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Adaptive Angular Sampling for SPECT Imaging

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Abstract

This paper presents an analytical approach for performing adaptive angular sampling in single photon emission computed tomography (SPECT) imaging. It allows for a rapid determination of the optimum sampling strategy that minimizes image variance in regions-of-interest (ROIs). The proposed method consists of three key components: (a) a set of close-form equations for evaluating image variance and resolution attainable with a given sampling strategy, (b) a gradient-based algorithm for searching through the parameter space to find the optimum sampling strategy and (c) an efficient computation approach for speeding up the search process. In this paper, we have demonstrated the use of the proposed analytical approach with a single-head SPECT system for finding the optimum distribution of imaging time across all possible sampling angles.

Compared to the conventional uniform angular sampling approach, adaptive angular sampling allows the camera to spend larger fractions of imaging time at angles that are more efficient in acquiring useful imaging information. This leads to a significantly lowered image variance. In general, the analytical approach developed in this study could be used with many nuclear imaging systems (such as SPECT, PET and X-ray CT) equipped with adaptive hardware. This strategy could provide an optimized sampling efficiency and therefore an improved image quality.

Index Terms

Adaptive angular sampling; non-uniform object-space pixelation (NUOP) approach; single photon emission computed tomography (SPECT)

I. Introduction

Single photon emission computed tomography (SPECT) is a commonly used nuclear imaging modality for small animal studies [1], [2]. One of the recent emphases in SPECT instrumentation is to push for higher spatial resolution. Examples of recent developments include the SemiSPECT reported by Kastis *et al.* [4], the SiliSPECT under development by Peterson *et al.* [5], the MediSPECT proposed (and evaluated) by Accorsi *et al.* [6] and the U-SPECT-III proposed by Beekman *et al.* [7], a low-cost ultra-high resolution imager based on the second-generation image intensifier [8] and the use of a pre-existing SPECT camera, arranged in an extreme focusing geometry for ultra-high resolution small animal SPECT imaging applications [9]. We have recently developed a prototype ultra-high resolution

single photon emission microscope (SPEM) system for mouse brain studies [10], [11]. This system delivers an ultra-high imaging resolution of around 100 μm in phantom studies. It was demonstrated that the current dual-headed SPEM system is capable of visualizing a very small number of radiolabeled cells in mouse brain [12]. Despite these promising results, the performance of the SPEM system is limited by the common bottleneck for ultra-high resolution SPECT instrumentations—the limited detection efficiency. Even with the large number of pinholes in the entire system, the overall detection efficiency for the SPEM system is typically 10^{-4} or lower. The long imaging time required for ultra-high resolution studies could preclude many interesting applications.

This problem could be partially alleviated by using the adaptive imaging concept proposed by Barrett *et al.* [13], Clarkson *et al.* [14] and Freed *et al.* [15]. In an adaptive SPECT system, the system hardware could vary in real-time to maximize the efficiency for collecting useful imaging information regarding a given task, and therefore provide an optimum imaging performance. In [12] (Fig. 12), we have proposed the use of a variable aperture system with four sets of apertures that can be interchanged during an imaging study. Therefore, apertures with larger pinholes can be used for localizing the target-region and highly focusing ultra-high resolution apertures can then be used for a closer examination of the target region.

In this paper, we propose an analytical approach for adaptive angular sampling in SPECT imaging. This approach assigns a non-uniform distribution of imaging times across all possible sampling angles, and the actual sampling strategy will be determined based on the relative importance of each angle for collecting useful imaging information regarding a given imaging task. With the adaptive angular sampling approach, an imaging study could start with a uniform time distribution across all possible angles. During the study, the imaging information being acquired and the input from the user (e.g., the target-region to be examined) will be used to determine the optimum time distribution based on the expected system performance measured with certain analytical performance indices.

The adaptive angular sampling approach requires an efficient computation method for searching through the parameter space to find the optimum time distribution in real time. For this purpose, we have proposed a search algorithm that utilizes the gradient function of certain system performance indices, such as image variance, with respect to imaging times at individual angles. To allow for a rapid optimization process, we have also incorporated a non-uniform object-space pixelation (NUOP) scheme that uses different pixel sizes adaptively according to the characteristics of the object and the input from the user [3]. By combining the gradient-based search algorithm and the NUOP approach, one can refine the angular sampling strategy adaptively during an imaging study in near real time to achieve an improved image quality.

Although we have focused on the problem of adaptive angular sampling in SPECT, the basic approach developed in this study could be applied to optimize other adaptive imaging systems, such as SPECT, PET and X-ray CT [15], [16], with respect to a wide range of design and imaging parameters. In practice, most of adaptive imaging systems are (likely to be) designed with a finite number of possible imaging configurations. For such systems, one

could find the best sampling strategy indirectly, by deriving the optimum time-sharing scheme among all possible configurations using the proposed computation approach.

II. Material and Methods

A. SPECT Image Formation

Let $\mathbf{x} = [x_1, x_2, \dots, x_N]^T$ denote a series of unknown deterministic parameters, e.g., the object intensities underlying the projection data $\mathbf{y} = [y_1, y_2, \dots, y_M]^T$. The mapping from $\mathbf{x}$ to $\mathbf{y}$ is governed by a conditional probability distribution function, $p_r(\mathbf{y}|\mathbf{x})$. For emission tomography, $\mathbf{y}$ could be approximated as a collection of independent random Poisson variables, whose expectations are given by

$$\bar{y}_m \equiv E[y_m] = \int y_m \cdot p_r(y_m|\mathbf{x}) \cdot dy_m \quad m=1, \dots, M, \quad (1)$$

or by the following discrete transform

$$\bar{\mathbf{y}} = T \cdot \bar{\mathbf{p}},$$

and

$$\bar{\mathbf{p}} = A \cdot \mathbf{x}. \quad (2)$$

$E[\cdot]$ denotes the expectation operator. In (2), we have assumed that the same imaging time T is spent at all individual sampling angles. $\bar{\mathbf{p}}$ is the mean projection with a unit imaging time. A is a $M \times N$ matrix that represents the discretized system-response function (SRF). Here we have assumed that all systematic errors are corrected in the projection data. For Poisson variables $\mathbf{y}$, the log-likelihood function is given by

$$L(\mathbf{x}, \mathbf{y}) \equiv \log p_r(\mathbf{y}|\mathbf{x}) = \sum y_m \log \bar{y}_m - \bar{y}_m, \quad (3)$$

and

$$\bar{y}_m = \sum_n a_{mn} x_n, \quad (4)$$

where a_{mn} gives the probability of a gamma-ray emitted from the n 'th source voxel and detected by the m 'th detector pixel with a unit imaging time. The underlying image function may be reconstructed as

$$\begin{cases} \hat{\mathbf{x}}_{PML}(\mathbf{y}) = \arg \max_{\mathbf{x} \geq 0} [L(\mathbf{x}, \mathbf{y}) - \beta \cdot R(\mathbf{x})] \\ \text{and then} \\ \hat{\mathbf{x}}_{PF-PML} = \mathbf{F} \cdot \hat{\mathbf{x}}_{PML}(\mathbf{y}), \end{cases} \quad (5)$$

where $R(\mathbf{x})$ is a scalar function that selectively penalizes certain undesired features in reconstructed images. β is a parameter that controls the degree of regularization. $\mathbf{F}$ is an $N \times N$ matrix that represents the post-filtering operator. In this study, we used a quadratic roughness penalty function as defined by [17]:

$$R(\mathbf{x}) = \sum_j \frac{1}{2} \sum_k w_{jk} \phi(x_j - x_k), \quad (6)$$

where w_{jk} s are the weighting factors that are non-zero for the pairs of immediate neighbors, and

$$\phi(\theta) = \theta^2 / 2. \quad (7)$$

Note that the computation approach developed below would allow the use of many other forms of regularization functions.

