MM was used as the FOM for the optimization. To provide a clinically realistic object model and imaging simulation, the authors used a background-known-statistically and signal-known-statistically task. The background was modeled as multiple compartments in the liver with activity parameters independently following a Gaussian distribution; the signal was modeled as a tumor with a Gaussian-distributed activity parameter located randomly with equal probability at one of three positions. The IO test statistics (i.e., likelihood ratios) were estimated using Markov-chain Monte Carlo methods. The authors realistically modeled human anatomy using a digital phantom code, and realistically simulated ^{90}Y bremsstrahlung SPECT imaging with a clinical SPECT system and typical imaging parameters using a previously validated Monte Carlo bremsstrahlung simulation method. Model-mismatch was included by modeling image formation process in the calculation of IO test statistics using an analytic modeling method previously developed for quantitative ^{90}Y bremsstrahlung SPECT. To demonstrate the effects of the model-mismatch on the detection task, the authors optimized the energy window both with and without model-mismatch included in the IO.

Results: For all the energy windows, the AUC values for the IO-MM were smaller than that for the IO. The optimal windows for the IO-MM and the IO were 80–180 and 60–400 keV, respectively.

Conclusions: The authors have demonstrated the degradation of the ideal performance due to model-mismatch and optimized the energy window for ^{90}Y bremsstrahlung SPECT for detection tasks by accounting for the effects of the model-mismatch. The obtained optimal window was much narrower when taking into account the model-mismatch and similar to that obtained previously for estimation tasks. © 2013 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4805095>]

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I. INTRODUCTION

Yttrium-90 (^{90}Y) microsphere brachytherapy (also referred to as radioembolization) is used clinically to treat unresectable liver cancer.^{1–3} Posttherapy ^{90}Y bremsstrahlung imaging is used to document the distribution of microspheres in the patient and to help predict potential side effects.⁴ Recently, quantitative ^{90}Y bremsstrahlung single photon emission com-

puted tomography (SPECT) has shown great potential to provide quantitative accurate images and subjective improvement in image quality.⁵ The latter is crucial for patient monitoring and management. Unlike gamma photons with pronounced photopeaks used in conventional nuclear medicine imaging, ^{90}Y bremsstrahlung photons, resulting from the interaction of β -particles emitted during ^{90}Y decay with atomic nuclei in the patient, have a continuous and broad energy distribution,

with the highest energy ~ 2.28 MeV. As a result, there has been great variability in the choice of acquisition energy window for ^{90}Y bremsstrahlung imaging.^{6,7} Since the choice of energy window may have great impact on the image quality, use of an optimal energy window is desirable.

Objective assessment of image quality should be based on performance of an observer on a relevant task, and the figure of merit (FOM) used to measure observer performance must be computable and scalar so that it can be used unambiguously in optimization of imaging systems.⁸ To the best of our knowledge, to date there has been no rigorous task-based optimization of the energy window for ^{90}Y bremsstrahlung imaging for detection tasks.

The area under the receiver operating characteristic (ROC) curve (AUC) is a widely used figure of merit for quantitatively summarizing observer performance for detection tasks.^{9–12} The ideal observer (IO) makes optimal use of complete information regarding physics and statistics of the imaging system and object population to achieve the highest AUC attainable.⁸ Since the IO sets an upper limit on the observer performance, IO performance is a powerful theoretical tool for comparison and optimization of imaging systems. However, computation of IO performance requires full knowledge of the probability density function of high-dimensional projection data under the competing hypotheses. As a result, the analytical computation of IO test statistic, i.e., the likelihood ratio (LR), is limited to simple and thus unrealistic models of objects and imaging systems.

To overcome this limitation, Kupinski *et al.* have developed a method based on Markov-chain Monte Carlo (MCMC) techniques¹³ to compute the LR for fixed signals in random backgrounds with known statistics, i.e., signal-known-exactly (SKE) and background-known-statistically (BKS).¹⁴ Park *et al.* then extended this computational method to the case where both the signal and the background were random with known statistical properties, i.e., signal-known-statistically (SKS) in addition to BKS.¹⁵ In principle, with known parameterization of the object, characterization of the imaging system and the ability to compute the background- and signal-known-exactly (BSKE) LR, this MCMC IO estimation method can be applied to arbitrarily complicated models of objects and imaging systems. In practice, however, the application of the method has been limited to relatively simple models (e.g., statistically defined lumpy backgrounds as the object model and spatially invariant Gaussian blurring as the imaging system model) due to prohibitive computational burden of modeling the image formation process for the general case. For example, for a realistic object model in myocardial perfusion SPECT imaging, thousands of projection datasets may be necessary to represent samples due to noise and variation of anatomy and uptake. For each of these thousands of projection datasets, millions of MCMC iterations may be necessary to compute a single corresponding LR using the MCMC IO estimation method. Generating realistic projections, even using an analytical projector, can take on the order of minutes of processor time. Since this must be repeated for each iteration, a typical computational time would be 10^8 – 10^9 h for a single CPU.

To apply the MCMC IO estimation method to more realistic object model and imaging simulation, the computational burden needs to be greatly reduced. He *et al.* applied Kupinski's MCMC IO estimation method (SKE-BKS) to myocardial perfusion SPECT imaging using a parameterized torso phantom as the object model and a realistic analytical SPECT projector as the imaging simulation.¹⁶ In this application, the computational burden mainly resulted from the imaging simulation process. Since the MCMC IO estimation method is an iterative approach that may take millions of iterations to estimate just one LR, performing a realistic imaging simulation using a realistic analytical projector or Monte Carlo (MC) simulation in each iteration is computationally infeasible, as described above.

