Assessment of cardiac single-photon emission computed tomography performance using a scanning linear observer

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(Received 4 November 2011; revised 26 November 2012; accepted for publication 28 November 2012; published 21 December 2012)

Purpose: Single-photon emission computed tomography (SPECT) is widely used to detect myocardial ischemia and myocardial infarction. It is important to assess and compare different SPECT system designs in order to achieve the highest detectability of cardiac defects.

Methods: Whitaker *et al.*'s study ["Estimating random signal parameters from noisy images with nuisance parameters: linear and scanning-linear methods," *Opt. Express* **16**(11), 8150–8173 (2008)] on the scanning linear observer (SLO) shows that the SLO can be used to estimate the location and size of signals. One major advantage of the SLO is that it can be used with projection data rather than with reconstruction data. Thus, this observer model assesses the overall hardware performance independent of any reconstruction algorithm. In addition, the computation time of image quality studies is significantly reduced. In this study, three systems based on the design of the GE cadmium zinc telluride-based dedicated cardiac SPECT camera Discovery 530c were assessed. This design, which is officially named the Alcyon Technology: Discovery NM 530c, was commercialized in August, 2009. The three systems, GE27, GE19, and GE13, contain 27, 19, and 13 detectors, respectively. Clinically, a human heart can be virtually segmented into three coronary artery territories: the left-anterior descending artery, left-circumflex artery, and right coronary artery. One of the most important functions of a cardiac SPECT system is to produce images from which a radiologist can accurately predict in which territory the defect exists [<http://www.asnc.org/media/PDFs/PPReporting081511.pdf>, Guideline from American Society of Nuclear Cardiology]. A good estimation of the extent of the defect from the projection images is also very helpful for determining the seriousness of the myocardial ischemia. In this study, both the location and extent of defects were estimated by the SLO, and the system performance was assessed by localization receiver operating characteristic (LROC) [P. Khurd and G. Gindi, "Decision strategies maximizing the area under the LROC curve," *Proc. SPIE* **5749**, 150–161 (2005)] or estimation receiver operating characteristic (EROC) [E. Clarkson, "Estimation receiver operating characteristic curve and ideal observers for combined detection/estimation tasks," *J. Opt. Soc. Am. A* **24**, B91–B98 (2007)] curves.

Results: The area under the LROC/EROC curve (AULC/AUEC) and the true positive fraction (TPF) at a specific false positive fraction (FPF) can be treated as the figures of merit. For radii estimation with a 1 mm tolerance, the AUEC values of the GE27, GE19, and GE13 systems are 0.8545, 0.8488, and 0.8329, and the TPF at FPF = 5% are 77.1%, 76.46%, and 73.55%, respectively. The assessment of all three systems revealed that the GE19 system yields estimated information and cardiac defect detectability very close to those of the GE27 system while using eight fewer detectors. Thus, 30% of the expensive detector units can be removed with confidence.

Conclusions: As the results show, a combination of the SLO and LROC/EROC curves can determine the configuration that yields the most relevant estimation/detection information. Thus, this is a useful method for assessing cardiac SPECT systems. © 2013 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4771961>]

Key words: cardiac SPECT, image quality, LROC, scanning linear observer

I. INTRODUCTION

According to the Centers for Disease Control and Prevention (CDC),¹ heart disease is currently the leading cause of death for both men and women. The most common type of heart disease is coronary artery disease, which is also known as coronary heart disease. Myocardial perfusion disease is one type of coronary artery disease, and its detection is a topic

of great interest. Single-photon emission computed tomography (SPECT) is widely used to detect myocardial ischemia and myocardial infarction. It is important to assess and compare different SPECT system designs so that the highest detectability of cardiac defects can be achieved. A model observer is widely applied to assess system performance, and several groups have done impressive studies. He *et al.*² studied 4200 images using channelized Hotelling observer

for a three-class detection and characterization task. Gifford *et al.*³ applied scanning model observers and 184 cases were studied by both human and model observers. In both these works, the assessment was performed using 3D reconstructed images. The work of Whitaker *et al.*⁴ on the scanning linear observer (SLO) provides a new method that assesses the systems in 2D projections, but without a reconstruction procedure. They demonstrated that the SLO can successfully estimate location and size of signals in a lumpy background. Zhou and Gindi⁵ optimized the traditional SPECT systems (with collimators) having a lumpy or uniform background for detection/localization tasks. Several groups^{4,6-8} have mentioned that for estimation tasks, assessing the system performance with raw projection data is better than assessing it with reconstructed data, because the performance estimation based only on projection data depends solely on the choice of system parameters; the reconstruction parameters are irrelevant in this case and can be ignored. In this study, three clinical pinhole SPECT systems were assessed using a combination of the SLO and the localization receiver operating characteristic (LROC)/estimation receiver operating characteristic (EROC) curves so that the system configuration that provides the most task-based information can be determined. This method allows detection, location estimation, and signal size estimation to be performed concurrently and efficiently. The SLO can also assess system performance based on the basis of raw projection data.

For a cardiac SPECT imaging system, the relationship between the simulated, voxelized distribution of the radiotracer $\mathbf{f}$ and the projection data $\mathbf{g}$ can be written as

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

where $\mathbf{H}$ is the system transform matrix and $\mathbf{n}$ is additive noise. SPECT systems operate as photon-counting devices, and so a Poisson probability law applies to the measurement noise in the image data. The simulated, voxelized distribution of the radiotracer $\mathbf{f}$ was a combination of several individual organs (categorized as background) and cardiac defects (categorized as signals). All individual organs were simulated with both random uptakes and geometric variations. More details are given in Sec. II.C.

To determine an efficient system design, three different system designs were evaluated for the task of detecting defects in three locations for seven defect sizes. These three systems contain different detector configurations, but are based on the GE cadmium zinc telluride (CZT)-based dedicated cardiac SPECT camera Discovery 530c design. The defects were simulated as spherical shapes located in one of the three coronary artery territories. More details about the system designs and defects are given in Secs. II.B and II.D.

The system performance was assessed using the SLO that was previously studied by Whitaker *et al.*⁴ The SLO is a linear observer that scans over all the parameters to be estimated. The results of the SLO were quantified using the LROC/EROC curves. The LROC curves indicate the ability to correctly localize the signal when it is present. In Clarkson's work,⁹ the EROC curves quantify the performance on tasks that includes both detection of a signal and estimation

of a set of signal parameters. More details about the SLO and LROC/EROC curves are provided in Sec. II.E.