B. Approximations for Imaging Resolution and Covariance Properties With the Adaptive Angular Sampling Approach

In this study, we chose to determine the optimum angular sampling strategy based on the resolution and (co)variance properties of reconstructed images. More specifically, the optimum sampling strategy is chosen to be the one that delivers the lowest image variance at given spatial resolutions. The optimization process is implemented based on the modified uniform Cramer-Rao bounds (MUCRBs) detailed in [18], [19]. In this section, we will modify the original MUCRB formulations to incorporate the proposed adaptive sampling strategy.

Suppose one uses a single-head SPECT system for imaging an object from a total of K sampling angles. The imaging time spent at k 'th sampling angle is denoted by $t^{(k)}$. $\mathbf{t} = [t^{(1)}, t^{(2)} \dots t^{(K)}]^T$ could represent a non-uniform imaging time distribution. The mean projections are given by:

$$\bar{\mathbf{y}}^{(k)} = \mathbf{t}^{(k)} \cdot \bar{\mathbf{p}}^{(k)},$$

and

$$\bar{\mathbf{p}}^{(k)} = \mathbf{A}^{(k)} \cdot \mathbf{x}, \quad k=1 \cdots K. \quad (8)$$

Note that the vectors and matrices with superscript (k) are corresponding to observing the object with a single camera placed at the k 'th angle only. In this study, the Fisher information matrix (FIM) [20] was defined explicitly as a function of the imaging times, with its elements given by

$$\mathbf{J}_{ij}(\mathbf{t}) = -E \left[\frac{\partial^2}{\partial x_i \partial x_j} L(\mathbf{x}, \mathbf{y}, \mathbf{t}) \right]. \quad (9)$$

The corresponding log-likelihood function can be written as:

$$\begin{aligned} L(\mathbf{x}, \mathbf{y}, \mathbf{t}) &= \sum_{m=1}^M (y_m \log \bar{y}_m - \bar{y}_m) \\ &= \sum_{k=1}^K \left[\sum_{m=1}^{M^{(k)}} \left(y_m^{(k)} \log t^{(k)} \bar{p}_m^{(k)} - t^{(k)} \bar{p}_m^{(k)} \right) \right] \\ &= \sum_{k=1}^K \left[L^{(k)}(\mathbf{x}, \mathbf{y}, \mathbf{t}) \right], \end{aligned} \quad (10)$$

where

$$L^{(k)}(\mathbf{x}, \mathbf{y}, \mathbf{t}) \equiv \sum_{m=1}^{M^{(k)}} \left(y_m^{(k)} \log t^{(k)} \bar{p}_m^{(k)} - t^{(k)} \bar{p}_m^{(k)} \right). \quad (11)$$

$L^{(k)}(\mathbf{x}, \mathbf{y}, \mathbf{t})$ is the log-likelihood function for the measurement acquired with the camera at the k 'th angle only.

Substituting (10) into (9), the FIM for non-uniform angular sampling approach is given by:

$$\begin{aligned}
\mathbf{J}_{ij} &= -E \left[\frac{\partial^2}{\partial x_i \partial x_j} L(\mathbf{x}, \mathbf{y}, \mathbf{t}) \right] \\
&= -E \left[\frac{\partial^2}{\partial x_i \partial x_j} \sum_{k=1}^K \sum_{m=1}^{M^{(k)}} \left(y_m \log t^{(k)} \bar{p}_m^{(k)} - t^{(k)} \bar{p}_m^{(k)} \right) \right] \\
&= -E \left\{ \sum_{k=1}^K \sum_{m=1}^{M^{(k)}} \left[\frac{\partial^2}{\partial x_i \partial x_j} \left(y_m \log t^{(k)} \bar{p}_m^{(k)} - t^{(k)} \bar{p}_m^{(k)} \right) \right] \right\} \\
&= E \left\{ \sum_{k=1}^K \sum_{m=1}^{M^{(k)}} \left[y_m \frac{a_{mi}^{(k)} a_{mj}^{(k)}}{\left[\bar{p}_m^{(k)} \right]^2} \right] \right\} \\
&= \sum_{k=1}^K \sum_{m=1}^{M^{(k)}} \left[E[y_m] \cdot \frac{a_{mi}^{(k)} a_{mj}^{(k)}}{\left[\bar{p}_m^{(k)} \right]^2} \right] \\
&= \sum_{k=1}^K \left[t^{(k)} \sum_{m=1}^{M^{(k)}} \frac{a_{mi}^{(k)} a_{mj}^{(k)}}{\bar{p}_m^{(k)}} \right]. \tag{12}
\end{aligned}$$

Note that (12) can be re-written as:

$$\begin{aligned}
\mathbf{J}_{ij} &= -E \left[\frac{\partial^2}{\partial x_i \partial x_j} L(\mathbf{x}, \mathbf{y}, \mathbf{t}) \right] = \sum_{k=1}^K t^{(k)} \mathbf{J}_{ij}^{(k)(0)}, \\
\text{with } \mathbf{J}_{ij}^{(k)(0)} &= \sum_{m=1}^{M^{(k)}} \frac{a_{mi}^{(k)} a_{mj}^{(k)}}{\bar{p}_m^{(k)}}. \tag{13}
\end{aligned}$$

The second equation in (13) can be re-written in the matrix form as

$$\mathbf{J}^{(k)(0)} = \left(\mathbf{A}^{(k)} \right)^T \text{diag} \left\{ \frac{1}{\bar{p}_m^{(k)}} \right\} \cdot \mathbf{A}^{(k)}, \tag{14}$$

and the overall FIM is given by

$$\mathbf{J} = \sum_{k=1}^K \mathbf{J}^{(k)} = \sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)}, \tag{15}$$

where $\mathbf{J}^{(k)(0)}$ is the FIM with measurements acquired with a unit time spent at the k 'th angle only.

Substituting (15) into (23), (32) and (33) in [19], the covariance of images reconstructed with post-filtered penalized maximum likelihood algorithm, given by (5), can be approximated as

$$Cov[\hat{\mathbf{x}}] \approx \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \mathbf{F}^T. \quad (16)$$

The variance on the j th pixel could therefore be approximately given by,

$$Var[\hat{\mathbf{x}}_j] \approx \mathbf{e}_j^T \cdot \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \mathbf{F}^T \cdot \mathbf{e}_j, \quad (17)$$

where $\mathbf{e}_j$ is the j th unit vector. The mean gradient matrix of the corresponding reconstruction can be approximated as

$$\mathbf{G}(\mathbf{x}) = \frac{\partial E(\hat{\mathbf{x}})}{\partial \mathbf{x}} \approx \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right). \quad (18)$$

The j th column vector of $\mathbf{G}(\mathbf{x})$ represents the local impulse response function centered at the j th pixel in the object-space [21], obtained with the reconstruction process (5). Based on (16) and (18), we can compare given time distributions based on the minimum imaging variance attainable at given spatial resolutions. This method, typically referred to as the resolution-variance tradeoff, has been used extensively for optimizing the design of emission tomography systems [3], [10], [18], [19], [22], [23].