To reduce the computational burden, He *et al.*¹⁶ modeled the object as a parameterized torso phantom with discretized anatomic parameters and continuous organ activity parameters. Projections for each organ were computed using unit activity for a finite number of anatomic parameters using the analytical projector prior to MCMC iterations and stored in memory. In this way, for a linear imaging process, in each iteration projection data for the sampled organ activity parameters could be rapidly obtained by taking linear combinations of the precomputed organ projections instead of performing a complicated imaging simulation. As a result, the computational burden has been greatly reduced and the application of the MCMC IO estimation method for realistic SPECT imaging simulation has become practical.

As mentioned previously, the IO implicitly assumes using a perfect model of the image formation process. However, in many applications such as ^{90}Y bremsstrahlung SPECT, the errors in the model of the image formation process used in tomographic reconstruction, termed the model-mismatch, can be large. In these cases, the IO may not be suitable for predicting the image quality after reconstruction: the projection data, that is optimal for the IO, may not be optimal after reconstruction with the model-mismatch and interpretation by human observers. The channelized hotelling observer (CHO) has been previously validated with human observer studies and showed good agreement with the human observers in a variety of applications.^{17–20} However, using the CHO for optimizing acquisition parameters requires reconstruction of a large number of projection data and optimization of various reconstruction and regularization parameters (e.g., iteration number and cutoff frequency of smoothing filters). Thus, using an observer that performs directly on projection data is computationally less expensive than an observer that performs on reconstructed images (e.g., the CHO). To both facilitate using projection data instead of reconstructed images for optimization and account for the effects of the model-mismatch on the image quality of the reconstructed images, Ghaly *et al.* have developed an observer that explicitly includes model-mismatch in the IO.^{21,22} This observer was termed the IO-MM, where MM stands for the model-mismatch. The IO-MM still uses the LR as the test statistic, but in the estimation of the LR it uses a model of the image formation process that includes model-mismatch instead of the perfect one. Ghaly *et al.* compared the performance of the IO-MM

with that of the CHO for the task of optimizing the energy window for myocardial perfusion SPECT imaging.²² The results of the IO-MM were consistent with those of the CHO.

As mentioned above, model-mismatch can be large for ⁹⁰Y bremsstrahlung SPECT imaging due to the continuous and broad energy distribution of ⁹⁰Y bremsstrahlung photons. First, the continuous distribution results in a large fraction of scattered photons in any energy window. Thus, energy-based scatter rejection used for gamma photons is relatively ineffective. Second, high-energy photons result in image degrading effects in low-energy windows, such as down-scatter, septal penetration and scatter, as well as backscatter from structures behind the crystal. In addition, beam hardening is more important for bremsstrahlung photons, which have a broad energy distribution, than for gamma photons, which have discrete energies. Since image degrading effects including attenuation, scatter, and collimator-detector response (CDR) are energy dependent, the modeling methods used in conventional SPECT reconstruction may result in large model-mismatch in bremsstrahlung SPECT.

Moreover, for ⁹⁰Y bremsstrahlung SPECT the choice of the energy window may have an important influence on the amount of the model-mismatch. The fraction of various kinds of photons is different for different energy windows: e.g., the fraction of detected photons undergoing septal penetration for a 400–450 keV window is much larger than for a 100–150 keV window. Since septal penetration is relatively difficult to model accurately, energy windows that include high-energy photons may result in large model-mismatch. Furthermore, since beam hardening is more serious for a wide energy window than for a narrow one, modeling methods not accounting for the energy dependence of image degrading effects may result in larger model-mismatch for a wide energy window than for a narrow one.

In this paper, we aim to optimize the acquisition energy window for ⁹⁰Y bremsstrahlung SPECT for detection tasks in microsphere radioembolization. Since there may be large model-mismatch in bremsstrahlung imaging and the amount of the model-mismatch may depend on the energy window, it is important to take into account the effects of the model-mismatch on the observer performance in the optimization of the energy window. To this end, we used the AUC for the IO-MM as the figure of merit for optimization. To allow for a complicated and clinically realistic object model and imaging simulation, the MCMC IO estimation method was applied to estimate the LR. To represent general situations of interest in microsphere radioembolization, we defined a SKS-BKS detection task, where the background was modeled as multiple compartments in the liver with activity parameters independently following a Gaussian distribution and the signal was modeled as a tumor with a Gaussian-distributed activity parameter located at multiple possible positions. We realistically modeled human anatomy using a digital phantom code, and realistically simulated ⁹⁰Y bremsstrahlung SPECT imaging with a clinical SPECT system and typical imaging parameters using a previously validated MC bremsstrahlung simulation method. Since the performance of the IO-MM depends on the amount of the model-mismatch, to make our optimization

results more general, we used a modeling method developed previously for ⁹⁰Y bremsstrahlung SPECT,⁵ which is based on methods applied to conventional gamma-emitting radionuclides.²³ To demonstrate the effects of the model-mismatch on the observer performance and the optimization results, we also performed an optimization study using the IO and compared the obtained results to that using the IO-MM.

II. MATERIALS AND METHODS

In this section, we first introduce in more detail the MCMC IO estimation method for random signals and backgrounds, including the He method for accelerating the computation of projection data using a database of organ projections, and the modification of the method for the IO-MM. We then describe in detail the experimental design for the optimization study including the object model, imaging simulation, estimation of the AUC, and implementation of the MCMC IO estimation method.

