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Collimator Width Optimization in X-Ray Luminescent Computed Tomography (XLCT) with Selective Excitation Scheme

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Abstract

X-ray luminescent computed tomography (XLCT) is a promising new functional imaging modality based on computed tomography (CT). This imaging technique uses X-ray excitable nanophosphors to illuminate objects of interest in the visible spectrum. Though there are several validations of the underlying technology, none of them have addressed the issues of performance optimality for a given design of the imaging system. This study addresses the issue of obtaining best image quality through optimizing collimator width to balance the signal to noise ratio (SNR) and resolution. The results can be generalized as to any XLCT system employing a selective excitation scheme.

Keywords

Optimization; Signal to Noise Ratio; Structural Similarity; X-Ray Luminescence; Selective Excitation

1. INTRODUCTION

X-ray computed tomography (CT) has been a mainstay in biomedical imaging for three decades.¹ Though CT offers excellent image quality, it is not sensitive to low concentrations of molecular imaging agents.² The sensitivity of an X-ray CT is few orders of magnitude smaller than optical or radionuclide imaging modalities because of poor X-ray stopping potential of diluted contrast agents.³ Therefore, it is restricted to anatomical imaging, and it is not well suited for molecular imaging. Functional imaging via CT necessitates higher concentrations of contrast agents, a situation which is unsuitable for molecular imaging.

Phosphors have been used for many years for radiographic imaging. These substances are sensitive to high energy radiation and emit down-converted energy in the visible or near infrared (NIR) spectrum. Advancements in phosphor chemistry in the recent years have made it possible to fabricate stable, nano-sized phosphor particles which can emit visible or NIR photons with high conversion efficiency.^{4,5} X-ray luminescent CT (XLCT) was proposed based on this principle. XLCT works via selective excitation of nanophosphors.

Tomographic images of samples, containing unknown volumetric distribution of nanophosphors uptakes, are reconstructed from the measurements of exposure to a sequence of narrowly-separated thin X-ray beams. The optical luminescence produced from the narrow illumination is captured by an optical camera tuned to a specific bandwidth. Regardless of where the photon is detected, it could be safely assumed that it originated somewhere in the beam path. Spatially resolving the optical signal becomes redundant. By collecting optical information from each narrow beam excitation and over a large number of angular views, projections are collected and optical tomographic images of high fidelity can be reconstructed.^{6–8} This optical information from EM-CCD cameras can be co-registered with conventional CT reconstruction for simultaneously obtaining anatomical and functional images.⁹ The scheme of operation is illustrated in Figure 1.

Though there is plenty of studies reproducing the scheme and demonstrating its efficacy, few examples exist to propose optimization schemes for selective excitation based the XLCT. Usually, the images have to endure long acquisition times due to the low concentration of molecular agents. They also suffer from poor resolution because of X-rays and optical photons scatters during the process of acquisition. Because weak emitted signal leads to lower SNR, a selective excitation scheme can be preconfigured to improve one of these parameters but not all at the same time.

The number of photons emitted from the source fundamentally dictates the image quality and SNR. This factor can be controlled at a large extent by adjusting collimator width of the X-ray source. In this study, the authors put forward a scheme to theoretically determine a desirable balance in SNR and resolution through finding such an optimal width. The hypothesis is experimentally verified from numerical simulations by mimicking the process of experimentation. The rest of this paper is organized as follows: Section 2 summarizes the principles of XLCT data acquisition and image reconstruction. Section 3 briefly describes the optimization problem and introduces two independent image quality indices with discussions on conditions of optimality. Section 4 presents system design and simulations. Section 5 elaborates the analysis. Finally we present some relevant issues are in discussion.