In addition, one could also compare different imaging configurations based on their performance for ROI quantification. If the boundary of the ROI is well-defined, one can approximately derive the variance and bias for the estimated total uptake in ROI with the following steps. The total tracer-uptake in the ROI could be obtained by

$$tr(\hat{\mathbf{x}}) = \mathbf{z}^T \cdot \hat{\mathbf{x}}, \quad (19)$$

where $\mathbf{z}$ is an indicator vector for the ROI,

$$\mathbf{z} = \{z_j\}^T, \quad z_j = \begin{cases} 1 & j \in ROI \\ 0 & \text{otherwise.} \end{cases} \quad (20)$$

Using (17) and (18), the variance and bias values associated with $tr(\hat{\mathbf{x}})$, obtained with the reconstruction process (5), (7) and (19), can be approximately given by

$$\begin{aligned} Var_{ROI} [tr(\hat{\mathbf{x}})] &\approx \mathbf{z}^T \cdot \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \\ &\cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) \\ &\cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \\ &\cdot \mathbf{F}^T \cdot \mathbf{z}, \end{aligned} \quad (21)$$

$$\begin{aligned} Bias_{ROI} [tr(\hat{\mathbf{x}})] &\approx \mathbf{z}^T \cdot \mathbf{F}^T \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \\ &\cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) \cdot \mathbf{x} - \mathbf{z}^T \cdot \mathbf{x}. \end{aligned} \quad (22)$$

In principle, one could apply (17)–(22) to derive the resolution-variance and bias-variance tradeoffs and use these quantities as the basis to find an optimum time distribution. However, even with these close-form solutions, the computation load for searching through all possible time distributions could be too high for regular PC-based computation environments. To allow near real-time optimization of the imaging time distribution, we will introduce a gradient-based search algorithm for finding the optimum time distribution.

C. Partial Derivatives of Variance With Respect to Imaging Times

In order to develop a systematic approach for minimizing the image variance with respect to the distribution of a finite total imaging time, we first formulated a solution for the partial derivatives of the variance with respect to individual imaging times. This would help us to rank the relative-importance of each sampling angle for reducing image variance.

$$\begin{aligned} &\frac{\partial}{\partial t^{(k)}} Var [\hat{x}_j (t^{(1)} \dots, t^{(k)}, \dots, t^{(K)})] \\ &= \lim_{\delta \rightarrow 0} \frac{Var [\hat{x}_j (t^{(1)} \dots, t^{(k)} + \delta, \dots, t^{(K)})] - Var [\hat{x}_j (t^{(1)} \dots, t^{(k)}, \dots, t^{(K)})]}{\delta}. \end{aligned}$$

The partial derivative of image variance on reconstructed pixel j , with respect to $t^{(k)}$, is given by (see equation (23) at the bottom of the page).

To evaluate the partial derivatives, we first introduce a small disturbance δ to $t^{(k)}$ and the corresponding variance becomes

$$\begin{aligned} \text{Var} \left[\hat{x}_j \left(t^{(1)}, t^{(2)} \dots, t^{(k)} + \delta, \dots, t^{(K)} \right) \right] &\approx \mathbf{e}_j^T \\ &\cdot \mathbf{F} \cdot \left[\mathbf{J} + \beta \cdot \mathbf{R} + \delta \cdot \mathbf{J}^{(k)(0)} \right]^{-1} \\ &\cdot \left(\mathbf{J} + \delta \cdot \mathbf{J}^{(k)(0)} \right) \\ &\cdot \left[\mathbf{J} + \beta \cdot \mathbf{R} + \delta \cdot \mathbf{J}^{(k)(0)} \right]^{-1} \cdot \mathbf{F}^T \cdot \mathbf{e}_j. \end{aligned} \quad (24)$$

For small δ , one could use the matrix inversion lemma [24], which gives

$$\left[\mathbf{J} + \beta \cdot \mathbf{R} + \delta \cdot \mathbf{J}^{(k)(0)} \right]^{-1} \approx \left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1} - \delta \cdot \left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot \left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1}. \quad (25)$$

To simplify the derivation, we defined matrix $\mathbf{M}$ as

$$\mathbf{M} = \left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot \left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1}. \quad (26)$$

Therefore (25) becomes

$$\left[\mathbf{J} + \beta \cdot \mathbf{R} + \delta \cdot \mathbf{J}^{(k)(0)} \right]^{-1} \approx \left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1} - \delta \cdot \mathbf{M}. \quad (27)$$

Substituting (27) into (24), one has

$$\begin{aligned} \text{Var} \left[\hat{x}_j \left(t^{(1)} \dots, t^{(k)} + \delta, \dots, t^{(K)} \right) \right] &\approx \mathbf{e}_j^T \cdot \mathbf{F} \cdot \left(\left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1} - \delta \cdot \mathbf{M} \right) \cdot \left(\mathbf{J} + \delta \cdot \mathbf{J}^{(k)(0)} \right) \cdot \left(\left[\mathbf{J} + \beta \cdot \mathbf{R} \right]^{-1} - \delta \cdot \mathbf{M} \right) \cdot \mathbf{F}^T \cdot \mathbf{e}_j. \\ &\quad (28) \end{aligned}$$

Substituting (28) into (23) and letting δ approach zero, the partial derivatives become

$$\begin{aligned}
\frac{\partial}{\partial t^{(k)}} \text{Var} \left[\hat{\mathbf{x}}_j \left(t^{(1)} \dots, t^{(k)} + \delta, \dots, t^{(K)} \right) \right] &= \mathbf{e}_j^T \cdot \mathbf{F} \cdot ([\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} - \mathbf{M} \cdot \mathbf{J} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} - [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J} \\
&= \mathbf{e}_j^T \cdot \mathbf{F} \cdot \left\{ [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} - 2 \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \right\} \cdot \mathbf{F}^T \cdot \mathbf{e}_j
\end{aligned}
\tag{29}$$

With (29), one could derive the gradient of imaging variance on the j 'th pixel with respected to the time distribution as

$$\nabla_{t=[t^{(1)}, t^{(2)}, \dots, t^{(K)}]} \{ \text{Var}[\hat{\mathbf{x}}_j] \} = \left\{ \frac{\partial \text{Var}[\hat{\mathbf{x}}_j]}{\partial t^{(1)}}, \frac{\partial \text{Var}[\hat{\mathbf{x}}_j]}{\partial t^{(2)}}, \dots, \frac{\partial \text{Var}[\hat{\mathbf{x}}_j]}{\partial t^{(K)}} \right\}. \tag{30}$$

D. A Gradient-Based Approach for Optimizing the Angular Sampling Strategy

To find the optimum distribution of sampling times that delivers the minimum image variance, we have proposed an iterative algorithm that uses the gradient function given by (29), (30). At the beginning of each iteration, the partial derivatives of the image variance with respect to $t^{(k)}$ s are evaluated using (29), and then an average value across all partial derivatives is derived. To proceed to the next iteration, the imaging time for each sampling angle will be either increased or decreased, depending on the difference between the corresponding partial derivative value and the average value. This process is kept repeated iteratively, until the image variance is stabilized around its minimum value. This algorithm is sketched in Fig. 1. Several aspects of the proposed search algorithm are discussed below.

- The proposed computation approach involves frequent evaluations of the Fisher information matrix (FIM) given by (13)–(15), which requires the mean projections $\bar{p}_m^{(k)}$. Although the mean projections are readily available in Monte Carlo studies, these will not be available in experimental studies for an unknown object. In the latter case, one could use the measured (noisy) projections instead of their mean values in (14), which leads to the *observed* (FIM) [25]. With the adaptive imaging scheme, a possibility is to acquire a set of projection data with a relatively short total imaging time uniformly distributed through all possible angles. One can scale the projection data statistically and use the resultant noisy projections, instead of $\bar{p}_m^{(k)}$, to derive the observed FIM.
- There is no guarantee that the (co)variance given by (16) and (17) are convex functions of the time distribution vector, $\mathbf{t}$. It is possible that the proposed algorithm converges to local minima. In principle, there could be certain object geometries possessing certain symmetry that leads to multiple sampling strategies yielding identical minimum imaging variance values.