II.A. MCMC IO estimation method for random signal and background

Given a voxelized object $\mathbf{f} = [f_1, f_2, \dots, f_N]^T \in \mathbb{R}^{N \times 1}$, a linear image formation process can be represented as

$$\mathbf{g} = \mathbf{P}\mathbf{f} + \mathbf{n}, \quad (1)$$

where $\mathbf{g} = [g_1, g_2, \dots, g_M]^T \in \mathbb{R}^{M \times 1}$ is the projection data; $\mathbf{P} \in \mathbb{R}^{M \times N}$, termed the *system matrix*, represents the mapping from the object space to the projection space; $\mathbf{n} \in \mathbb{R}^{M \times 1}$ is the measurement noise; M and N are the number of projection bins and object voxels, respectively.

For a random signal $\mathbf{f}_s \in \mathbb{R}^{N \times 1}$ in a random background $\mathbf{f}_b \in \mathbb{R}^{N \times 1}$, the image formation process under signal-absent and signal-present hypotheses can be represented as

$$H_0 : \mathbf{g} = \mathbf{P}\mathbf{f}_b + \mathbf{n}, \quad (2)$$

$$H_1 : \mathbf{g} = \mathbf{P}(\mathbf{f}_b + \mathbf{f}_s) + \mathbf{n}. \quad (3)$$

For a pair of parameterized background and signal models, $\mathbf{f}_b(\boldsymbol{\theta}) \in \mathbb{R}^{N \times 1}$ and $\mathbf{f}_s(\boldsymbol{\alpha}) \in \mathbb{R}^{N \times 1}$, respectively, the background and signal images are defined as

$$\mathbf{b}(\boldsymbol{\theta}) = \mathbf{P}\mathbf{f}_b(\boldsymbol{\theta}), \quad (4)$$

$$\mathbf{s}(\boldsymbol{\alpha}) = \mathbf{P}\mathbf{f}_s(\boldsymbol{\alpha}), \quad (5)$$

where $\boldsymbol{\theta}$ is the background parameter vector, and $\boldsymbol{\alpha}$ is the signal parameter vector.

The IO test statistic, i.e., the LR, is defined as

$$\Lambda(\mathbf{g}) = \frac{\text{pr}(\mathbf{g}|H_1)}{\text{pr}(\mathbf{g}|H_0)}, \quad (6)$$

where $\text{pr}(\mathbf{g}|H_i)$ is the probability density function of the projection $\mathbf{g}$ under the hypothesis H_i . In the cases where $\boldsymbol{\alpha}$ and $\boldsymbol{\theta}$ are statistically independent, Park *et al.* formulated the LR for BKS/SKS problem as the posterior mean of the BSKE

(i.e., background-and-signal-known-exactly) LR,¹⁵

$$\Lambda(\mathbf{g}) = \int d\boldsymbol{\alpha} \int d\boldsymbol{\theta} \Lambda_{\text{BSKE}}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}), s(\boldsymbol{\alpha})) \text{pr}(\boldsymbol{\theta}|\mathbf{g}, H_0) \text{pr}(\boldsymbol{\alpha}). \quad (7)$$

When the measurement noise, $\mathbf{n}$, follows a Poisson distribution, the BSKE LR is given by

$$\begin{aligned} \Lambda_{\text{BSKE}}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}), s(\boldsymbol{\alpha})) &= \frac{\text{pr}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}), s(\boldsymbol{\alpha}), H_1)}{\text{pr}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}), H_0)} \\ &= \prod_{m=1}^M \left(1 + \frac{s_m(\boldsymbol{\alpha})}{b_m(\boldsymbol{\theta})} \right)^{g_m} e^{-s_m(\boldsymbol{\alpha})}. \end{aligned} \quad (8)$$

Then the integral in Eq. (7) can be estimated by Monte Carlo integration

$$\gamma((\tilde{\boldsymbol{\theta}}, \tilde{\boldsymbol{\alpha}}), (\boldsymbol{\theta}^{(j)}, \boldsymbol{\alpha}^{(j)})) = \min \left(1, \frac{\text{pr}(\mathbf{g}|\mathbf{b}(\tilde{\boldsymbol{\theta}}), H_0) \text{pr}(\tilde{\boldsymbol{\theta}}) \text{pr}(\tilde{\boldsymbol{\alpha}}) q_b(\tilde{\boldsymbol{\theta}}|\boldsymbol{\theta}^{(j)}) q_s(\tilde{\boldsymbol{\alpha}}|\boldsymbol{\alpha}^{(j)})}{\text{pr}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}^{(j)}), H_0) \text{pr}(\boldsymbol{\theta}^{(j)}) \text{pr}(\boldsymbol{\alpha}^{(j)}) q_b(\boldsymbol{\theta}^{(j)}|\tilde{\boldsymbol{\theta}}) q_s(\boldsymbol{\alpha}^{(j)}|\tilde{\boldsymbol{\alpha}})} \right), \quad (10)$$

where

$$\frac{\text{pr}(\mathbf{g}|\mathbf{b}(\tilde{\boldsymbol{\theta}}), H_0)}{\text{pr}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}^{(j)}), H_0)} = \prod_{m=1}^M \left(\frac{b_m(\tilde{\boldsymbol{\theta}})}{b_m(\boldsymbol{\theta}^{(j)})} \right)^{g_m} e^{b_m(\boldsymbol{\theta}^{(j)}) - b_m(\tilde{\boldsymbol{\theta}})}. \quad (11)$$

In principle, any proposal distribution will ultimately deliver samples from the stationary distribution. However, the convergence rate (i.e., how fast the chain converges to the stationary distribution) and the mixing rate (which determines the number of samples needed to provide a good representation of the stationary distribution after convergence) depend crucially on the proposal distributions. Since the computation time is of critical concern in practice, appropriate proposal distributions are needed for rapid convergence and mixing.