II. METHODS

II.A. Forward models

In medical imaging simulations, the object is often modeled as a discrete phantom. Digital phantoms of $480 \times 480 \times 480$ voxels with 1 mm^3 resolution were generated using the NCAT software¹⁰ and served as the objects to be imaged, denoted as $\mathbf{f}$. The forward model can be written as Eq. (1), where the transformation matrix $\mathbf{H}$ was not stored but calculated on the fly by scanning over the object $\mathbf{f}$, accounting for the effects of attenuation, pinhole segmental penetration, and detector thickness. The transformation matrix $\mathbf{H}$ was calculated geometrically from the center of each $480 \times 480 \times 480$ voxels to the detectors, and the output of each single pixel was generated by averaging 3×3 subpixels. More details on the effects of attenuation, pinhole segmental penetration, subpixels, and detector thickness are given in Sec. II.B. Poisson noise $\mathbf{n}$ was added, resulting in projection data $\mathbf{g}$.

Patients were assumed to have been injected with 34.09 mCi of a ^{99m}Tc radiotracer [with the γ -ray emission efficiency $\approx 88\%$ (Ref. 11)], and imaged continuously for 3 min. The traveling distances (from the photon-emitting voxels to the surfaces of the pixels in the detectors) and the corresponding propagation attenuation (the attenuation effect from the patient's body) were calculated. The intensity of incident γ -ray photons onto the detectors can be simulated by geometric calculation with attenuation. (The following elements were modeled: the inverse-square falloff of intensity with distance along each possible photon path, and the factor related to the cosine of the angle of incidence of the photon path where it enters the detector.) Finally, the detector absorption of the γ -ray photons can be derived from Beer's law

$$I(L) = I_0 e^{-\int \alpha(l) dl}, \quad (2)$$

where I_0 is the intensity of one incident collimated γ -ray beam, $I(L)$ is the intensity of the γ -ray beam after traveling a distance L , α is the attenuation coefficient and different materials have different values. The detectors are described in more detail in Sec. II.B.

II.B. Systems

To determine an efficient system design, three designs, GE27, GE19, and GE13, were simulated in this study. The systems were based on the GE CZT-based dedicated cardiac SPECT camera Discovery 530c design and had 27, 19, and 13 detectors, respectively. Among them, the GE19 design is fairly similar to the commercialized DNM530c from GE Healthcare, as shown in Fig. 1.

The Discovery 530c design contains three parallel rows of detectors and covers the left side hemisphere of a patient's body. In the GE27 system, each row contains nine detectors. In the GE19 system, the three rows contain five, nine, and five detectors, with the furthest eight detectors (two at each corner)

FIG. 1. GE CZT-based dedicated cardiac SPECT camera Discovery 530c.

removed. Note that in the commercial system, the corner detectors are populated. The three rows in the GE13 system contain four, five, and four detectors, which are cross-distributed. Figure 2 shows a conceptual mapping of the three rows in each system.

The detectors in all the simulated systems are made of solid-state CZT with dimensions of $7.872 \times 7.872 \text{ cm}^2$ discretized into 32×32 pixels. Thus, the detectors have an intrinsic resolution of 2.46 mm. Pinholes with a diameter of 4.5 mm are placed in front of the detectors at a designed distance, e.g., 7 cm. The SPECT systems studied here are single-pinhole systems, i.e., there is only one pinhole in front of each detector. The effects of detector thickness and pinhole penetration are simulated. The detector is 5 mm thick and has electrodes attached to both sides (pixelized on a single side only). There are no physical segments inside the crystal, and only the electrons and holes (generated from γ -ray photons interacting with CZT crystals) will travel toward the electrodes. Other γ -ray photons that do not interact in the crystal (by scattering and/or absorption) will travel unaffected in their original incident directions. Consequently, the detector might exhibit responses in more than one pixel if a collimated γ -ray beam is not normally incident. A 2D diagram

FIG. 2. A conceptual mapping of three rows in each system.

FIG. 3. The effect of detector thickness.

of the effect of detector thickness is shown in Fig. 3 (but the effect of detector thickness was simulated in 3D in this study). For example, for a collimated incident γ -ray beam, the photon traveling distances (m, n, p) of corresponding pixels (M, N, P) in the crystal are precisely calculated. Three pixels (M, N, P) in the detector respond to single collimated γ -ray photons. Beer's law [Eq. (2)] and the absorption coefficient of CZT (4.5 cm^{-1}) are applied to calculate the responses of all the pixels. If the intensity of the incident γ -ray is I_0 , the outputs of pixels $M/N/P$ are $I_0 - I_0 e^{-\alpha m} / I_0 e^{-\alpha m} - I_0 e^{-\alpha(m+n)} / I_0 e^{-\alpha(m+n)} - I_0 e^{-\alpha(m+n+p)}$.

Then, the output of each single pixel is generated by averaging 3×3 subpixels. A conceptual figure of subsampling of the pixels is shown in Fig. 4. If the transformation matrix H is calculated without subsampling (in the left of Fig. 4), H_{mn} is calculated with (a, b, c) and (d, e, f), which are the coordinate of the center the M th voxel, and the coordinate of the center of the N th pixel, respectively. The distance D between voxel M and pixel N is equal to $\sqrt{(a-d)^2 + (b-e)^2 + (c-f)^2}$. On the other hand, if the transformation matrix H is calculated with subsampling (in the right of Fig. 4), the pixel N is virtually segmented into nine subpixels (three in one side). The final value of H_{mn} is the average of the nine results from the voxel M and each individual subpixel of pixel N .

The design details were approximately reproduced. The pinhole was designed as shown in Fig. 5 and was located at the center of a platinum plate. For 140.5 keV γ -ray photons, the attenuation coefficient of platinum is 43.7 cm^{-1} . The acceptance angle was assumed to be 45° . Any γ -ray photons with an incident angle larger than 45° were omitted because only $<10^{-6}$ of the incident γ -ray would penetrate, assuming 0.9-cm-thick platinum plates. Note that in the commercial system, the acceptance angle is larger than 45° and the plate is not made of platinum.

FIG. 4. Pixels subsampling.

FIG. 5. Pinhole setting.