- The partial derivatives given by (29) can be evaluated using the following recipe. One could use conjugate gradient method [26] to compute

$$\mathbf{u} = [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{F}^T \cdot \mathbf{e}_j, \quad (31)$$

and then

$$\begin{aligned} \mathbf{v} &= [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J} \cdot \mathbf{u} \\ &= [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{F}^T \cdot \mathbf{e}_j. \end{aligned} \quad (32)$$

The imaging variance on pixel j is therefore

$$\text{Var} \left[\hat{x}_j \left(t^{(1)}, t^{(2)}, \dots, t^{(k)}, \dots, t^{(K)} \right) \right] \approx \mathbf{u}^T \cdot \mathbf{J} \cdot \mathbf{u}, \quad (33)$$

and the partial derivative of the variance with respect to imaging time $t^{(k)}$ is given by

$$\frac{\partial}{\partial t^{(k)}} \text{Var} \left[\hat{x}_j \left(t^{(1)}, t^{(2)}, \dots, t^{(k)}, \dots, t^{(K)} \right) \right] = \mathbf{u}^T \cdot \mathbf{J}^{(k)(0)} \cdot \mathbf{u} - 2 \cdot \mathbf{u}^T \cdot \mathbf{J}^{(k)(0)} \cdot \mathbf{v}. \quad (34)$$

When computing imaging variance and its gradient using (29), (31)–(34), the most computation-intensive steps are the evaluations of vectors $\mathbf{u}$ and $\mathbf{v}$, each requiring the inversion of matrix $(\mathbf{J} + \beta \mathbf{R})$. With the current geometry (detailed in Section II-F) the total number of non-zero elements in $(\mathbf{J} + \beta \mathbf{R})$ is at the order of 10^9 . Even with the use of sparse matrix and 8 CPUs running in parallel, it took about 3 hours for an inversion of the matrix $(\mathbf{J} + \beta \mathbf{R})$. In general, the amount of computation required for evaluating vectors $\mathbf{u}$ or $\mathbf{v}$ is similar to that for a single image reconstruction. Therefore, the total computation load for evaluating the gradient is about twice that of image reconstruction. Assuming a total of 50 iterations are needed for the gradient-based iterative approach (shown in Fig. 1) for finding the optimum time distribution, the total amount of computation will be close to that for 100 image reconstructions. This highlights the challenge for performing such optimization steps in real-time.

- One could also use a similar approach to optimize the time distribution based on other performance measures, such as the tradeoffs between the variance and bias for quantifying the total uptake in a region-of-interest

(ROI). In this case, the partial derivative of the variance (on the derived ROI value) respect to imaging time $t^{(k)}$ is given by:

$$\begin{aligned} & \frac{\partial}{\partial t^{(k)}} \text{Var}_{ROI}[\text{tr}(\hat{\mathbf{x}})] \\ &= \mathbf{z}^T \cdot \mathbf{F} \cdot \left\{ [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} - 2 \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J}^{(k)(0)} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \cdot \mathbf{J} \cdot [\mathbf{J} + \beta \cdot \mathbf{R}]^{-1} \right\} \cdot \mathbf{F}^T \cdot \mathbf{z} \end{aligned} \quad (35)$$

where $\mathbf{z}$ is the indicator function for the given ROI as defined in (20).

E. Using the Non-Uniform Object-Space Pixelation (NUOP) Approach to Further Reduce the Computation Load

As previously discussed, direct optimization of the time distribution using the proposed search algorithm could be a computation-intensive task. To alleviate this problem, we have adopted a non-uniform object-space pixelation (NUOP) approach, previously developed to improve the computation efficiency for SPECT image reconstruction [3]. With the NUOP approach, the object-space is divided into smaller pixels for target-regions, and into larger pixels in areas that are relatively smooth and/or less important to the reconstruction of the target-region. Compared to the conventional uniform object-space pixelation scheme, the NUOP approach could lead to reconstructions with a much smaller number of unknowns, without sacrificing the image quality in the target-region [3].

The NUOP process is typically performed in three steps. In the first step, the object-space is modeled with sufficiently small and uniformly-sized pixels. The source function represented in this finely-pixelated object-space is symbolized by $\mathbf{x} = [x_1, x_2, \dots, x_N]^T$. This step is performed only one time for a given system and the resultant system-response functions are stored for future use. In the second step, a target-region will be specified based on some prior knowledge, such as a scout image of the object. This image could be obtained in a short study using a uniform imaging time distribution, and/or with apertures having large pinholes to ensure a good counting statistics. One could obtain a quick reconstruction of the scout image with relatively coarse pixels in the object-space [13]. In addition, prior knowledge may also be obtained from other modality imaging, e.g., computed tomography (CT), positron emission tomography (PET), and magnetic resonance imaging (MRI). In the third step, a non-uniform object-space pixelation scheme is defined, according to the target-region chosen in Step 2. Several systematic approaches for defining the NUOP schemes were discussed in [3]. With the NUOP approach, certain pixels originally in the uniform object-space can be combined to form larger pixels. The object-space, after this rebining process, is represented by a new vector $\mathbf{x}_{Rebin} = [(x_{Rebin})_1, (x_{Rebin})_2, \dots, (x_{Rebin})_p]^T$, which would typically have a much smaller number of pixels.

As part of Step 3, a new system-response function (SRF) is needed to reflect the transformation from the non-uniform (or rebinned) object-space to the projection data space.

To simplify the discussion, we defined a transformation matrix S ($N \times P$ in size) as the following:

$$S_{ii'} = \begin{cases} 1 & \text{if pixel } i \text{ in the uniform object space is rebinned into pixel } i' \text{ in the non-uniform object space,} \\ 0 & \text{otherwise.} \end{cases} \quad (36)$$

The new system-response function, A_{Rebin} , could be given by

$$A_{Rebin} = A \cdot S. \quad (37)$$

The expectation of the measurement is related to the underlying source vector (x_{Rebin}) as,

$$\begin{cases} \bar{y} = T \cdot \bar{p}, \\ \bar{p} = A_{Rebin} \cdot x_{Rebin}. \end{cases} \quad (38)$$

Subsequently, the underlying source function can be reconstructed using the penalized maximum-likelihood algorithm,

$$(\hat{x}_{Rebin})_{PML} = \arg \max_{x_{Rebin} \geq 0} [L_{Rebin}(x_{Rebin}, y) - \beta \cdot R_{Rebin}(x_{Rebin})]. \quad (39)$$

The log-likelihood function $L_{Rebin}(x_{Rebin}, y)$ in (39) is given by

$$L_{Rebin}(x_{Rebin}, y) = \sum_{m=1}^M \{y_m \log[\bar{y}_m(x_{Rebin})] - [\bar{y}_m(x_{Rebin})]\}. \quad (40)$$

In this study, we used a quadratic roughness penalty function $R_{Rebin}(x_{Rebin})$ in the non-uniform object-space, which is defined as:

$$R_{Rebin} = S^T \cdot R \cdot S, \quad (41)$$

where matrices R is defined for the uniformly pixelated object-space. According to the definition, if two source functions, represented in uniform and non-uniform object-spaces, are related by

$$\hat{\mathbf{x}} = \mathbf{S} \cdot \hat{\mathbf{x}}_{Rebin}, \quad (42)$$

then the corresponding penalty functions would be identical,

$$\begin{aligned} R_{Rebin}(\hat{\mathbf{x}}_{Rebin}) &= \hat{\mathbf{x}}_{Rebin}^T \cdot \mathbf{R}_{Rebin} \cdot \hat{\mathbf{x}}_{Rebin} \\ &= \hat{\mathbf{x}}_{Rebin}^T \cdot \mathbf{S}^T \cdot \mathbf{R} \cdot \mathbf{S} \cdot \hat{\mathbf{x}}_{Rebin} \\ &= \hat{\mathbf{x}}^T \cdot \mathbf{R} \cdot \hat{\mathbf{x}} = R(\hat{\mathbf{x}}). \end{aligned} \quad (43)$$

For convenience, the estimator, $(\hat{\mathbf{x}}_{Rebin})_{PML}$, could be restored back to the uniform object-space by the following operation

$$\hat{\mathbf{x}}_{Restore} = \mathbf{S} \cdot (\hat{\mathbf{x}}_{Rebin})_{PML}. \quad (44)$$

This restoration process simply assigns the value of each rebinned pixel i' back to those pixels that were originally in the unrebbinned (uniform) object-space, but combined into pixel i' during the rebining process. Finally, we could also filter the resultant estimator, $\hat{\mathbf{x}}_{Restore}$, to obtain a smoother reconstruction:

$$\hat{\mathbf{x}}_{PF-Restore} = \mathbf{F} \cdot \hat{\mathbf{x}}_{Restore} = \mathbf{F} \cdot \mathbf{S} \cdot (\hat{\mathbf{x}}_{Rebin})_{PML}. \quad (45)$$

We have previously demonstrated that the image quality obtained in the target-region with the NUOP approach is essentially unchanged from that obtained with uniform object-space pixelation, but the computation load could be greatly reduced, due to the much reduced dimension of the object-space [3].