In each iteration, to compute the BSKE LR according to Eq. (8) for $(\boldsymbol{\theta}^{(j)}, \boldsymbol{\alpha}^{(j)})$, the background and signal images require simulating the image formation process that is represented mathematically by Eqs. (4) and (5). As mentioned previously, performing a realistic imaging simulation, such as a realistic analytical projector or Monte Carlo simulation in each iteration, is typically computationally infeasible.

Suppose $\boldsymbol{\theta} = [\mathbf{u}, \boldsymbol{\lambda}]^T = [u_1, u_2, \dots, u_G, \lambda_1, \lambda_2, \dots, \lambda_K]^T \in \mathbb{R}^{(G+K) \times 1}$ and $\boldsymbol{\alpha} = [\mathbf{v}, \boldsymbol{\beta}]^T = [v_1, v_2, \dots, v_Q, \beta_1, \beta_2, \dots, \beta_L]^T \in \mathbb{R}^{(Q+L) \times 1}$, where $(\mathbf{u}, \mathbf{v})$ are discretized parameters with a finite number of values (e.g., indices for anatomies in a phantom population or tumor locations) and $(\boldsymbol{\lambda}, \boldsymbol{\beta})$ are parameters with continuous values (e.g., activities for individual volumes of interest). Then the object can be parameterized as

$$\mathbf{f}_b(\boldsymbol{\theta}) = \sum_{k=1}^K \lambda_k \cdot \mathbf{f}_{bk}(\mathbf{u}), \quad (12)$$

$$\hat{\Lambda}(\mathbf{g}) = \frac{1}{J} \sum_{j=1}^J \Lambda_{\text{BSKE}}(\mathbf{g}|\mathbf{b}(\boldsymbol{\theta}^{(j)}), s(\boldsymbol{\alpha}^{(j)})), \quad (9)$$

where each pair $(\boldsymbol{\theta}^{(j)}, \boldsymbol{\alpha}^{(j)})$ is a sample from the distribution $\text{pr}(\boldsymbol{\theta}|\mathbf{g}, H_0) \text{pr}(\boldsymbol{\alpha})$.

To generate a series of the object parameters, $(\boldsymbol{\theta}^{(j)}, \boldsymbol{\alpha}^{(j)})$, sampled from the desired distribution, a Markov chain with $\text{pr}(\boldsymbol{\theta}|\mathbf{g}, H_0) \text{pr}(\boldsymbol{\alpha})$ as the stationary distribution is constructed using a MCMC technique known as the Metropolis-Hastings algorithm.²⁴ This iterative approach begins with an initial parameter vector, $(\boldsymbol{\theta}^{(0)}, \boldsymbol{\alpha}^{(0)})$. In each iteration, given $(\boldsymbol{\theta}^{(j)}, \boldsymbol{\alpha}^{(j)})$, a pair of parameter vectors $(\tilde{\boldsymbol{\theta}}, \tilde{\boldsymbol{\alpha}})$ are sampled from a pair of proposal distributions $(q_b(\boldsymbol{\theta}|\boldsymbol{\theta}^{(j)}), q_s(\boldsymbol{\alpha}|\boldsymbol{\alpha}^{(j)}))$ and then accepted or rejected by the Markov chain with acceptance probability

$$\mathbf{f}_s(\boldsymbol{\alpha}) = \sum_{l=1}^L \beta_l \cdot \mathbf{f}_{sl}(\mathbf{v}), \quad (13)$$

where $\mathbf{f}_{bk}(\mathbf{u}) \in \mathbb{R}^{N \times 1}$ ($k = 1, 2, \dots, K$) and $\mathbf{f}_{sl}(\mathbf{v}) \in \mathbb{R}^{N \times 1}$ ($l = 1, 2, \dots, L$), termed *basis objects* in the remainder of this paper, are independent of $(\boldsymbol{\lambda}, \boldsymbol{\beta})$. The background and signal images can thus be represented as

$$\mathbf{b}(\boldsymbol{\theta}) = \sum_{k=1}^K \lambda_k \cdot \mathbf{P} \mathbf{f}_{bk}(\mathbf{u}), \quad (14)$$

$$\mathbf{s}(\boldsymbol{\alpha}) = \sum_{l=1}^L \beta_l \cdot \mathbf{P} \mathbf{f}_{sl}(\mathbf{v}). \quad (15)$$

The imaging simulation $\mathbf{P} \mathbf{f}_{bk}(\mathbf{u})$ and $\mathbf{P} \mathbf{f}_{sl}(\mathbf{v})$ can be performed for all possible values of $(\mathbf{u}, \mathbf{v})$ and the resulting projection data, termed *basis projections* in the remainder of this paper, can be stored prior to starting the MCMC iterations. In each iteration, the background image $\mathbf{b}(\boldsymbol{\theta}^{(j)})$ and the signal image $\mathbf{s}(\boldsymbol{\alpha}^{(j)})$ can then be obtained by taking linear combinations of the prestored basis projections corresponding to $\mathbf{u}^{(j)}$ and $\mathbf{v}^{(j)}$, as represented by Eqs. (14) and (15), respectively. In this way, the computational burden can be greatly reduced.