II.C. Phantoms, uptake variation, and noise

The NURBS-based cardiac torso (NCAT) software package uses nonuniform rational B-spline (NURBS) surfaces to realistically model human anatomy and physiology for medical research. NCAT also includes a realistic model of the cardiac motion based on tagged MRI data of a normal patient.¹⁰

NCAT phantoms with a 1 mm voxel size and $480 \times 480 \times 480$ voxels were created to model object **f**. The unit value phantom of the individual organ was generated and projected to the detectors with attenuation as the unit value projection $\mathbf{g}_u$. The attenuation map was also generated from NCAT at the same time as the activity map. Seven individual organ unit value phantoms were generated: the heart, lungs, liver, kidneys, gall bladder, spleen, and rest of the body. In doing so, the projection data corresponding to different organ uptakes can be generated by scaling and summing the projection data from the individual organs. The unit value projection $\mathbf{g}_u$ is the base projection from an object with some specific decays such that the final projection can be simulated by multiplying by a scaling constant. For example, if we specify that the unit image of the heart, $\mathbf{g}_u^{\text{heart}}$, is projected from a 0.01 mCi radiotracer [with the γ -ray emission efficiency $\approx 88\%$ (Ref. 11)] with 3 min of continuous imaging, there are a total of 58 608 000 decays from all voxels of the heart (of the phantom). If the heart can be presented in 1000 voxels, $\mathbf{g}_u^{\text{heart}}$ is the projection from these 1000 voxels, with 58 608 decays in each voxel (so there are a total of 58 608 000 decays from these 1000 voxels). As the heart uptake ranges from 0.526 to 2.273 mCi, as shown in Table I, the final projection from the heart, $\mathbf{g}_{\text{heart}}$, can be generated by scaling $\mathbf{g}_u^{\text{heart}}$ using a constant with a range of [52.6, 227.3].

Eighteen different patients (nine males and nine females) were generated. Each patient had a different body shape and different organ sizes except for the heart, which was fixed

TABLE I. Total organ-uptake variations.

Organ	Min. (mCi)	Max. (mCi)
Heart	0.526	2.273
Lung	0.638	3.182
Liver	1.193	9.693
Kidney	0.613	1.705
Gall bladder	0.613	1.705
Spleen	0.613	1.705
Body (in FOV)	7.170	13.830

FIG. 6. Generation of projection image $\mathbf{g}$.

in shape and size owing to the limited computing power. The 18 patients were generated with long-axis radii of 33–35.15 cm and short-axis radii of 24–26.15 cm in equal steps, in the NCAT parameters; patient nos. 2, 4, 6, . . . , 18 are males with long-axis values of 33.15, 33.40, 33.65, . . . , 35.15 cm whereas patient nos. 1, 3, 5, . . . , 17 are females with long-axis values of 33, 33.25, 33.50, . . . , 35 cm, respectively. The increment is 0.25 cm for both axes of both genders. The similar range of organ uptakes as in Ref. 12 was applied. The values assigned to individual organs were based on a Gaussian distribution with a known mean and variance. The minimum and maximum confinements are listed in Table I. Note that the body uptake is presented in the form of “Body (in FOV)” because usually not all the radiotracers are in the field of view (FOV) of the imaging system.

A projection of the entire phantom can be created by summing the scaled noise-free projections of all seven individual organs, as shown in Fig. 6. Randomly generated scaling values for all seven components from the truncated Gaussian distributions with known mean/variance and minimum/maximum confinements were generated. The varied-uptake projections were then generated by multiplying the scaling values by individual organ projections and summing all of them. The last step was to add Poisson noise to the projections. These noise-added projections are approximations to what would be measured by clinical cardiac SPECT systems.

II.D. Defects

Several terms are required to describe myocardial perfusion disease: size (small/medium/large), severity (mild/moderate/severe), type (reversible/persistent/mixed), location of the defect, and presence of single-vessel or multivessel disease.¹³ In this study, we focused on the size and location of the defects. As shown in Fig. 7, spherical defects were simulated in one of the three coronary artery territories:¹⁴ the left-anterior descending artery (LAD), left-circumflex artery (LCX), and right coronary artery (RCA). Owing to the limited computing power, defects were

FIG. 7. Three coronary artery territories of heart.

modeled with radii varying from 2 to 8 mm in increments of 1 mm. Note that the simulated cardiac wall was approximately 12 mm thick in the NCAT phantoms generated for this study. Therefore, defects with radii larger than 6 mm were truncated into aspheric shapes because they exist only within the cardiac wall. Moreover, the center of each defect is not necessarily located exactly at the center of one of the three territories. In fact, the three territories do not have simple geometric shapes and so the exact centers cannot be defined. We chose the three locations roughly at the centers of the three territories. The severity (brightness) of defects was assumed to be generated by sampling from a uniform distribution between 20% and 30% of decays from the heart, which were also randomly generated from a Gaussian distribution, as done by He *et al.*¹²

II.E. SLO and LROC/ERO curves

The SLO was studied by Whitaker *et al.*⁴ and can be represented by the formula

$$\hat{\theta}_{SL}(\mathbf{g}) = \underset{\theta}{\operatorname{argmax}} \left\{ \bar{\mathbf{g}}(\theta)^T \bar{\mathbf{K}}_g^{-1} \mathbf{g} - \frac{1}{2} \bar{\mathbf{g}}(\theta)^T \bar{\mathbf{K}}_g^{-1} \bar{\mathbf{g}}(\theta) + \ln[pr(\theta)] \right\}, \quad (3)$$

where $\bar{\mathbf{g}}(\theta)$ represents the data averaged over all sources of randomness except the parameters to be estimated (θ), $\bar{\mathbf{K}}_g^{-1}$ is the inverse covariance matrix for the random vector $(\mathbf{g} - \bar{\mathbf{g}}(\theta))$ with approximation of slowly varying parameters, $\mathbf{g}$ is one sample from the testing pool, and $pr(\theta)$ is the probability of the estimates. Here, the parameters to be estimated (θ) include the locations and sizes of the defects. In this study, we assumed that each combination of defect size and location was equally likely.