The NUOP approach could be adapted for the evaluation of the resolution-variance and bias-variance under the non-uniform angular sampling scheme. Similar to the derivation in the uniformly-pixelated object-space, the Fisher information matrix in non-uniform object-space is given by

$$\mathbf{J}_{Rebin} = \sum_{k=1}^K \left(t^{(k)} \cdot \mathbf{J}_{Rebin}^{(k)(0)} \right), \quad (46)$$

where $\mathbf{J}_{Rebin}^{(k)(0)}$ is the FIM corresponding to the estimation of $\mathbf{x}_{Rebin}$ with projection from the k 'th angle and a unit observation time only,

$$\begin{aligned} \mathbf{J}_{Rebin}^{(k)(0)} &= \left(\mathbf{A}_{Rebin}^{(k)} \right)^T \cdot \text{diag} \left\{ \bar{p}_m^{(k)} \right\} \cdot \mathbf{A}_{Rebin}^{(k)} \\ &= \left(\mathbf{S} \cdot \mathbf{A}^{(k)} \right)^T \cdot \text{diag} \left\{ \bar{p}_m^{(k)} \right\} \cdot \left(\mathbf{S} \cdot \mathbf{A}^{(k)} \right). \end{aligned} \quad (47)$$

Similar to (16), we have the corresponding covariance matrix for $(\hat{\mathbf{x}}_{Rebin})_{PML}$ approximately given by

$$\text{Cov}[(\hat{\mathbf{x}}_{Rebin})_{PML}] \approx [\mathbf{J}_{Rebin} + \beta \cdot \mathbf{R}_{Rebin}]^{-1} \cdot \mathbf{J}_{Rebin} \cdot [\mathbf{J}_{Rebin} + \beta \cdot \mathbf{R}_{Rebin}]^{-1}, \quad (48)$$

and the mean gradient matrix of the corresponding reconstruction could be approximated as:

$$\begin{aligned} \mathbf{G}(\mathbf{x}_{Rebin}) &= \frac{\partial E(\hat{\mathbf{x}}_{Rebin})}{\partial \mathbf{x}_{Rebin}} \\ &\approx [\mathbf{J}_{Rebin} + \beta \cdot \mathbf{R}_{Rebin}]^{-1} \cdot \mathbf{J}_{Rebin}. \end{aligned} \quad (49)$$

Since both post-filtering and restoring are simple linear operations, we can approximate the covariance matrix and mean gradient matrix for $\hat{\mathbf{x}}_{PF-Restore}$ as:

$$\begin{aligned} \text{Cov}[\hat{\mathbf{x}}_{PF-Restore}] &\approx \mathbf{F} \cdot \mathbf{S} \cdot \text{Cov}[(\hat{\mathbf{x}}_{Rebin})_{PML}] \cdot \mathbf{S}^T \cdot \mathbf{F}^T \\ &= \mathbf{F} \cdot \mathbf{S} \cdot [\mathbf{J}_{Rebin} + \beta \cdot \mathbf{R}_{Rebin}]^{-1} \cdot \mathbf{J}_{Rebin} \cdot [\mathbf{J}_{Rebin} + \beta \cdot \mathbf{R}_{Rebin}]^{-1} \cdot \mathbf{S}^T \cdot \mathbf{F}^T, \end{aligned} \quad (50)$$

and

$$\mathbf{G}(\mathbf{x}_{PF-Restore}) \approx \mathbf{F} \cdot \mathbf{S} \cdot [\mathbf{J}_{Rebin} + \beta \cdot \mathbf{R}_{Rebin}]^{-1} \cdot \mathbf{J}_{Rebin} \cdot \mathbf{S}^T. \quad (51)$$

In our previous study [3], it has been demonstrated that the local impulse response (LIR) derived with (51) is almost identical to the LIR derived based on the uniform pixilation. Table I summarizes the formulations of approximated covariance and mean gradient matrix discussed in this paper.

Equations (50) and (51) could be used to evaluate the resolution-variance tradeoffs attainable with reconstructions in the non-uniform object-space, with computation loads greatly reduced from those for similar calculations in the uniformly pixelated object-space. Furthermore, these results are fully compatible with the gradient-based algorithm for adaptively optimizing the angular sampling strategy. Combining the NUOP approach with the gradient-based search algorithm developed in this paper would offer a practical computation approach for performing adaptive angular sampling in near real-time. The computational steps involved in the adaptive angular sampling approach are summarized in Fig. 1.

If necessary, the computation load could be further reduced by using the locally shift-invariant approximation as previously discussed in [27], [28]. For studying reconstructed image quality in a relatively shift-invariant local region (such as inside the ROI), one could assume the Fisher information matrix (FIM) to be a block-toeplitz matrix, with each column being a shifted version of the actual FIM column corresponding to a given pixel in the target-region. Therefore, the inversion of FIM, such as $\mathbf{J}_{Rebin}$, could be performed based on fast Fourier transform (FFT) [29]. This greatly reduces the computation load, when compared to the use of regular matrix inversion methods, such as conjugate-gradient algorithm [30]. This approach was widely used by many authors in the context of emission tomography [22], [29], [31]. The combination of the NUOP approach with the FFT-based matrix inversion techniques would offer a practical solution for evaluating of the optimum time distribution in real time.

F. Monte Carlo Simulation

We have carried out a series of Monte Carlo studies to evaluate the adaptive angular sampling approach with a single-head single-pinhole SPECT system. This single camera is rotated around the object with a constant radius of rotation. In the first study of 12 phantoms, detailed in Table II, for evaluating the adaptive angular sampling, the camera could be placed at 32 equally-spaced sampling angles around the object during data acquisition. The gamma ray detector has 64×64 square pixels of $700 \mu\text{m} \times 700 \mu\text{m}$ in size. It is coupled to a collimator with a single pinhole of $300 \mu\text{m}$ diameter. In the second study for visualizing the benefit of the adaptive angular sampling, higher spatial resolution is preferred. The camera could sample the object with 64 equally-spaced sampling angles. The detector is divided into 128×128 square pixels of $350 \mu\text{m} \times 350 \mu\text{m}$ in size. The diameter of the single pinhole becomes $200 \mu\text{m}$. The detector-to-pinhole and pinhole-to-center distances are 45 mm and 15 mm respectively for both studies. The attenuation of gamma rays in collimator and the depth-of-interaction effect in detector are modeled using Monte Carlo package described in [3], [12].

The object-space is divided into $64 \times 64 \times 64$ voxels, each being $200 \mu\text{m} \times 200 \mu\text{m} \times 200 \mu\text{m}$ in size. The active volume of the object is a sphere of around 12 mm in diameter, having a uniform background concentration. In the first study, we have modeled a total of 12 object configurations, each having a spherical region-of-interest (ROI) of 1.6 mm diameter and an extra ellipsoidal background region (half-axes: 1.5 mm, 1.5 mm and 3 mm) with elevated tracer uptakes. Detailed dimensions and relative tracer uptakes of the phantoms are shown in Table II and Fig. 2. The ROI, the ellipsoidal background feature, and the continuous background have activity concentrations of C_1 , C_2 , and C_B respectively. The entire phantom contains a total activity of $500 \mu\text{Ci}$ and the total observation time is 64 minutes for all MC studies.