Suppose $\mathbf{P}_t$ is the true system matrix, which exactly embodies the image formation process, and $\mathbf{P}_e$ is the model-estimated system matrix, $\Delta \mathbf{P} = \mathbf{P}_e - \mathbf{P}_t$ represents the model-mismatch. The IO-MM still uses the LR as the test statistic. In the estimation of the LR, however, in contrast to the IO, which uses the true system matrix $\mathbf{P}_t$ in the imaging simulation, the IO-MM uses the model-estimated system matrix $\mathbf{P}_e$. In particular, when using the MCMC method to estimate the LR, instead of using $\mathbf{P}_t$ as in the IO, the IO-MM uses $\mathbf{P}_e$ to generate *basis projections* by performing imaging simulation on *basis objects* [see Eqs. (14) and (15)].

II.B. Experimental design

II.B.1. Task definition and object model

Even when using precomputed basis projections, the computational complexity is still very high in this optimization study. Thus, it is crucial to balance generality and computational complexity. Generality argues for a large number of parameters used in the object model. However, the computational complexity increases dramatically as the number of parameters increases. In the MCMC IO estimation method, the number of parameters in the object model determines the dimension of the sample space for the Markov chain. With increased number of parameters, the number of burn-in iterations, i.e., the iterations required for the Markov chain to converge to the stationary distribution, increases dramatically. After convergence, the number of iterations in the mixing process also increases dramatically since more samples are required to obtain a good representation of the stationary distribution. In addition, to obtain an accurate and precise estimate of the AUC, a large number of samples of the projection data, $\mathbf{g}$, under each hypothesis are required to provide a good representation of the object variability and noise. The LR for each of these samples must be estimated using the MCMC IO estimation method. More parameters in the object model lead to more required samples of $\mathbf{g}$ and thus more LRs to be estimated.

Considering both the generality and computational complexity, we defined the task as detection of a small tumor in the liver containing two large tumors. Since it is relatively rare that there is only one small tumor in the liver in clinical radioembolization, we believe it was more general to incorporate two large tumors in the background model. In particular, the background was modeled as three compartments: the whole liver and two spheres with diameters of 4.2 and 5.2 cm representing two large tumors in the liver. Each compartment had a Gaussian-distributed parameter related to the activity in this compartment. The signal was modeled as a sphere with a diameter of 1.5 cm representing the small tumor in the liver; the signal had a discretized parameter indicating three possible locations of the tumor and a continuously Gaussian-distributed parameter related to the activity in the tumor. We believe that using three compartments in the background model and three possible locations in the signal model achieves a good trade-off between generality of the model and computational complexity.

We used the XCAT phantom code,²⁵ a computer program for generating digital phantoms that realistically model human anatomy, to generate images representing basis objects used in the object model and the mass density map used later in the imaging simulation. Each of these images had $128 \times 128 \times 128$ voxels and the voxel size was 4.664 mm. The object model can be represented as

$$\mathbf{f}_b(\boldsymbol{\theta}) = \lambda_1 \cdot \mathbf{f}_{b1} + \lambda_2 \cdot \mathbf{f}_{b2} + \lambda_3 \cdot \mathbf{f}_{b3}, \quad (16)$$

$$\mathbf{f}_s(\boldsymbol{\alpha}) = \beta \cdot \mathbf{f}_{s1}(v). \quad (17)$$

The meanings of the parameters in Eqs. (16) and (17) are discussed below.

In the background model, the basis object $\mathbf{f}_{b1} \in \mathbb{R}^{N \times 1}$ ($N = 128 \times 128 \times 128$) represented an image with a total activity of 1 GBq, a typical activity in microsphere radioembolization, in the liver and zero activity outside the liver; the activity was uniformly distributed inside the liver. $\mathbf{f}_{b2} \in \mathbb{R}^{N \times 1}$ represented an image with activity uniformly distributed inside the 4.2 cm diameter tumor and zero activity outside the tumor; the activity concentration in the tumor for $\mathbf{f}_{b2}$ was four times that in the liver for $\mathbf{f}_{b1}$. Similarly, $\mathbf{f}_{b3} \in \mathbb{R}^{N \times 1}$ represented an image of the 5.2 cm diameter tumor. The background parameter vector $\boldsymbol{\theta} = [\lambda_1, \lambda_2, \lambda_3]^T$ defines the background activity and random variations in the parameters provide background variability. The random variables λ_k ($k = 1, 2, 3$) were statistically independent and followed a Gaussian distribution with a mean of 1 and a standard deviation of 0.25; the distribution was truncated to a maximum value of 1.5 and a minimum value of 0.5. This truncated Gaussian distribution was chosen to represent the general situations of interest in clinical radioembolization. Note that since $\mathbf{f}_{b1}$ represented the whole liver including the tumor regions in $\mathbf{f}_{b2}$ and $\mathbf{f}_{b3}$, the mean value of the tumor-to-liver activity concentration ratio in the object model was 5 rather than 4.

In the signal model, we have the signal parameter vector $\boldsymbol{\alpha} = [v, \beta]^T$. The integer random variable v had three possible values (1, 2, or 3) with equal probabilities, indicating three possible locations of the small tumor. Similar to $\mathbf{f}_{b2}$ and $\mathbf{f}_{b3}$ for the large tumors, $\mathbf{f}_{s1}(v)$ ($v = 1, 2, 3$) represented images of the small tumor located at each of the three possible positions, respectively. The activity concentration in the small tumor for $\mathbf{f}_{s1}(v)$ ($v = 1, 2, 3$) was also four times that in the liver for $\mathbf{f}_{b1}$. The random variable β represented the signal uptake and followed the same truncated Gaussian distribution as the λ_k . All five parameters in the object model were statistically independent. Figure 1 illustrates the tumor positions in the object model.