If the background is independent of the estimates, $\bar{\mathbf{g}}(\theta)$ can be rewritten as

$$\bar{\mathbf{g}}(\theta) \equiv \mathbf{s}(\theta) + \bar{\mathbf{b}}, \quad (4)$$

where $\mathbf{s}(\theta)$ is the noise-free image of a signal parameterized by θ , and $\bar{\mathbf{b}}$ is the noise-free image of the mean background. The conditional covariance contains only terms for the noise

and background; by making a slowly varying signal approximation in the noise covariance,

$$\mathbf{K}_{g|\theta} \simeq \langle \mathbf{K}_{g|\theta} \rangle_{\theta} = \bar{\mathbf{K}}_n + \bar{\mathbf{K}}_g^{\text{bkgn}}. \quad (5)$$

Many imaging systems operate as photon-counting devices, and so a Poisson probability law applies to the measurement noise of the image data; consequently, for a given object, the noise values in different detector elements are independent of one another. Therefore, the noise covariance matrix is diagonal,

$$\bar{\mathbf{K}}_n \equiv \langle \mathbf{K}_n \rangle_f = \operatorname{Diag}(\bar{\mathbf{g}}), \quad (6)$$

where $\bar{\mathbf{g}}$ denotes the grand mean of the data. By applying those changes, Eq. (3) can be rewritten as

$$\hat{\theta}_{SL}(\mathbf{g}) = \underset{\theta}{\operatorname{argmax}} \left\{ \mathbf{s}(\theta)^T \bar{\mathbf{K}}_g^{-1} \left(\mathbf{g} - \bar{\mathbf{b}} - \frac{1}{2} \mathbf{s}(\theta) \right) + \ln[pr(\theta)] \right\}. \quad (7)$$

The step-by-step derivation of Eq. (7) is given by Whitaker *et al.*⁴

To implement the SLO, the covariance matrix $\mathbf{K}$ must be generated from a set of training data. For this study, the training data contained 22 000 images: 1000 images for each defect configuration in three locations (LAD, LCX, RCA) and in seven different sizes (2–8 mm), i.e., $1000 \times 3 \times 7$, and 1000 images of normal cases (signal-absent or healthy cases). The location and size of the defects can be continuously distributed. However, owing to the limited computing power, three possible defect locations and seven possible defect sizes were used.

In the work of Whitaker *et al.*,⁴ the brightness of the signals depended on the background. For example, if the signal brightness is 20% (the signal value over the background value), the number of photon counts for a pixel in signal-absent (healthy) cases is 100, and the number of photon counts for a pixel in signal-present (with defect) cases is 80 (background: 100, signal: $100 \times 20\% = 20$, total: $100 - 20 = 80$). In this study, the signals depended only on the heart decays and were independent of other organs. For example, if the brightness of the signal is 20% (the signal value over the heart activity value, assuming the heart activity value is 50), the number of photon counts for a pixel in signal-absent (healthy) cases is 100 (heart: 50, others: 50), and the number of photon counts for a pixel in signal-present (with defect) cases is 90 (others: 50, heart: 50, defect: $50 \times 20\% = 10$, total: $50 + 50 - 10 = 90$). Since we have different assumption of the signals from the work of Whitaker *et al.*, the covariance matrix must be derived. Derivations start with the projection data

$$\mathbf{g}_h = \mathbf{b} + \mathbf{n} \quad (8)$$

and

$$\mathbf{g}_d = \mathbf{b} + \mathbf{s} + \mathbf{n}, \quad (9)$$

where $\mathbf{b}$ is the background vector, $\mathbf{n}$ is Poisson noise, and $\mathbf{g}_h$ and $\mathbf{g}_d$ denote images without (healthy cases) and with

$$\begin{pmatrix} 0 & \dots & 0 & 0 & 0 & 0 & 0 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \dots & \vdots \\ \vdots & \vdots & 0 & 0 & 0 & 0 & 0 & \dots & \vdots \\ \vdots & \vdots & 0 & 1 & 0 & 0 & 0 & \dots & \vdots \\ \vdots & \vdots & 0 & 0 & 1 & 0 & 0 & \dots & \vdots \\ \vdots & \vdots & 0 & 0 & 0 & 1 & 0 & \dots & \vdots \\ \vdots & \vdots & 0 & 0 & 0 & 0 & 0 & \dots & \vdots \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \dots & \vdots \\ 0 & \dots & 0 & 0 & 0 & 0 & 0 & \dots & 0 \end{pmatrix}$$

FIG. 8. Sample of support operator.

defects, respectively. The support operator $\mathbf{D}_s$ can be defined as in Fig. 8.

In the 3D object space, the support operator has ones at the components where signals exist and zeros otherwise. In the example shown above, the support operator $\mathbf{D}_s$ contains only three nonzero elements corresponding to some specific voxels; however, the number of nonzero components in the support operator is varied and should be obtained from the NCAT phantoms of the defects. The defect-present image $\mathbf{g}_d$ can be written as

$$\mathbf{g}_d = \mathbf{H}[\mathbf{I} + \beta \mathbf{D}_s] \mathbf{f}_b + \mathbf{n} \quad (10)$$

with

$$\mathbf{s} = \beta \mathbf{H} \mathbf{D}_s \mathbf{f}_b, \quad (11)$$

where $\mathbf{f}_b$ is the background vector in the 3D object space. As discussed in Sec. II.D, the signals in this study are cardiac defects. Thus, β , the ratio of the signal to the decays in the heart, is a random variable that represents the strength of the signal and is randomly selected from a range of $[-0.2, -0.3]$ for each image. For the signal-absent cases,

$$\mathbf{K}_h = \bar{\mathbf{K}}_{nh} + \bar{\mathbf{K}}_g^{\text{bkgnd}} = \bar{\mathbf{K}}_{nh} + \mathbf{K}_b, \quad (12)$$

where $\bar{\mathbf{K}}_{nh}$ is the noise covariance matrix for images of defect-free (healthy) cases. For simplicity, we will use $\mathbf{K}_b$ to represent $\bar{\mathbf{K}}_g^{\text{bkgnd}}$ in the following derivation. For the signal-present cases, $\mathbf{K}_d$ can be written as

$$\begin{aligned} \mathbf{K}_d &= \langle (\mathbf{g} - \bar{\mathbf{g}})(\mathbf{g} - \bar{\mathbf{g}})^t \rangle \\ &= \langle \langle \langle (\mathbf{g} - \bar{\mathbf{g}})(\mathbf{g} - \bar{\mathbf{g}})^t \rangle_{g|\mathbf{b},\beta} \rangle_{\mathbf{b}} \rangle_{\beta} \\ &= \langle \langle \langle (\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta) + \bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})(\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta) \\ &\quad + \bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})^t \rangle_{g|\mathbf{b},\beta} \rangle_{\mathbf{b}} \rangle_{\beta}. \end{aligned}$$