In the second study, the phantom configuration is slightly modified. The ROI contains three hot cylinders, each being 0.6 mm in diameter and 4 mm in length. The spacing between the small spheres is 0.5 mm, seen in Fig. 7. The strong background feature has the same size of that in the first study. The total activity the entire phantom contains is increased to 4 mCi and the total observation time is 128 minutes.

Intuitively, gamma ray attenuation in the object could play an important role in defining the optimum angular sampling strategy, especially for imaging human-sized objects with tracers labeled with Tc-99 m. To highlight this effect, we have also tested three linear attenuation coefficients, 0 mm^{-1} , 0.0154 mm^{-1} (typical value for 140 keV gamma rays in water) and 0.077 mm^{-1} , with the phantoms. Please also see Table II for details.

As previously discussed in Section II-E, we have used a nonuniform object-space pixelation (NUOP) approach to reduce the computation load. In this approach, the ROI and regions important for the reconstruction of the ROI were represented by the finest pixels and other regions were represented by larger pixels (Fig. 3). As a result, the number of unknowns could be reduced from 262144 to around 4000. This allowed us to find the optimum time distribution within a few minutes using a single PC. Note that the object pixelation strategy was arbitrarily chosen for the object. There could certainly be room for further optimization. In [3], we have introduced several approaches for defining the object pixelation strategy for a given object, which could be used with future studies.

III. Results

A. Validation of the Analytical Approach

To verify the proposed gradient-based search algorithm (Fig. 1), we have compared the optimum time distributions obtained with the proposed algorithm against the ones obtained with exhaustive searches through all possible combinations of imaging times. In this study, we used the phantom configuration, P_{O4} , as detailed in Table II and Fig. 2.

To make the exhaustive search process computationally practical, we have to combine the 32 sampling angles into four groups. The first group includes angles 28–31 and 0–3, the second group includes angles 4–11 and so on (Fig. 4). Within each group, the imaging times at all angles are kept the same. Equivalently the number of effective sampling angles is shrunk to be 4. To further reduce the number of possible angular sampling schemes, the imaging time for each group can only be varied as integral multiple of certain finite time intervals, such as 10 s or 30 s. A smaller interval would further improve the accuracy. But the greatly increased number of possible sampling configurations makes this impractical. By contrast, the proposed gradient-based search algorithm allows imaging time at each group (of eight angles) to vary arbitrarily, except that the sampling times cannot be negative. The corresponding partial derivative of variance for each group could be calculated as the sum of partial derivatives with respect to imaging times at sampling angles in the related group. The optimum time distributions derived with the exhaustive search and the gradient-based algorithm are shown in Table III. Both approaches generate similar results and the degree of agreement improves with smaller time interval allowed for the exhaustive search process. β in (5) is set to be 1×10^{-9} and the FWHM of the corresponding 3-D Gaussian filter function used in (50), (51) is chosen to be 0.8 mm.

In this simple example, we have shown in Table III that both the exhaustive search and the gradient-based approach have led to highly non-uniform time distribution across the four (groups of) angles. In Fig. 5, we plot the image variance, the partial derivatives of the variance given by (34), and the resultant time distribution as functions of iteration number.

The image variance converged to its minimum value within the first 50 iterations, but the optimum imaging times at certain angles kept changing till well beyond 150 iterations. For comparison, we have also included the results obtained by allowing all the 32 imaging times to vary independently. In this study, the non-uniform angular sampling did result in a reduced image variance (by ~20%) as shown in Table IV.

B. Optimum Time Distributions for ROI Studies

We have evaluated the use of the proposed algorithm to find the optimum angular sampling strategy, especially for imaging relatively weak ROIs inside objects containing hot background features. In this effort, we studied a total of 12 phantom configurations, as detailed in Table II. The imaging times at all possible sampling angles were allowed to vary independently. To ensure the variance to converge to their minimum values, we allowed 250 iterations for the optimization process. Fig. 6 summarizes the optimum time distribution obtained using the gradient-based search algorithms for all 12 phantom configurations. In Table IV, the imaging variance values obtained with the non-uniform sampling strategies are compared with those derived using uniform sampling across all 32 sampling angles.

In general, the adaptive angular sampling approaches have led to an appreciable reduction in image variance (by factors of 10–40%), over the uniform sampling approaches. The adaptive sampling approach was particularly effective for imaging ROIs located near the boundary of the object ($P_{O1} - P_{O6}$). In such cases, imaging angles, corresponding to the camera placed close to the ROI, are the most effective ones for collecting imaging information. The resultant noise reduction is greater for phantoms with increased gamma ray attenuation. This effect can be seen by comparing the noise reduction factors within different groups ($P_{O1} - P_{O3}$), ($P_{O4} - P_{O6}$), ($P_{C1} - P_{C3}$), and ($P_{C4} - P_{C6}$). Furthermore, the noise reduction must be more obvious for stronger background feature, which could be seen in the comparison of groups ($P_{O1} & P_{O4}$), ($P_{O2} & P_{O5}$), ($P_{O3} & P_{O6}$), ($P_{C1} & P_{C4}$), ($P_{C2} & P_{C5}$) and ($P_{C3} & P_{C6}$).

To further demonstrate the performance benefit from using the adaptive angular sampling approach, we have carried out another Monte Carlo study using a slightly modified phantom configuration. In this case, the ROI contains three hot tubes parallel to the rotation axis, each being 0.6 mm in diameter and 4 mm in length (instead of having a uniform and above-the-background tracer concentration). The spacing between the small spheres is 0.5 mm. For this study, the camera could be placed at any of the 64 equally spaced sampling angles. The linear attenuation coefficient used in the phantom is 0.077 mm^{-1} . By using the computation procedures shown in Fig. 1, we have identified the optimum angular sampling strategy as shown in Fig. 7. This leads to a reduction in image variance by 42%, compare to the use of the uniform sampling approach. The non-uniform object-space pixelation (NUOP) approach is used to improve the computation efficiency.

The optimum time distribution obtained with the proposed approach is a complex function of many factors, including the location of the ROI with respect to the orbit of the camera, the relative location and strength of the background features (such as the elliptical features shown in Fig. 6 and Fig. 7), the attenuation of the gamma ray originated from the ROI, etc. While the effects of these factors are coupled to each other and therefore difficult to quantify, one may draw a few general guidelines from these results:

- Sampling angles corresponding to larger probabilities for detecting the gamma rays originated from the ROI are generally more important and therefore associated with longer imaging time. This applies to Cases, $P_{O1} - P_{O6}$ in Fig. 6. Similarly, sampling angles that lead to greater sensitivity to strong background features are generally less favorable. This is also evident in Cases, $P_{C1} - P_{C6}$ in Fig. 6.
- Sampling angles that lead to overlapping between the projections of the ROI and other strong background features could be more favorable angles. This is evident by examining Cases, $P_{C1} - P_{C6}$ in Fig. 6. This result could be explained by considering two factors, which are balancing each other. On one hand, such overlapping reduces the *weighted* correlation¹ between the response of the detector to a target pixel and the response to other source pixels nearby. Since this correlation is directly related to the physical resolution of the system, the reduction in correlation could help to separate the target pixel from other pixels during reconstruction. On the other hand, the overlapping between the projections tends to reduce the amount of information carried by each detected photon, since it is associated with a larger statistical uncertainty. These two effects are counter-balancing each other, which leads to these counterintuitive results.
- In Fig. 6, we have also observed some cases that zero imaging times interleave between positive imaging times. These time-distributions were carefully verified to minimize imaging variance. In contrast, a smother time distribution seems to be attainable with the increasing number of possible sampling angles, as shown in Fig. 7. This indicates that the irregularity is likely to come from the discretization of sampling angles and object-space.