II.B.2. Imaging simulation: Generating true and model-estimated basis projections

As mentioned previously, to reduce the computational burden, the projection data for individual basis objects, i.e., basis projections, were generated prior to MCMC iterations. In this optimization study in particular, for each energy window investigated, both the true and the model-estimated basis projections for each of the six basis objects were generated. Since the estimation of the AUC for each energy window involves estimating thousands of the LRs, the investigated energy windows should be chosen carefully to avoid unnecessary computation while making sure the optimal window is included in the investigation. To this end, we investigated a total of 45 energy windows within the energy range 60–500 keV. We chose 60 keV as a lower bound considering that most photons with energies lower than 60 keV are attenuated in the patient and thus have little contribution to the detected photons. We chose 500 keV as an upper bound considering that most detected photons with energies higher than 500 keV result from septal penetration and scatter, which seriously degrade the image quality. The investigated energy windows were combinations

FIG. 1. (Left to right) maximum intensity projections of the voxel values along lateral, anterior-posterior and superior-inferior directions (the voxel values in the signal and the three compartments for the background were 1, 0.1, 0.2, and 0.3, respectively; note that these values were chosen to facilitate the illustration of the tumor positions and did not have any specific meanings in the object model), and a sample slice of the mass density map generated using the XCAT phantom code. Note that tumors did not overlap in 3D space.

of six possible lower thresholds (60, 80, 100, 120, 140, and 160 keV) and ten possible upper thresholds (100, 120, 140, 160, 180, 200, 240, 300, 400, and 500 keV). Only continuous windows with widths larger than 40 keV were investigated (e.g., a 80–100 keV window was not investigated and a 80–120 keV window was investigated). We adopted this limit since narrower windows will result in high noise in the projection data and thus were deemed highly unlikely to be the optimal window. As will be demonstrated by the optimization results later, optimal window was indeed not at the edge of the investigated range and its width was larger than 40 keV.

II.B.2.a. Generation of true basis projections. For each energy window investigated, true basis projections were generated for each of the six basis objects using a previously validated SIMIND Monte Carlo bremsstrahlung simulation method.^{26,27} In particular, we generated low-noise projection data using a SIMIND simulation of a Philips Precedence SPECT/CT system with a high-energy general-purpose (HEGP) collimator and a 9.525 mm thick NaI(Tl) crystal. The compartments behind the crystal were simulated as a slab of SiO₂ with density of 2.6 g/cm³ and thickness of 6 cm. We simulated an energy resolution of 9.5% full width at half maximum (FWHM) at 140 keV and an intrinsic spatial resolution of 3.4 mm, both with an energy dependence of $1/\sqrt{E}$, where E was the energy imparted. We simulated eight projection views over 360° and an imaging time of 1 min per view; we simulated fewer projection views than the typical number of views to reduce the computational burden. The projection image at each view had 128 × 128 pixels and the pixel size was 4.664 mm. A body-contouring noncircular orbit was modeled by adjusting the radius of rotation for each view based on the attenuation map so that the camera face was close to the body surface.

II.B.2.b. Generation of model-estimated basis projections. For each energy window investigated, model-estimated basis projections were generated for each of the six basis objects using a forward projection code^{28–31} implementing a modeling method developed previously for quantitative ⁹⁰Y bremsstrahlung SPECT imaging.⁵ We modeled all the image degrading effects including attenuation, object scatter and the full collimator-detector response (CDR) including geometric response, lead characteristic x-ray, septal penetration

and scatter, partial deposition in the crystal, intrinsic resolution, and backscatter from structures behind the crystal. The model-mismatch resulted from the difference between this model and the detailed SIMIND bremsstrahlung simulation described in Sec. II.B.2.a.

In the attenuation modeling, a different effective attenuation coefficient was used for each energy window. To account for the effects of both the source depth and the detector interactions on the effective attenuation coefficient, we computed the effective attenuation coefficient for each energy window using SIMIND simulations of a point source at the center of a 15 cm radius sphere water phantom and in air. We used 15 cm as the representative average distance primary photons travel before exiting the patient. In these simulations, the numbers of geometrically collimated primary photons detected in each energy window were recorded. The effective mass attenuation coefficient for water was computed as $(\ln(C_{\text{air}}/C_{\text{phan}}))/15 \text{ cm}^{-1}$, where C_{air} and C_{phan} were the numbers of the detected geometrically collimated primary photons in air and in the phantom, respectively. Then the voxel values in the mass density map generated from the XCAT phantom code were multiplied by the obtained effective mass attenuation coefficient to form the attenuation map for each energy window.

The effective source scatter estimation (ESSE) method was used to model scatter.³¹ We generated the kernels used in ESSE using a SIMIND simulation of a point source in the center of a water slab phantom of size 100 × 80 × 80 cm³ for each energy window.

The CDR tables used in CDR modeling³⁰ were generated from SIMIND simulations of a point source in air at various distances from the camera face for each energy window.