2. METHODS

2.1. Imaging Model

Beer-Lambert's Law states that for mono-energetic X-rays of energy E emitted from a source q_i , fluence at a depth having radial coordinate r is given by

$$I = I_0 e^{-\int_{q_i}^r \mu(\mathbf{x}, E) d\mathbf{x}} \quad (1)$$

where $\mu(\mathbf{x}, E)$ is the attenuation coefficient for a thin beam taking absorption and Compton scatter into account, and I_0 is the initial fluence rate. The sample is assumed to be consisting of homogenous material described by its coefficients of linear attenuation $\mu(\mathbf{r}, E)$, energy absorption $\mu_{\text{en}}(\mathbf{r}, E)$, optical absorption and scattering. The kinetic energy, transferred to ionized electrons at the position $\mathbf{r}$, can be expressed as

$$E_i(\mathbf{r}) = \left\{ \mu_{en} I_0 e^{-\int_{q_i}^{\mathbf{r}} \mu(\mathbf{x}, E) \cdot d\mathbf{x}} \right\} \cdot w_i(\mathbf{r}) \quad (2)$$

where the window function $w(r)$ restricts our equation to the i th beam. The distributed nanophosphors concentration can be modeled as a functional $f(\mathbf{r})$ compactly supported in a small volume centered on $\mathbf{r}$. The phantom is irradiated by pre-assigned number of beams and optical signal recorded simultaneously. Based on this concentration, we can deduce the number of photons emitted due to i th beam by rescaling the values from light emission in pure crystal. The photon flux density can be thus expressed as

$$\begin{aligned} \phi(\mathbf{r}) &= \left(\frac{f(\mathbf{r})}{\rho_b} \right) \epsilon_b E_i(\mathbf{r}) \\ &= \left(\frac{f(\mathbf{r})}{\rho_b} \right) \epsilon_b \left\{ \mu_{en} I_0 e^{-\int_{q_i}^{\mathbf{r}} \mu(\mathbf{x}, E) \cdot d\mathbf{x}} \right\} \cdot w_i(\mathbf{r}) \end{aligned} \quad (3)$$

We consider $\epsilon_b = 60/\text{KeV}$ and $\rho_b = 7.44 \text{ gm/ml}$, which are characteristics of $\text{Gd}_2\text{O}_3\text{:Tb}$, a commonly used XLCT phosphor.⁶ The photons from a small volume $d\mathbf{r}$ is given as

$$\phi(\mathbf{r}) \cdot d\mathbf{r} = \frac{f(\mathbf{r})}{\rho_b} \epsilon_b E_i(\mathbf{r}) \cdot d\mathbf{r} \quad (4)$$

The fluence from the volume of interest, observed over a time period τ can be expressed as

$$y_i = Q_E \left[\tau \int_{\Omega} \mathbf{S}(\mathbf{r}) \phi_i(\mathbf{r}) d\mathbf{r} \right] \quad (5)$$

where Ω is the volume enclosing the sample, $s(\mathbf{r})$ is the optical sensitivity map, and Q_E is quantum efficiency. For brevity, we assume quantum efficiency Q_E of 1.0. The sample density ρ_s is taken to be $1 \mu\text{g/ml}$ with the background set $0.1 \mu\text{g/ml}$. We take into account beam widening due to Compton scatter of electrons and subsequent charge creation leading to photon generation from the neighborhood of the beam's path.

2.2. Reconstruction Model

Emission tomography, as is the case of XLCT, follows a statistical model. A given concentration of phosphor doesn't exactly produce the same quantity of emission each time and the detected photon number is a random variable. Meanwhile, true signal also often gets overshadowed by system noise. For our study, we resort to Maximum Likelihood Estimation maximization (MLEM) for an optimal performance because it converges to a non-negative optimal solution and computation of gradients is absent.¹⁰

The nanophosphors distribution is approximated in the Cartesian space by a set of N basis function given as

$$f(\mathbf{r}) = \langle \mathbf{x} | e(\mathbf{r}) \rangle = \sum_{j=1}^N x_j e_j(\mathbf{r}) \quad (6)$$

If the expected number of detected photons is $\mathbf{y}$, it could be taken as a linear combination of phosphor concentration $\mathbf{x}$ and $\mathbf{A}$, as given by

$$\mathbf{y} = \mathbf{A}\mathbf{x} \quad (7)$$

To compute the coefficients of $\mathbf{A}$, we consider Eq. (5)

$$\begin{aligned} y_i &= \tau \mathbf{Q}_E \int_{\Omega} \mathbf{S}(\mathbf{r}) \phi_i(\mathbf{r}) d\mathbf{r} \\ &= \sum_j \left(\frac{\epsilon_b}{\rho_b} S_j \tau \mathbf{Q}_E \int_{\epsilon_j} \mathbf{e}_j(\mathbf{r}) \mathbf{E}_i(\mathbf{r}) d\mathbf{r} \right) x_j = \sum_j a_{ij} x_j \end{aligned} \quad (8)$$