Expanding the terms yields

$$\begin{aligned} \mathbf{K}_d &= \langle \langle \langle (\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta))(\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta))^t \rangle_{g|\mathbf{b},\beta} \rangle_{\mathbf{b}} \rangle_{\beta} \\ &\quad + \langle \langle \langle (\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})(\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})^t \rangle_{\mathbf{b}} \rangle_{\beta} \\ &= \bar{\mathbf{K}}_{nd} + \langle \langle \langle (\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})(\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})^t \rangle_{\mathbf{b}} \rangle_{\beta}, \end{aligned}$$

where $\bar{\mathbf{K}}_{nd}$ is the noise covariance matrix for the images of defect-present cases. The double bars of the

matrix indicate that the matrix is averaged over the background $\mathbf{b}$ and the strength of the signal β . Note that the terms $\langle \langle \langle (\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta))(\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})^t \rangle_{g|\mathbf{b},\beta} \rangle_{\mathbf{b}} \rangle_{\beta}$ and $\langle \langle \langle (\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})(\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta))^t \rangle_{g|\mathbf{b},\beta} \rangle_{\mathbf{b}} \rangle_{\beta}$ of the expansion are equal to zero because

$$\langle (\mathbf{g} - \bar{\mathbf{g}}(\mathbf{b}, \beta)) \rangle_{g|\mathbf{b},\beta} = 0.$$

If $\mathbf{A} \equiv \mathbf{H}[\mathbf{I} + \beta \mathbf{D}_s]$, the second term in $\mathbf{K}_d$ can be written as

$$\begin{aligned} \mathbf{K}_d - \bar{\mathbf{K}}_{nd} &= \langle \langle \langle (\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})(\bar{\mathbf{g}}(\mathbf{b}, \beta) - \bar{\mathbf{g}})^t \rangle_{\mathbf{b}} \rangle_{\beta} \\ &= \langle \langle (\mathbf{A} \mathbf{f}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)(\mathbf{A} \mathbf{f}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)^t \rangle_{\mathbf{f}_b} \rangle_{\beta} \\ &= \langle \langle (\mathbf{A} \mathbf{f}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b + \bar{\mathbf{A}} \bar{\mathbf{f}}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b) \\ &\quad \times (\mathbf{A} \mathbf{f}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b + \bar{\mathbf{A}} \bar{\mathbf{f}}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)^t \rangle_{\mathbf{f}_b} \rangle_{\beta} \\ &= \langle \mathbf{A} \mathbf{K}_{f_b} \mathbf{A}^t \rangle_{\beta} + \langle (\mathbf{A} - \bar{\mathbf{A}}) \bar{\mathbf{f}}_b \bar{\mathbf{f}}_b^t (\mathbf{A} - \bar{\mathbf{A}})^t \rangle_{\beta}, \end{aligned}$$

where $\mathbf{K}_{f_b} = \langle (\mathbf{f}_b - \bar{\mathbf{f}}_b(\theta))(\mathbf{f}_b - \bar{\mathbf{f}}_b(\theta))^t \rangle_{\beta}$ and the other two terms, $\langle \langle (\mathbf{A} \mathbf{f}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)(\bar{\mathbf{A}} \bar{\mathbf{f}}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)^t \rangle_{\mathbf{f}_b} \rangle_{\beta}$ and $\langle \langle (\bar{\mathbf{A}} \bar{\mathbf{f}}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)(\mathbf{A} \mathbf{f}_b - \bar{\mathbf{A}} \bar{\mathbf{f}}_b)^t \rangle_{\mathbf{f}_b} \rangle_{\beta}$, are equal to zero. If we replace $\mathbf{A}$ with $\mathbf{H}[\mathbf{I} + \beta \mathbf{D}_s]$ (because $\mathbf{A} \equiv \mathbf{H}[\mathbf{I} + \beta \mathbf{D}_s]$), we obtain

$$\begin{aligned} \mathbf{K}_d - \bar{\mathbf{K}}_{nd} &= \langle \mathbf{H}(\mathbf{I} + \beta \mathbf{D}_s) \mathbf{K}_{f_b} (\mathbf{I} + \beta \mathbf{D}_s)^t \mathbf{H}^t \rangle_{\beta} \\ &\quad + \langle \mathbf{H}[(\mathbf{I} + \beta \mathbf{D}_s) - (\mathbf{I} + \bar{\beta} \mathbf{D}_s)] \bar{\mathbf{f}}_b \bar{\mathbf{f}}_b^t [(\mathbf{I} + \beta \mathbf{D}_s) \\ &\quad - (\mathbf{I} + \bar{\beta} \mathbf{D}_s)]^t \mathbf{H}^t \rangle_{\beta} \\ &= \langle \mathbf{K}_b + \beta \mathbf{H} \mathbf{D}_s \mathbf{K}_{f_b} \mathbf{H}^t + \beta \mathbf{H} \mathbf{K}_{f_b} \mathbf{D}_s \mathbf{H}^t \\ &\quad + \beta^2 \mathbf{H} \mathbf{D}_s \mathbf{K}_{f_b} \mathbf{D}_s \mathbf{H}^t \rangle_{\beta} \\ &\quad + \langle [(\beta - \bar{\beta}) \mathbf{H} \mathbf{D}_s] \bar{\mathbf{f}}_b \bar{\mathbf{f}}_b^t [(\beta - \bar{\beta}) \mathbf{D}_s]^t \mathbf{H}^t \rangle_{\beta} \\ &= \langle \mathbf{K}_b + \bar{\beta} \mathbf{H} \mathbf{D}_s \mathbf{K}_{f_b} \mathbf{H}^t + \bar{\beta} \mathbf{H} \mathbf{K}_{f_b} \mathbf{D}_s \mathbf{H}^t \\ &\quad + [\sigma_{\beta}^2 + \bar{\beta}^2] \mathbf{H} \mathbf{D}_s \mathbf{K}_{f_b} \mathbf{D}_s \mathbf{H}^t \\ &\quad + \langle (\beta - \bar{\beta})^2 \mathbf{H} \mathbf{D}_s \bar{\mathbf{f}}_b \bar{\mathbf{f}}_b^t \mathbf{D}_s \mathbf{H}^t \rangle_{\beta}. \end{aligned}$$