Finally, to visualize the performance benefit of using the adaptive sampling approach, we have generated two images of the phantom shown in Fig. 7 with both uniform and non-uniform angular sampling strategies. Both images are reconstructed in the uniform object-space. The image variance at the center of the ROI is controlled by the FWHM of Gaussian filter in the post-filtered penalized maximum-likelihood reconstruction process (5). In Fig. 8, we compare two images having the same variance at the center of the ROI. Clearly, the adaptive angular sampling provides a better spatial resolution in the ROI while providing similar noise levels, as can be visualized in both 1-D and 2-D cross sections of the reconstructed images.

IV. Conclusion and Discussion

We have developed an analytical approach for finding the optimum system configuration that minimizes image variance. This approach has three key components: (a) a set of equations for evaluating image variance and resolution properties attainable with a given

¹The weighted correlation refers to a column of FIM that is corresponding to a given target pixel. It essentially quantifies the correlation between the responses of the detector to gamma ray emissions at the given pixel and at adjacent pixels, weighted by the variance on the projection data. See Eq. (13).

sampling strategy, (b) an iterative algorithm for searching through the parameter space and finding the optimum sampling strategy and (c) a novel computation approach based on the non-uniform object-space pixelation method for reducing the computation load [3]. This combination leads to a highly efficient computation approach that can be implemented in near real-time.

In this study, we have utilized the proposed computation approach for adaptive angular sampling in SPECT imaging. It is shown that the performance of a SPECT system can be improved with non-uniform allocations of imaging time across all possible sampling angles. We have also demonstrated, with a series of Monte Carlo studies, that the proposed computation approach is highly effective for finding the optimum sampling strategies that lead to a significantly lowered image variance.

It is worth noting that the proposed computation approach could be applied to optimize SPECT systems with respect to a wide range of imaging parameters, and be equally applicable to other imaging modalities, such positron emission tomography (PET) and X-ray computed tomography (CT). For an adaptive imaging system that offers a finite number of possible configurations, the proposed method could help to rank the relative importance of each configuration. By identifying the optimum combination of different imaging configurations in near real-time, the proposed computation approach allows the system to offer an optimum efficiency for collecting imaging information about unknown objects. This makes the proposed computation approach well suited for future adaptive nuclear imaging applications.

References

1. Cherry SR. In vivo molecular and genomic imaging: New challenges for imaging physics. *Phys Med Biol.* Feb 7; 2004 49(3):R13–R48. [PubMed: 15012005]
2. Meikle SR, Kench P, Kassiou M, et al. Small animal SPECT and its place in the matrix of molecular imaging technologies. *Phys Med Biol.* Nov 21; 2005 50(22):R45–R61. [PubMed: 16264248]
3. Meng LJ, Li N. Non-uniform object-space pixelation (NUOP) for penalized maximum-likelihood image reconstruction for a single photon emission microscope system. *IEEE Trans Nucl Sci.* Oct; 2009 56(5):2777–2788.
4. Kastis GA, Furenlid LR, Wilson DW, et al. Compact CT/SPECT small-animal imaging system. *IEEE Trans Nucl Sci.* Feb; 2004 51(1):63–67. [PubMed: 26538684]
5. Peterson TE, Wilson DW, Barrett HH. Application of silicon strip detectors to small-animal imaging. *Nucl Instrum Methods Phys Res A.* Jun 1; 2003 505(1–2):608–611.
6. Accorsi R, Curion AS, Frallicciardi P, et al. Preliminary evaluation of the tomographic performance of the mediSPECT small animal imaging system. *Nucl Instrum Methods Phys Res A.* Feb 1; 2007 571(1–2):415–418.
7. Beekman FJ, Vastenhouw B. Design and simulation of a high-resolution stationary SPECT system for small animals. *Phys Med Biol.* Oct 7; 2004 49(19):4579–4592. [PubMed: 15552418]
8. Jimenez-Cruz A, Loustaunau-Lopez VM, Bacardi-Gascon M. The use of low glycemic and high satiety index food dishes in Mexico: A low cost approach to prevent and control obesity and diabetes. *Nutricion Hospitalaria.* May-Jun; 2006 21(3):353–356. [PubMed: 16771117]
9. Finck BK, Weissman BNW, Rubenstein JD, et al. 100 micron digitization resolution is optimal for x-rays for a large multicenter trial in rheumatoid arthritis (RA). *Arthrit Rheum.* Sep; 1997 40(9): 1544–1544.

10. Meng LJ, Clinthorne NH, Skinner S, et al. Design and feasibility study of a single photon emission microscope system for small animal I-125 imaging. *IEEE Trans Nucl Sci.* Jun; 2006 53(3):1168–1178.
11. Meng LJ. An intensified EMCCD camera for low energy gamma ray imaging applications. *IEEE Trans Nucl Sci.* Aug; 2006 53(4):2376–2384.
12. Meng LJ, Fu G, Roy EJ, et al. An ultrahigh resolution SPECT system for I-125 mouse brain imaging studies. *Nucl Instrum Methods Phys Res A.* Mar 1; 2009 600(2):498–505. [PubMed: 20161174]
13. Barrett HH, Furenlid LR, Freed M, et al. Adaptive SPECT. *IEEE Trans Med Imag.* Jun; 2008 27(6):775–788.
14. Clarkson E, Kupinski MA, Barrett HH, et al. A task-based approach to adaptive and multimodality imaging. *Proc IEEE.* Mar; 2008 96(3):500–511.
15. Freed M, Kupinski MA, Furenlid LR, et al. A prototype instrument for single pinhole small animal adaptive SPECT imaging. *Med Phys.* May; 2008 35(5):1912–1925. [PubMed: 18561667]
16. Moore, JW.; Barrett, HH.; Furenlid, LR. Adaptive CT for high-resolution, controlled-dose, region-of-interest imaging. *Proc. IEEE NSS-MIC Conf. Rec;* 2009; p. 5154-5157.
17. Jean YC, Hong X, Liu J, et al. High sensitivity of positron annihilation lifetime to time and pressure effects in gas-exposed polymers. *J Radioanalyt Nucl Chem-Articles.* Nov; 1996 210(2): 513–524.
18. Meng LJ, Clinthorne NH. A modified uniform Cramer-Rao bound for multiple pinhole aperture design. *IEEE Trans Med Imag.* Jul; 2004 23(7):896–902.
19. Meng LJ, Li N. A vector uniform cramer-rao bound for SPECT system design. *IEEE Trans Nucl Sci.* Feb; 2009 56(1):81–90.
20. Wolbarst AB. Foundations of image science. *Health Phys.* Jul; 2004 87(1):93–93.
21. Fessler JA. Spatial resolution and noise tradeoffs in pinhole imaging system design: A density estimation approach. *Opt Express.* Mar 16; 1998 2(6):237–253. [PubMed: 19377607]
22. Meng LJ, Rogers WL, Clinthorne NH, et al. Feasibility study of Compton scattering enhanced multiple pinhole imager for nuclear medicine. *IEEE Trans Nucl Sci.* Oct; 2003 50(5):1609–1617.
23. Meng LJ, Wehe DK. Feasibility study of using hybrid collimation for nuclear environmental imaging. *IEEE Trans Nucl Sci.* Aug; 2003 50(4):1103–1110.
24. Bai ZJ, Fahey M, Golub G. Some large-scale matrix computation problems. *J Comput Appl Math.* Nov 5; 1996 74(1–2):71–89.
25. Berger, J. *Statistical Decision Theory and Bayesian Analysis.* New York: Springer-Verlag; 1985.
26. Press, WH.; Teukolsky, SA.; Vetterling, WT., et al. *Numerical Recipes in C++: The Art of Scientific Computing.* 2. Cambridge, U.K: Cambridge Univ; 2007.
27. Stayman JW, Fessler JA. Regularization for uniform spatial resolution properties in penalized-likelihood image reconstruction. *IEEE Trans Med Imag.* Jun; 2000 19(6):601–615.
28. Stayman JW, Fessler JA. Compensation for nonuniform resolution using penalized-likelihood reconstruction in space-variant imaging systems. *IEEE Trans Med Imag.* Mar; 2004 23(3):269–284.
29. Qi JY, Leahy RM. Resolution and noise properties of MAP reconstruction for fully 3-D PET. *IEEE Trans Med Imag.* May; 2000 19(5):493–506.
30. Fessler JA, Booth SD. Conjugate-gradient preconditioning methods for shift-variant PET image reconstruction. *IEEE Trans Image Process.* May; 1999 8(5):688–699. [PubMed: 18267484]
31. Qi JY, Huesman RH. Theoretical study of penalized-likelihood image reconstruction for region of interest quantification. *IEEE Trans Med Imag.* May; 2006 25(5):640–648.