which implies that the coefficients of $\mathbf{A}$ can be computed as

$$a_{ij} = \frac{\tau \epsilon_b}{\rho_b} S_j \int_{\Omega} E_i(\mathbf{r}) e_j(\mathbf{r}) d\mathbf{r} \quad (9)$$

where s_j is a discretized version of the optical sensitivity map $\mathbf{s}$ discussed previously. The measurement contributions $\mathbf{m}$ to the ML-EM process over $\mathbf{P}$ beams are statistical realizations of vector $\mathbf{Y}$. The independent component Y_i follows a Poisson distribution with mean y_i , such that,

$$p_m(y_i) = \frac{e^{-y_i} y_i^{m_i}}{m_i!} \quad (10)$$

For a set of values recorded at the detector, we could elaborate for a maximum probability

$$p_m(y_1, y_2 \dots y_P) = \frac{e^{-y_1} y_1^{m_1}}{m_1!} \cdot \frac{e^{-y_2} y_2^{m_2}}{m_2!} \dots \frac{e^{-y_P} y_P^{m_P}}{m_P!} \quad (11)$$

From the log-likelihood of (11), we obtain

$$\log[p_m(\mathbf{y})] = \sum_{i=1}^P -y_i + m_i \log(y_i) - \log(m_i!) \quad (12)$$

Ignoring the constant term $m!$, vector $\mathbf{x}$ satisfying the ML criterion is a solution to the function of $\mathbf{y}$

$$\max_{\mathbf{x}} f_{\mathbf{m}}(\mathbf{y}) = \sum_{i=1}^P -y_i + m_i \log(y_i), (\mathbf{y} = \mathbf{A} \cdot \mathbf{x} \text{ and } x \geq 0) \quad (13)$$

When $\mathbf{A}$ is a full-ranked matrix, the expression has a unique solution for $x \in R^N$ and $y \in R^P$.

EM was done iteratively following the scheme published by Shepp and Vardi¹¹ to reconstruct the data points.

For $n+1$ th iteration, the values of m_i can be written as

$$m_i^{n+1} = E \left[m_i | N_j x_j^n \right] = \frac{a_{ij} x_j}{N_j \sum_b a_{ib} x_b} \quad (14)$$

Applying minimization with respect to $\mathbf{x}_i$ in (2–14),

$$\frac{\partial}{\partial x_j} \{\log p_m\} = \sum_i -a_{ij} + \frac{m_i}{x_j} = 0 \Rightarrow x_j^{n+1} = \sum_i m_i a_{ij} \quad (15)$$

Using (15) and (16), successive estimates are performed as,

$$x_j^{n+1} = \frac{x_j^n}{N_j} \sum_{i=1}^P a_{ij} \frac{m_i}{\sum_{b=1}^N a_{ib} x_b^n} \quad (16)$$

A sensitivity map which takes into non-uniform distribution of X-ray beam throughout the volume is given by

$$N_j = \sum_{i=1}^P a_{ij} \quad (17)$$

The sensitivity map was created by Monte-Carlo methods. The photons are assumed to have unity power within an infinite region with no boundaries. This assumption simplifies the simulation problem provided the detectors are placed close to the sample, accommodating a negligible air gap. The Monte-Carlo simulation yields a steady state distribution of ionized charges created by X-ray interaction with matter.¹² Further it compensates for the contribution of X-ray scatter and beam widening towards total ionization and emission. Optical properties of the medium are considered by taking into account absorption coefficient ($\mu_a = 0.1 \text{ cm}^{-1}$), scattering coefficient ($\mu_s = 100 \text{ cm}^{-1}$) and anisotropy ($g = 0.90$), and the mean cosines of angles of scatter. The distribution of charges can be translated to optical light by (3).