In this study, $\mathbf{K}_b$ can be decomposed to

$$\mathbf{K}_b = \mathbf{W} \mathbf{W}^t \quad (13)$$

$$[\mathbf{W}]_j = \frac{1}{\sqrt{N-1}} ([\bar{\mathbf{g}}_h]_j - \bar{\mathbf{g}}_h(\theta)), \quad (14)$$

where $[\mathbf{W}]_j$ is the j th column of $\mathbf{W}$, $\bar{\mathbf{g}}_h(\theta)$ is the grand mean (except for the estimates θ) of the N noise-free samples, $\bar{\mathbf{g}}_h$ is the noise-free images, and j is the index of the sample in the training set. We can define $\mathbf{W}_f$ as

$$[\mathbf{W}_f]_j = \frac{1}{\sqrt{N-1}} ([\bar{\mathbf{f}}_h]_j - \bar{\mathbf{f}}_h(\theta)), \quad (15)$$

where $\bar{\mathbf{f}}_h(\theta)$ is the grand mean (except for the estimates θ) of the N noise-free 3D object vectors, $\bar{\mathbf{f}}_h$ is the noise-free 3D object vector, and j is the index of the sample in the training set. The subscript “f” means this is defined in the object space. Then, $\mathbf{K}_b$ can also be decomposed to

$$\mathbf{K}_b = \mathbf{H} \mathbf{W}_f \mathbf{W}_f^t \mathbf{H}^t. \quad (16)$$

$$\mathbf{K}_g = \underbrace{0.5\bar{\mathbf{K}}_{nh} + 0.5\bar{\mathbf{K}}_{nd}}_{A1} + \underbrace{\mathbf{H}\mathbf{W}_f\mathbf{W}_f^t\mathbf{H}^t}_{A2} + \underbrace{0.5\bar{\beta}\mathbf{W}_D\mathbf{W}_D^t}_{A3} + \underbrace{0.5\bar{\beta}\mathbf{W}\mathbf{W}_D^t}_{A4} + \underbrace{0.5[\sigma_\beta^2 + \bar{\beta}^2]\mathbf{W}_D\mathbf{W}_D^t}_{A5} + \underbrace{0.5\sigma_\beta^2\bar{\alpha}_h^2\bar{\mathbf{g}}_u^{df}\mathbf{I}(\bar{\mathbf{g}}_u^{df})^t}_{U5\ C5\ V5}$$

FIG. 9. Method of matrix inversion lemma application.

We can also define $\mathbf{W}_D$ as

$$[\mathbf{W}_D]_j = \mathbf{H}\mathbf{D}_s[\mathbf{W}_f]_j \quad (17)$$

$$\begin{aligned} &= \frac{1}{\sqrt{N-1}}\mathbf{H}\mathbf{D}_s([\bar{\mathbf{f}}_h]_j - \bar{\mathbf{f}}_h(\theta)) \\ &= \frac{1}{\sqrt{N-1}}\mathbf{H}\mathbf{D}_s([\alpha_h\bar{\mathbf{f}}_u^h]_j - \bar{\alpha}_h\bar{\mathbf{f}}_u^h) \\ &= \frac{\alpha_{h_j} - \bar{\alpha}_h}{\sqrt{N-1}}\bar{\mathbf{g}}_u^{df}, \end{aligned} \quad (18)$$

where α_{h_j} is the weighting constant for the heart in the j th testing image (in Table I and Fig. 6), $\bar{\alpha}_h$ is the mean of α_h (the weighting constant), $\bar{\mathbf{f}}_u^h$ is the unit-value heart 3D object vector, and $\bar{\mathbf{g}}_u^{df}$ is the noise-free image of the unit-value defect.

Then, $\mathbf{K}_d$ can be written as

$$\begin{aligned} \mathbf{K}_d &= \bar{\mathbf{K}}_{nd} + \mathbf{K}_b + \bar{\beta}\mathbf{W}_D\mathbf{W}_D^t + \bar{\beta}\mathbf{W}\mathbf{W}_D^t \\ &\quad + [\sigma_\beta^2 + \bar{\beta}^2]\mathbf{W}_D\mathbf{W}_D^t + \sigma_\beta^2\bar{\alpha}_h^2\bar{\mathbf{g}}_u^{df}(\bar{\mathbf{g}}_u^{df})^t, \end{aligned}$$

and $\mathbf{K}_g$ can be written as

$$\begin{aligned} \mathbf{K}_g &= \frac{\mathbf{K}_h + \mathbf{K}_d}{2} \\ &= 0.5\bar{\mathbf{K}}_{nh} + 0.5\bar{\mathbf{K}}_{nd} + \mathbf{K}_b + 0.5\bar{\beta}\mathbf{W}_D\mathbf{W}_D^t + 0.5\bar{\beta}\mathbf{W}\mathbf{W}_D^t \\ &\quad + 0.5[\sigma_\beta^2 + \bar{\beta}^2]\mathbf{W}_D\mathbf{W}_D^t + 0.5\sigma_\beta^2\bar{\alpha}_h^2\bar{\mathbf{g}}_u^{df}(\bar{\mathbf{g}}_u^{df})^t. \end{aligned} \quad (19)$$

Finally, we can use the matrix inversion lemma to obtain $\mathbf{K}_g^{-1}$. The matrix inversion lemma¹⁵ states that if a matrix $\mathbf{B}$ can be decomposed into $(\mathbf{A} + \mathbf{UCV})$, the inverse matrix $\mathbf{B}^{-1}$ can be calculated as

$$\begin{aligned} \mathbf{B}^{-1} &= (\mathbf{A} + \mathbf{UCV})^{-1} \\ &= \mathbf{A}^{-1} - \mathbf{A}^{-1}\mathbf{U}(\mathbf{C}^{-1} + \mathbf{V}\mathbf{A}^{-1}\mathbf{U})^{-1}\mathbf{V}\mathbf{A}^{-1}, \end{aligned} \quad (20)$$

where the dimension of $\mathbf{A}$ and $\mathbf{B}$ is $M \times M$, the dimension of $\mathbf{U}$ is $M \times N$, the dimension of $\mathbf{C}$ is $N \times N$, and the dimension

of $\mathbf{V}$ is $N \times M$. In our work, M is the number of pixels and N is the number of samples. We can simply choose

$$\mathbf{C} = \mathbf{I}, \quad (21)$$

where $\mathbf{I}$ is the identity matrix in our work. As shown in Fig. 9, the inverse covariance matrix $\mathbf{K}_g^{-1}$ can be calculated if we know $A5$ and let $U5$, $C5$, $V5$ be equal to $\bar{\mathbf{g}}_u^{df}$, $\mathbf{I}$, $(\bar{\mathbf{g}}_u^{df})^t$, respectively. As shown in Fig. 9, we must compute the inverse of the $A1$ block before we can compute the block $A2$ inverse, and so forth. Therefore, we need to know the inverse of the $A1$ block first if, and then progress through to the compute inversion of the entire $A5$ block. In our work, photon counting detectors were applied. The noise covariance matrices $\bar{\mathbf{K}}_{nh}$ and $\bar{\mathbf{K}}_{nd}$ are diagonal and the inverse matrices can be calculated easily. With the $A1$ inverse known, we can get the inverse covariance matrix $\mathbf{K}_g^{-1}$.