II.B.3. Estimation of the AUC

To estimate the AUC for each energy window, a set of samples of the projection data $\mathbf{g}$ under each hypothesis were used to represent the data statistics due to object variability and noise. To this end, for each energy window we generated a total of 3000 pairs of the noisy signal-absent and signal-present projection datasets. Specifically, to generate each pair of projection datasets, we first sampled the five parameters in the object model from their probability distributions. We then

computed the background image and the signal image according to Eqs. (14) and (15), respectively, using the sampled parameter values and the precalculated true basis projections for the corresponding energy window. We then added Poisson noise generated from a Poisson random number generator to the background image and the sum of the background and signal images, respectively, to form a pair of noisy signal-absent and signal-present projection datasets.

For each energy window, the MCMC IO estimation method was applied to estimate the LR for each of the 6000 projection datasets $\mathbf{g}$. Since the computational burden is of critical concern, instead of using the whole projection image, we used a region-of-interest (ROI) of the image that contains the signal (or on the corresponding locations of the signal-absent image) to estimate the LR. Specifically, for each projection view, three squares of 8×8 pixels were used as the ROI, and each square was located at one of the three possible positions of the signal in the projection image. Considering that in the projection image the regions without the signal had no effects on the computed value for the BSKE LR [see Eq. (8)], using an appropriate ROI instead of the whole projection image was a reasonable approach and dramatically reduced the computational burden. The implementation of the MCMC IO estimation method will be discussed in more detail in Sec. II.B.4.

For each energy window, the 3000 pairs of estimates of the LR obtained from the MCMC procedure were used as inputs to the LABROC4 code,^{32,33} a computer program for fitting binormal ROC curves to continuously distributed data using a true maximum likelihood algorithm, to estimate the ROC curve and the corresponding AUC. The energy window having the maximum AUC value was deemed optimal.

II.B.4. Implementation of the MCMC IO estimation method

For a given projection data $\mathbf{g}$, the LR was estimated by taking the average of the BSKE LRs for a series of sets of the object parameters generated from a Markov chain after burn-in iterations [see Eq. (9)]. In this study, since the parameter

$\mathbf{v}$ had only three possible values, Eq. (7) can be transformed into

$$\Lambda(\mathbf{g}) = \int d\beta \int d\theta \left[\frac{1}{3} \sum_{i=1}^3 \Lambda_{\text{BSKE}}(\mathbf{g}|\mathbf{b}(\theta), s_i(\beta)) \right] \times \text{pr}(\theta|\mathbf{g}, H_0) \text{pr}(\beta), \quad (18)$$

where

$$s_i(\beta) = \beta \cdot \mathbf{P}\mathbf{f}_{s1}(v = i). \quad (19)$$

As a result, Eq. (9) becomes

$$\hat{\Lambda}(\mathbf{g}) = \frac{1}{J} \sum_{j=1}^J \left[\frac{1}{3} \sum_{i=1}^3 \Lambda_{\text{BSKE}}(\mathbf{g}|\mathbf{b}(\theta^{(j)}), s_i(\beta^{(j)})) \right]. \quad (20)$$

Since $\mathbf{P}\mathbf{f}_{s1}(v = i)$ ($i = 1, 2, 3$) were precomputed basis projections, instead of sampling five parameters in each iteration, we only need to obtain four parameters $(\lambda_1^{(j)}, \lambda_2^{(j)}, \lambda_3^{(j)}, \beta^{(j)})$ from a Markov chain with $\text{pr}(\theta|\mathbf{g}, H_0) \text{pr}(\beta)$ as the stationary distribution.

We used a total of 2×10^6 iterations for a single Markov chain. The computation of the BSKE LR started after 1×10^6 iterations to guarantee the convergence of the Markov chain to the stationary distribution.

Specifically, to estimate the LR for a given $\mathbf{g}$ with $(\lambda_1^*, \lambda_2^*, \lambda_3^*, \beta^*)$ as the underlying true parameters, we used $(\lambda_1^*, \lambda_2^*, \lambda_3^*, \beta^*)$ as the initial sample of the Markov chain to facilitate fast convergence and mixing.

In each iteration we sampled each parameter independently from a proposal distribution $q(x|x^{(j)})$, where x denoted one of the four parameters, considering that these four parameters were statistically independent. We chose a Gaussian distribution with a mean of $x^{(j)}$ as the proposal distribution $q(x|x^{(j)})$. The standard deviation of the Gaussian distribution was 0.005 for the parameter λ_1 (related to whole liver activity) and 0.01 for the parameters λ_2, λ_3 , and β (related to tumor activities). These values were chosen empirically for relatively fast convergence and mixing.

The sampled parameters were then accepted or rejected with the acceptance probability

$$\gamma((\tilde{\theta}, \tilde{\beta}), (\theta^{(j)}, \beta^{(j)})) = \min \left(1, \frac{\text{pr}(\mathbf{g}|\mathbf{b}(\tilde{\theta}), H_0) \text{pr}(\tilde{\lambda}_1) \text{pr}(\tilde{\lambda}_2) \text{pr}(\tilde{\lambda}_3) \text{pr}(\tilde{\beta})}{\text{pr}(\mathbf{g}|\mathbf{b}(\theta^{(j)}), H_0) \text{pr}(\lambda_1^{(j)}) \text{pr}(\lambda_2^{(j)}) \text{pr}(\lambda_3^{(j)}) \text{pr}(\beta^{(j)})} \right), \quad (21)$$

where the *a priori* probability distribution was the truncated Gaussian distribution described in Sec. II.B.1. Equation (21) has a simpler form than Eq. (10) due to the symmetry of the used proposal distribution: $q(\tilde{x}|x^{(j)}) = q(x^{(j)}|\tilde{x})$. If $(\tilde{\theta}, \tilde{\beta})$ was accepted, $(\theta^{(j+1)}, \beta^{(j+1)}) = (\tilde{\theta}, \tilde{\beta})$; otherwise $(\theta^{(j+1)}, \beta^{(j+1)}) = (\theta^{(j)}, \beta^{(j)})$. If the current iteration number was larger than 1

$\times 10^6$, $\frac{1}{3} \sum_{i=1}^3 \Lambda_{\text{BSKE}}(\mathbf{g}|\mathbf{b}(\theta^{(j+1)}), s_i(\beta^{(j+1)}))$ was computed.