Fig. 1.

The combination of the NUOP approach and the gradient-based search algorithm for finding the optimum angular sampling strategy.

Fig. 2.

Schematics of two spherical phantoms used in the Monte Carlo simulations. Each phantom contains a small spherical region-of-interest (ROI) of 1.6 mm diameter and a strong elliptical feature superimposed on a continuous background. The location of the ROI, the relative intensities of different features and the attenuation coefficient of the media in the phantom are varied to produce a total of 12 different phantom configurations as shown in Table II. The numbers shown in different regions of the phantoms are the relative tracer uptake values.

Fig. 3.

The rebinning strategy used with the phantoms. The numbers shown in the graphs are the rebinning density as defined in [3]. The number “1” symbolizes that the pixels in the corresponding regions (marked in black) are not rebinned. Within the background region marked with 4, $4 \times 4 \times 4$ adjacent pixels will be rebinned into a larger pixel. In addition, pixels in the strong background region marked with number “10” will be rebinned into a single voxel. Detailed algorithm for the rebinning process can be found in [3]. In this example, the use of the NUOP approach reduces the total number of unknowns from 262144 to around 4000. This leads to a greatly reduced computation load, while searching for the optimum angular sampling strategy for imaging the ROIs.

Fig. 4.
Simulated single-head SPECT system

Fig. 5.

The convergence behavior of the proposed gradient-based search algorithm for finding the optimum angular sampling strategy. **Top row:** The image variance, its partial derivatives and the resultant imaging times at individual imaging angles (or groups of angles) as functions of iteration number. The results were obtained by grouping the 32 angles into four groups as described in Section III-E and in Fig. 4. $\beta = 1 \times 10^{-8}$. **Bottom row:** Similar results obtained by allow imaging times at all the 32 angles to vary independently. $\beta = 1 \times 10^{-9}$. The FWHM of the corresponding Gaussian filter (used in Eq. (45)) is 0.8 mm for both cases.

Fig. 6.

The optimum time distributions across the 32 sampling angles, obtained using the gradient-based search algorithm with 300 iterations. The color-bar and the numbers (with the unit of second) surrounding the phantom represent the optimum sampling times at individual angles. β is 1×10^{-8} for all the cases. The FWHM of corresponding Gaussian filter function is 0.8 mm.

Fig. 7.

The optimum time distributions across the 64 sampling angles for imaging the three hot tubes. The numbers marked inside the object are the relative activity concentrations of different features and the background. The numbers around the color bar are imaging times given in seconds. β is 1×10^{-8} . The FWHM of the Gaussian filter function used is 0.8 mm.

Fig. 8.

Left column 2-D and 1-D cross sections of the simulated source object; **Central column:** cross sections of the reconstructed phantom image obtained with non-uniform angular sampling (NUAS); **Right column:** image obtained with uniform angular sampling (UAS). The reconstructed images have the same imaging noise in the ROI region, and the use of the non-uniform angular sampling leads to an apparent improvement in spatial resolution. The x-axis is the pixel number across the object-space.

Summary of Approximated Covariance and Mean Gradient Matrix for Uniform and Non-Uniform Pixelation and Time-Distribution

TABLE I

	Approximated Covariance Matrix	Approximated Mean Gradient Matrix $\mathbf{a}$
Uniform Pixelation Uniform Time-distribution	$Cov[\hat{\mathbf{x}}] \approx \mathbf{F} \cdot \left[\left(T \cdot \sum_{k=1}^K \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left[\left(T \cdot \sum_{k=1}^K \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \mathbf{F}^T$	$\mathbf{G}(\mathbf{x}) \approx \mathbf{F} \cdot \left[\left(T \cdot \sum_{k=1}^K \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left(T \cdot \sum_{k=1}^K \mathbf{J}^{(k)(0)} \right)$
Uniform Pixelation Non-uniform Time-distribution	$Cov[\hat{\mathbf{x}}] \approx \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \mathbf{F}^T$	$\mathbf{G}(\mathbf{x}) \approx \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right) + \beta \cdot \mathbf{R} \right]^{-1} \cdot \left(\sum_{k=1}^K t^{(k)} \mathbf{J}^{(k)(0)} \right)$
Non-uniform Pixelation Non-uniform Time-distribution $\mathbf{b}$	$Cov[\hat{\mathbf{x}}_{PF-Restore}] \approx \mathbf{F} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \cdot \mathbf{J}^{(k)(0)}_{Rebin} \right) + \beta \cdot \mathbf{R}_{Rebin} \right]^{-1} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \cdot \mathbf{J}^{(k)(0)}_{Rebin} \right) + \beta \cdot \mathbf{R}_{Rebin} \right]^{-1} \cdot \mathbf{F}^T$	$\mathbf{G}(\mathbf{x}_{PF-Restore}) \approx \mathbf{F} \cdot \mathbf{S} \cdot \left[\left(\sum_{k=1}^K t^{(k)} \cdot \mathbf{J}^{(k)(0)}_{Rebin} \right) + \beta \cdot \mathbf{R}_{Rebin} \right]^{-1} \cdot \left(\sum_{k=1}^K t^{(k)} \cdot \mathbf{J}^{(k)(0)}_{Rebin} \right) \cdot \mathbf{S}^T$

^aThe columns of the gradient matrix represent the local impulse response functions at corresponding pixels.

^bFormulations are used in the subsequent calculation.

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TABLE II
Different Phantom Configurations Used to Evaluate the Proposed Computation Approach

Phantoms	Phantoms with the ROI at the Center						Phantoms with the ROI off the Center					
	P _{C1}	P _{C2}	P _{C3}	P _{C4}	P _{C5}	P _{C6}	P _{O1}	P _{O2}	P _{O3}	P _{O4}	P _{O5}	P _{O6}
Tracer Concentrations: C _B :C _I :C ₂	1 : 5 : 10						1 : 5 : 10					
Linear Attenu. Coef. (mm ⁻¹)	0	0.0154	0.077	0	0.0154	0.077	0	0.0154	0.077	0	0.0154	0.077

TABLE III
Comparison of Optimal Variance and Corresponding Time Distribution by Two Approaches

	Observation Time (s) Spent at				Minimum Variance ¹
	Group1	Group2	Group3	Group4	
Exhaustive Search (30s step)	270	120	30	60	376.2026
Exhaustive Search (10s)	280	120	20	60	375.4184
Gradient-Based Approach	283.96	119.05	19.082	57.91	375.35

¹The variance with uniform time distribution is 466.0874

TABLE IV

Imaging Variance Obtained with Non-Uniform Angular Sampling Strategies

Phantom	Variance (uniform time)	Variance (non-uniform time)	Relative Reduction
P _{O1}	433.37	319.05	0.264
P _{O2}	457.20	321.08	0.298
P _{O3}	549.16	334.78	0.390
P _{O4}	675.16	460.59	0.318
P _{O5}	709.29	461.19	0.350
P _{O6}	827.97	469.84	0.433
P _{C1}	504.38	481.94	0.044
P _{C2}	549.96	516.73	0.060
P _{C3}	782.95	697.03	0.110
P _{C4}	769.26	696.70	0.094
P _{C5}	835.18	739.14	0.115
P _{C6}	1154.36	953.14	0.174