Because three signal locations and seven signal sizes are simulated, 21 inverse covariance matrices are generated: $\mathbf{K}_{gay}^{-1}$ for the $y = 2 - 8$ mm signal in the LAD, $\mathbf{K}_{gxy}^{-1}$ for the $y = 2 - 8$ mm signal in the LCX, and $\mathbf{K}_{gry}^{-1}$ for the $y = 2 - 8$ mm signal in the RCA. Once the covariance matrices are computed, the training of the observer is complete.

The next step is to obtain estimates placing $\mathbf{g}$, one sample from the testing pool, in Eq. (7). If the maximum value of 21 $\hat{\theta}_{SL}(\mathbf{g})$ outputs is larger than some specific threshold (scans from $-\infty$ to ∞ , the same as the thresholds of the ROC curves) in each test, the corresponding parameters are the estimated defect location and radius from the SLO. For convenience, the output or the likelihood $\hat{\theta}_{SL}(\mathbf{g})$ for the cases of defects at the LAD with 2 mm, 3 mm, etc. are denoted as $\text{SLO}_{\text{LAD}2\text{mm}}$, $\text{SLO}_{\text{LAD}3\text{mm}}$, etc. For example, if $\text{SLO}_{\text{RCA}6\text{mm}}$ has the largest value and is larger than the preselected threshold, then the SLO estimates that the defect is located in the RCA with a radius of 6 mm. The flow chart in Fig. 10 illustrates the application of the SLO.

FIG. 10. Method of SLO application.

After the SLO is applied, the results can be summarized using the LROC/EROC curves.^{9,16} The SLO not only attempts to localize the position of the signals but also estimates the size of the defect. Therefore, it is possible that the true positive fraction (TPF) of the LROC/EROC curves does not reach a maximum value of 1.0 as traditional ROC curves do. Before the LROC/EROC curves are plotted, we need to define a true positive (TP). This study uses three definitions for a TP.

In the first definition, the SLO needs to correctly predict the exact class of the signal location and size. For example, if the hypothesis is “LAD 4 mm” (defect is at the LAD with a radius of 4 mm), only if the SLO predicts that the signal belongs to the class “LAD 4 mm” can it be considered a TP. This is the original definition, and it represents a stringent requirement. This definition is denoted as “L+R.” Under this definition, we will obtain EROC curves because they include information on signal localization and size estimation.

Second, if only the locations of defects are considered, the definition is denoted as “L-only.” The 21 signal-present classes can be merged to three classes. Under this definition, we will obtain LROC curves because they include only information on signal localization.

Third, we can also define a TP in which the SLO predicts the class having the correct signal location and signal size within some error tolerance. We denote this as “L+R($\epsilon \leq 1$ mm)” because classes with the correct signal location and signal size within a 1-mm (user-defined) range are considered to be TPs. For example, we accept the SLO-predicted classes “LAD 3 mm,” “LAD 4 mm,” and “LAD 5 mm” as TPs if the signal is “LAD 4 mm.” In practical cases, a system prediction will not be regarded as a critical miss only if the estimated radius is 5 mm when the real signal size is 4 mm. Under this definition, we will obtain EROC curves because they include the information on signal localization and size estimation (with a larger error tolerance than the first definition).

III. RESULTS

The output of the SLO can be presented in several formats. In this study, histograms and LROC/EROC curves are shown. Figure 11 shows the histograms of estimated radii for a specific defect radius. For example, the leftmost figure in the top row is the histogram of radii that the SLO predicted for a 2 mm defect. The figure shows that under the condition of predicting the locations of defects correctly, roughly 1400 of the total 3000 testing images were correctly predicted as 2 mm defects by the SLO, roughly 400 of the images with a radius of 3 mm were predicted, and so on.

The other way of showing the SLO outputs is to use the LROC/EROC curves. In all the plots, x-axis shows the false positive fraction (FPF) and the y-axis shows the TPF. For “L+R,” the results are shown in Fig. 12.

The solid line represents the output EROC curve of this pool of 22 000 testing images, and the dashes represent the error bars. The binomial approach was applied here to obtain the data range of this limited samples test. For the binomial probability, the variance can be calculated as¹⁷

$$\sigma^2 = Np(1 - p), \quad (22)$$

FIG. 11. GE27 histogram.

$$\sigma = \sqrt{Np(1 - p)}, \quad (23)$$

$$\frac{\sigma}{N} = \sqrt{\frac{p(1 - p)}{N}}, \quad (24)$$

where p is the probability of an occurrence and N is the total number of tests. The SLO outputs for the signal-present images are TPs or not TPs; the TPF, the number of TPs over the total number of signal-present images, is an estimate of the probability of being a TP. We can also treat the FP and FPF similarly. We can use the TPF or the FPF as p , such that σ is the standard deviation of TPs or FPs and $\frac{\sigma}{N}$ is then the standard deviation of the TPF or the FPF. The total number of samples in the testing data set N is the number of total signal-present or signal-absent images; here, N is 21 000 for signal-present images and 1000 for signal-absent images. The effect of the total number of samples in the training set N_{train} is not shown in the LROC/EROC plot. However, without sufficient samples N_{train} in the training dataset, the observer's performance will be biased.¹⁸ The value $\sqrt{\sigma_{\text{TPF}}^2 + \sigma_{\text{FPF}}^2}$ is roughly

FIG. 12. Estimation of locations and radii.

FIG. 13. Estimation of locations and radii, 1 mm tolerance.

the range of the error bars on the LROC/EROC curve and can be plotted.

For “L+R($e \leq 1$ mm),” the corresponding EROC curves with error bars are shown in Fig. 13.

For “L-only,” the LROC curves with error bars are shown in Fig. 14.

If the LROC/EROC curves are shown together on the same plot, the performance of all three systems can be compared (Fig. 15).

The area under the LROC/EROC curve (AULC/AUEC) and TPF at a specific FPF can be treated as the figures of merit. The accuracy of radii estimation is presented in Tables II and III. Here, Δ represents the difference between the values of the systems. The standard deviations of the three systems are presented in Tables IV and V. We applied the binomial approach to calculate the standard deviation of the TPF at FPF = 5%, and we applied one-shot estimation¹⁹ to estimate the standard deviation for the AULC / AUEC values.

FIG. 14. Estimation of locations.

FIG. 15. Comparison of all three systems in the same plots.

TABLE II. AULC/AUEC.

	GE13	Δ	GE19	Δ	GE27
L+R	0.4786	0.0229	0.5015	0.0023	0.5038
L($e \leq 1$ mm)	0.8329	0.0159	0.8488	0.0057	0.8545
L-only	0.8708	0.0159	0.8867	0.0041	0.8908

TABLE III. TPF values for FPF = 5%.