3. OPTIMIZATION AND QUALITY INDICES

As previously discussed, width of the collimator is crucial to the quality of resultant images. A narrow collimator width could improve the image resolution but also increases noise. Because of less number of photons emitted per unit time from the source, statistical quality of image decreases. When we try to alleviate this problem by increasing the collimator width, the increase in photons mitigates low SNR but affects resolution adversely due to wider beam and scatter. It could be intuitively understood that there exists a balance between these two contrasting scenarios discussed above, which can maximize resolution with reasonable amount of noise. This optimal balance could lead to the best quality of images for the given system design. We introduce the following quality indices and conditions where the optimality can be observed.

3.1. Structural Similarity Index (SSIM)

Structural similarity index (SSIM) was chosen as our means of comparing the degree of similarity in two images.¹³ This index described the level of distortion between two input images and improved on prior measurement techniques.^{14,15} The expression evaluated the similarity of images, accounting for structure, luminance and contrast locally.

Mathematically, the SSIM can be put forward as,

$$SSIM(x, y) = \frac{(2\mu_x\mu_y + C_1)(2\sigma_{xy} + C_2)}{(\mu_x^2 + \mu_y^2 + C_1)(\sigma_x^2 + \sigma_y^2 + C_2)} \quad (18)$$

Where, μ_x, μ_y were the respective means and δ_x, δ_y are the variances in 7×7 windows x and y . Window x was assigned to the candidate image, whereas y was computed on the reference digital phantom. In each of the cases, middle slice was evaluated since it eliminated chances of any geometrical distortion. $C_i = (k_i L)^2$ were variables to stabilize division with a weak denominator. L was the dynamic range of pixels, with $k_1 = 0.01$ and $k_2 = 0.03$ by default.

A unity score in the index would have indicated a perfect match. The paradigm assumed one of the images to be distortion free for bench marking the other image. In our case, we employed the longitudinally middle slice of digital phantom to provide the benchmark. This image was tested against the results of the simulation, which served as the second image for each case under study.

3.2. CT Figure of Merit

To independently investigate results from another viewpoint, a method proposed by Kalender et al. was also being employed.¹⁶ A figure of merit was hence utilized as

$$Q = \frac{c}{\sigma^2 M^{-4} D} \quad (19)$$

where δ represented noise, D as dose level, and M denoted the 10% MTF expressed in inverse of length. If we considered the FWHM (ρ) in dimensions of length, the expression could be rewritten as

$$Q = \frac{k}{\sigma^2 \rho^4 D} \quad (20)$$

For dose per unit volume, we could reduce the expression in terms of the working variables using the simplification

$$D \propto \frac{N}{\rho^3} \quad (21)$$

Hence

$$Q \propto \frac{k}{\sigma^2 \rho^4 \left(\frac{N}{\rho^3}\right)} \quad (22)$$

or,

$$Q \propto \frac{k'}{\sigma^2 \rho} \quad (23)$$

Using these two metrics, we could analyze the results effectively and find conditions of optimality.

4. SYSTEM DESIGN AND SIMULATION

The simulation model employed selective excitation and single-pixel mode for collection of the optical signal. Since nanophosphors were designed to be in small concentrations, high energy electrons created by photoelectric effect and Compton scatter, contributing to photon creation, were supposed to be arising from tissue and near vicinity. Using a translate-rotate scheme akin to first-generation CT, images could be reconstructed without spatially resolving signal. The scanning X-ray source and optical detectors were positioned at orthogonal directions. The nanophosphors simulated were $\text{Gd}_2\text{O}_2\text{S:Tb}$ with density $7.44 \text{ gm}\cdot\text{ml}^{-1}$. This crystal in pure form responds with light emission of 60 photons/KeV in the NIR spectrum (doping dependent wavelength). All simulations were carried out by computing on 100 KeV of monochromatic X-rays.

In the simulation, we assumed a cylindrical phantom of 45 mm size in a Field of view (FOV) of 50 mm. The phantom was designed with 6 spheres of diameters of 0.25 mm, 0.5 mm, 1 mm, 2 mm, 4 mm and 8 mm, having a phosphor concentration of $1 \mu\text{g/ml}$ embedded in a background containing $0.1 \mu\text{g/ml}$ phosphor distribution. Since the phantom's uptake was several times higher than the background, the effect of noise and stray photons is reduced to a minimum. It can be safely assumed that the uptake ratios could provide SNR higher than the Rose criterion ($\text{SNR} \approx 5$). The phantom was designed to mimic a typical tumor immersed in extra-cellular fluid. The design of the phantom is attributed to Praxt et al.⁶ The FOV was sampled uniformly in designated pre-determined widths across 30 views covering 360° . Poisson noise centered about the mean value of the detector reading and amounting to 5% of the value was added to emulate electronic noise. The projection data was reconstructed by ML-EM in each case, involving 30 iterations, keeping voxel size of 1 mm.