To compute the BSKE LR, we need to compute the background and signal images for the current parameters according to Eqs. (14) and (15), respectively. For the IO, the precomputed true basis projections were used in the computation. For the IO-MM, the precomputed

FIG. 2. 2D contour plot of the AUC values as a function of the lower and upper threshold of the energy window for the IO-MM.

model-estimated basis projections were used instead of the true basis projections.

III. RESULTS

Figures 2 and 3 show 2D contour plots of the AUC values as a function of the lower and upper threshold of the energy window for the IO-MM and the IO, respectively. The standard deviations of the AUC values were substantially smaller than the differences of the AUC values among energy windows (a typical standard deviation was 0.005). For all the energy windows, the AUC values for the IO-MM were smaller than that for the IO. This demonstrated the degradation of the ob-

server performance due to the model-mismatch for all the energy windows. The optimal window for the IO-MM was 80–180 keV and the corresponding AUC value was 0.76. In contrast, the optimal window for the IO was 60–400 keV and the corresponding AUC value was 0.87.

IV. DISCUSSION

For the IO, there are two major factors affecting the observer performance: noise and object variability. For the IO-MM, in addition to these two factors, model-mismatch also plays an important role in determining the observer performance. Figure 4 shows the AUC values as a function of upper

FIG. 3. 2D contour plot of the AUC values as a function of the lower and upper threshold of the energy window for the IO.

FIG. 4. AUC values as a function of upper threshold for a fixed lower threshold of 80 keV for the IO and the IO-MM.

threshold for a lower threshold of 80 keV for the IO and the IO-MM. From this figure, we can obtain insight about how these three factors affect the observer performance and how they are related to energy windows. Specifically, for narrow energy windows (i.e., when the upper threshold was small) the dominant effect was noise due to the low count level in the projection data. As the window width increased, the number of detected photons increased substantially; as a result, the noise reduced and the AUC value increased. When the upper threshold exceeded 240 keV, as the window width further increased, the change in the AUC for the IO became very small. One plausible explanation is that the effects of the object variability on the observer performance became more important with more detected high-energy photons. Since most detected high-energy photons have undergone septal penetration and scatter, with increased upper threshold, more photons emitted from the background could be detected in the signal region in the projection image. As a result, the activity uncertainty in both the signal and the background would have greater influence on the observer performance for the detection of the signal. In contrast to the IO, the performance of the IO-MM was affected mainly by the model-mismatch as the window width further increased. Due to the fact that beam hardening was more serious for wider energy windows and various image degrading effects, such as attenuation, scatter, and CDR, were energy dependent, wider energy windows resulted in larger model-mismatch. As shown in Fig. 4, after exceeding 180 keV, as the upper threshold further increased, the performance of the IO-MM degraded dramatically due to increased model-mismatch. This demonstrates the dependence of the model-mismatch on the energy window and the importance of incorporating the effects of the model-mismatch on the observer performance in the optimization of energy windows.

We have previously developed a new method for optimizing the energy window for estimation tasks that accounts for the effects of the model-mismatch and applied this method to quantitative ^{90}Y bremsstrahlung SPECT imaging in microsphere radioembolization.³⁴ In this method, we proposed an

inverse-mass-weighted root mean squared error (RMSE) of the volume of interest (VOI) activity estimates as the FOM for optimization. Interestingly, in cases both with and without the model-mismatch, the relationship between the obtained FOM values and corresponding energy windows for the estimation task in the previous work was similar to that between the AUC values and energy windows for the detection task in this work. The obtained optimal windows were also similar. For the case with the model-mismatch, the optimal window was 100–160 keV for the estimation task vs 80–180 keV for the detection task in this work; for the case without the model-mismatch, the optimal window was 60–400 keV for both the estimation and the detection tasks.

V. CONCLUSION

In this work, we have optimized the acquisition energy window for a BKS-SKS detection task for ^{90}Y bremsstrahlung SPECT imaging in microsphere radioembolization. To account for the effects of the model-mismatch, we used the AUC for a previously proposed observer, a modification of the ideal observer that includes the effects of model-mismatch, as the figure of merit for the optimization. To provide a suitably general and clinically realistic object model and imaging simulation, Markov-chain Monte Carlo methods were applied to estimate the observer's test statistics. The model-mismatch was represented by the difference between a model of the image formation process generated using a modeling method developed previously for quantitative ^{90}Y bremsstrahlung SPECT and a previously validated detailed SIMIND bremsstrahlung Monte Carlo simulation. By comparing the performance of the ideal observer with and without taking into account the model-mismatch, we demonstrated the degradation of the observer performance due to the model-mismatch and the effects of model-mismatch on the optimal energy window. The obtained optimal energy window for the IO-MM was 80–180 keV, similar to that obtained previously for an estimation task.

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