	GE13 (%)	Δ (%)	GE19 (%)	Δ (%)	GE27 (%)
L+R	41.14	2.98	44.12	0.39	44.51
L($e \leq 1$ mm)	73.55	2.91	76.46	0.64	77.10
L-only	77.30	2.93	80.23	0.48	80.71

TABLE IV. One-shot estimation error of AULC/AUEC.

	GE13	GE19	GE27
L+R	0.0035	0.0035	0.0035
L($e \leq 1$ mm)	0.0029	0.0027	0.0026
L-only	0.0026	0.0024	0.0024

TABLE V. Standard deviation of TPF values for FPF = 5%.

	GE13 (%)	GE19 (%)	GE27 (%)
L+R	0.768	0.770	0.770
L($e \leq 1$ mm)	0.753	0.749	0.748
L-only	0.747	0.742	0.741

FIG. 16. Reconstructions for the three systems.

The LROC/EROC curves show that the performance of the GE19 system is comparable with that of the GE27 system, although the GE19 system has only $\sim 70\%$ as many detectors. The GE13 system requires even fewer detectors (only 13) and its performance is acceptable. However, its detectability is not on the same level as those of the other two systems. Examples of signal-absent and signal-present reconstructions for each system are shown in Fig. 16.

IV. CONCLUSION AND DISCUSSION

This study shows that a combination of the LROC/EROC curves and the SLO can be a useful tool for assessing and comparing different system designs when the task is both to detect an abnormality and to estimate signal parameters including location/size. In an assessment of three systems based on the design of the GE CZT-based dedicated cardiac SPECT camera Discovery 530c, the GE27 and GE19 systems gave almost the same results, whereas the GE13 system was slightly inferior to the other two, but with half the cost owing to the use of fewer CZT detectors. The assessment of the three systems indicates that eight expensive detectors (30% of the detector units) can be removed with confidence, and the resulting GE19 system yields estimations and cardiac defect detectability very close to those of the GE27 system. For radii estimation with a 1 mm tolerance, the AUEC values of the GE27 and GE19 systems are 0.8545 and 0.8488, and the TPF at FPF = 5% values are 77.1% and 76.46%, respectively. Although the GE13 design has only an acceptable detectability of cardiac defects, it is still a good design because it incurs less than half the manufacturing costs of the GE27 system.

We demonstrated that the SLO can be used to detect defects and estimate their sizes and locations. This study was performed using 24 computing cores with 8 GB of memory per core. It took several days to generate a single projection using our physical model and very fine voxel spacing ($480 \times 480 \times 480$). These methods generalize to more complicated signal models and can include scattering. However, owing to

computational limitations, these factors were not included in this initial study.

In this study, we chose to study cardiac defects having the same brightness (20%–30% of the heart uptake) regardless of the defect size. Another good approach to study cardiac defects is to fix the product of the extent (size) and severity (defect contrast). However, it would be confusing to present more than one task in a single paper. Because we used most of the parameters (e.g., for organ uptakes) from the work of He *et al.*,² we chose to use the same setting (defect contrast is 20%–30% of the heart uptake) and performed the SLO for the preliminary tests in this study.

If there are more than three possible defect locations, we expect the LROC/EROC curves to slightly decrease if the distance between two possible locations is larger than the system resolution and the signals maintain the same brightness. If the brightness of the signals decreases or the distance between two possible locations is smaller than the system resolution, the SLO will not be able to maintain the same detectability and the LROC/EROC curves will further decrease.

In this study, we studied systems with 27, 19, and 13 detectors. When the number of detectors is decreased by more than a factor of 3 (from the GE27 to the GE13), the stochastic image noise is expected to increase by more than 41% for equal time imaging. Our results show that the AUEC and TPF values for FPF = 5% are changed by just 2%–3% when the number of detectors is reduced from 27 to 13. Presumably, this is because a larger source of variability in this study arose from subject-to-subject variability and/or from the complexity of the task considered (i.e., the requirement of determining defect size and location as well as simply defect presence or absence), rather than just from stochastic image noise. It is also possible that the activity uptake and defect conditions (range of size and severity) were not sufficiently challenging to demonstrate a larger degradation in performance when using half the number of detectors. However, the brightness of the defects and the range of individual organ uptakes are from the work of He *et al.*² and these numbers come from clinical studies. As a result, the stochastic effect is not obvious in our

study. We have stated that we have not included photon scatter in this preliminary assessment. Once scatter is included, the LROC/EROC curves will decrease and the stochastic effect might become more obvious. Moreover, the ranges in viewing angles (Fig. 2) of the GE27 and GE13 systems are very similar even though the number of detectors decreases from 27 to 13. Thus, it is also possible that we placed too many detectors in a small range such that we do not get more information by adding detectors.

Zhou *et al.*⁵ showed that they can achieve the goal of optimization of traditional SPECT systems. They focused on changing the parameters of the collimator (a tradeoff between the collimator spatial resolution and the system count efficiency). We did not explicitly address the tradeoff between spatial resolution and system efficiency; instead, we focused on the effect of changing the total number and position of the detectors on the detection, localization, and estimation tasks for pinhole SPECT systems. We showed that the task performance for the GE19 system is nearly equivalent to that of the GE27 system. This implies that the system can achieve similar performance with eight fewer detectors, thereby cutting the costs substantially. McQuaid *et al.*²⁰ mentioned that in clinical practice, most tasks are performed using reconstructed images, and hence, determining how best to optimize the SPECT system for such tasks is an important consideration. In our study, the assessment of systems using the SLO does not necessarily correlate with human observer performance on reconstructed images. However, our analysis provides a systematic method for ranking hardware performance without the complications associated with selecting a proper reconstruction algorithm. In other words, our method approximates an upper bound on performance, which we use to quantify the utility of a particular imaging system. Issues such as reconstruction artifacts and postreconstruction smoothing do not affect our analysis. Artifacts from limited angular sampling and projection-data truncation would only be seen in reconstructed images, not in projection images. Such effects, if they are present, would definitely be related to the number and placement of pinholes and detectors, and could certainly affect human observer performance in detection tasks such as that considered in this study, even though they may have no apparent influence whatsoever on projection images and would not influence the LROC/EROC curves computed using the approach described here. We are taking the approach that the system hardware should be optimized to allow the best possible performance. Reconstruction and postprocessing can then be studied to produce images that allow human observers to best perform the relevant tasks. In the future, we plan to analyze the efficiency of reconstruction algorithms based on task performance to gain a better understanding of the overall performance.

ACKNOWLEDGMENTS

This research was supported by National Institutes of Health (NIH) Grant No. RC1-EB010974.

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