The simulations were carried out for increasing beam widths as described. The least width was 0.1 mm and the greatest width was set at 1 mm. Intervening values of beam widths were calculated. Outputs were recorded as bitmaps. The middle slice of the reconstructed image was used for all quality assessments, as shown in Figure 2. The set of images as shown in Figure 3 is representative images of variations seen in changing the beam width.

5. ANALYSIS

For calculation of signal to noise ratio, 4 equal sized regions of 45×45 were selected for background, far remotely from the nanophosphors. The variance in each of these four regions was used to assess a mean standard deviation. Signal was ascertained from a 45×45 region centered on largest circle of nanophosphors. Figure 4 illustrates the selection of regions for noise and signal.

The reconstruction SNR is obtained as

$$\text{Recon-SNR} = \frac{\mu_{sig}}{\sigma_{av}} \quad (24)$$

The full width at half maximum (FWHM) through line-pairs per mm can't be directly obtained. However, *Knife-edge* width i.e., length of the line profile, between 10% and 90%

of the maximum intensity change in a edge is considered an effective measure of the Full width at half maximum. A perfect edge would correspond to a step function, whereas a gradual change would be seen in a blurred edge. The FWHM by the Knife edge method was evaluated by a MATLAB script, which was adaptive in accordance with the extent of the blur. Subjective bias was minimized. The edge profile was calculated on the largest circle in the slice, as described by Figure 5.

6. RESULTS

Having obtained the aforementioned SNR and FWHM, the results were plotted to observe trends. Structural similarity Index and CT Figure of Merit were evaluated independently by different authors to remove any subjective bias. The structure of SSIM metric would indicate the global maxima as the optimal setting. From the tabulated data (not included), the optima indicated best performance at 0.11 mm for our given system design. The plot in Figure 6 shows the trend of results in Structural similarity of the images obtained from simulations.

The CT figure of merit would indicate the best performance when the $\mathcal{F}\rho$ value in (28) is at its minimum. The statistics for Figure of Merit was calculated (not included) and plotted, as given in Figure 7.

From the tabulation, the minimum was observed at 0.11 mm corresponding to 460 beams/FOV of sampling. It leads us to firmly believe the optimum performance would be seen at the aforementioned beam width with the given system parameters. Since two independent parameters converge to common values/range of values, we can safely assume that there exists point of optimality in the system, which we can deduce by adopting the aforementioned process to select beam-width presets for future scans.

7. DISCUSSION

As can be seen in the trends of SSIM indices and Figure of merit values, the best results doesn't correspond to the thinnest sampling beam. Optimality is seen to be separate from the beam width thickness and has encompasses the questions of noise and scatter. Deviation from optima leads to progressively deteriorating values. When the beam is thicker, higher FWHM leads to poor image quality, even though SNR is high. The blur becomes unacceptable beyond a particular point. Reducing the beam width leads to better resolution at the expense of SNR. Reducing the beam width beyond our observed optima leads to poorer image quality due to the scattering becoming significant.

The above mentioned techniques can be successfully used as a pilot scan (scout scan). Once we have an optimal value from the readings, we can proceed to perform quality scans. This can lead to better image quality in a shorter timeframe, eliminating need for repeating experiments which can be costly and labor intensive. Therefore, the proposed approach is robust and can be used for any XLCT setup with selective excitation.

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Fig. 1.
Scheme of the XLCT system via selective excitation.

Fig. 2.
Phantom and a middle-slice.

Fig. 3.

(a) 500 sampling points; (b) 400 sampling points; (c) 300 sampling points; (d) 250 Sampling points; (e) 100 Sampling points; (f) 50 Sampling points.

Fig. 4.
Selected regions for SNR measurements.

Fig. 5.
The *Knife-edge* technique in calculating FWHM.

Fig. 6.
Structural similarity index trend graph.

Fig. 7.
Figure of merit trend graph.