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Depth-of-Interaction Compensation Using a Focused-Cut Scintillator for a Pinhole Gamma Camera

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Abstract

Preclinical SPECT offers a powerful means to understand the molecular pathways of drug interactions in animal models by discovering and testing new pharmaceuticals and therapies for potential clinical applications. A combination of high spatial resolution and sensitivity are required in order to map radiotracer uptake within small animals. Pinhole collimators have been investigated, as they offer high resolution by means of image magnification. One of the limitations of pinhole geometries is that increased magnification causes some rays to travel through the detection scintillator at steep angles, introducing parallax errors due to variable depth-of-interaction in scintillator material, especially towards the edges of the detector field of view. These parallax errors ultimately limit the resolution of pinhole preclinical SPECT systems, especially for higher energy isotopes that can easily penetrate through millimeters of scintillator material. A pixellated, focused-cut (FC) scintillator, with its pixels laser-cut so that they are collinear with incoming rays, can potentially compensate for these parallax errors and thus improve the system resolution. We performed the first experimental evaluation of a newly developed focused-cut scintillator. We scanned a Tc-99m source across the field of view of pinhole gamma camera with a continuous scintillator, a conventional “straight-cut” (SC) pixellated scintillator, and a focused-cut scintillator, each coupled to an electron-multiplying charge coupled device (EMCCD) detector by a fiber-optic taper, and compared the measured full-width half-maximum (FWHM) values. We show that the FWHMs of the focused-cut scintillator projections are comparable to the FWHMs of the thinner SC scintillator, indicating the effectiveness of the focused-cut scintillator in compensating parallax errors.

Index Terms

Single photon emission computed tomography; scintillation detectors; biomedical applications of nuclear radiation; biomedical nuclear imaging

I. INTRODUCTION

Preclinical spect can potentially be a powerful platform to study fundamental biological processes and drug interactions in small animals [1]. Gamma cameras for such SPECT systems require a high spatial resolution in order to adequately map the uptake of radioisotopes in small animals. Pinhole collimators offer a technically feasible method to achieve a high resolution [2–4]. However, pinhole geometry introduces parallax errors, particularly toward the edge of the field-of-view (FOV), limiting the system spatial resolution. The parallax errors arise from the variable depth of interaction (DOI) of gamma-ray/scintillator events, especially when gamma rays enter a scintillator at steep angles. There have been several efforts to address parallax errors in pinhole SPECT, including algorithm-based DOI modeling and correction, and the use of a curved fiber bundle to collimate light from a curved scintillator [5, 6]. In PET, various methods are used to correct DOI-related errors, including use of an avalanche photodiode at the front surface of a scintillator crystal to detect the entry point an annihilation photon [7], measuring the ratio of the signals of detectors placed at opposite ends of a scintillator crystal [8], and the use of a 3D scintillator crystal array [9].

Another way to overcome parallax errors in a pinhole gamma camera is to use a focused-cut scintillator, which is pixellated so that the pixels are focused towards the pinhole of a collimator [10]. Thus, the path of a ray that has passed through the pinhole only intersects a single pixel in the scintillator. A focused-cut scintillator can be thicker than conventional scintillators, as parallax errors should theoretically no longer be an issue, and thus can improve the sensitivity of a pinhole gamma camera without sacrificing spatial resolution. Here, we experimentally evaluated a pinhole gamma camera with a focused-cut scintillator. We measured the degree of blurring in terms of full-width at half-maximum (FWHM) across a continuous scintillator, a straight-cut pixellated scintillator, and a focused-cut pixellated scintillator. Our results show that a 3 mm thick FC scintillator has a comparable degree of blurring at the edge of the scintillator to that of a thinner, 1.5 mm thick, SC scintillator, demonstrating the effectiveness of the DOI compensation yielded by the FC scintillator design.

II. OPERATING PRINCIPLE

When a gamma ray travels through a scintillator, it may either ionize or excite an atom or molecule in the scintillator, producing light that can be detected by conventional means, or it may simply pass through the scintillator. The precise interaction location along its trajectory is unknown, with the mean depth-of-interaction, Δl , approximately equal to μ^{-1} , where μ is the linear attenuation coefficient of the scintillator material. The resulting mean offset in the centroid of the projection through a knife-edge pinhole, $\bar{\sigma}$, can be shown to be equal to

$$\bar{\sigma} = \frac{\sin \theta - \exp(\mu T \sec \theta) + \mu T \tan \theta}{\mu [1 - \exp(\mu T \sec \theta)]} \quad (1)$$

where θ is the angle between the incident gamma ray and the vector normal to the surface of the scintillator and T is the scintillator thickness [11]. For CsI:Tl, with a linear attenuation at

140 keV of 0.383 mm^{-1} , the mean centroid offset reaches 1.0 mm at incident ray angle of 40° , as shown in Fig. 1. The error is greater than 0.40 mm even at a 20° incident angle and thus can be a major limitation to achieving sub-mm spatial resolution in pinhole SPECT systems. Fig. 2(a) illustrates the DOI effect on parallax error in a continuous scintillator, with $\bar{v}$ being the mean DOI [11] given by

$$\bar{v} = \frac{\mu T + \cos \theta - \exp(\mu T \sec \theta) \cos \theta}{\mu [1 - \exp(\mu T \sec \theta)]} \quad (2)$$

The use of a conventional pixellated straight-cut (SC) scintillator limits the spread of light emitted from an interaction event, but parallax errors still remain an issue, as illustrated in Fig. 2(b).

Here, we show that a pixellated focused-cut (FC) scintillator can be used to compensate for parallax errors in pinhole SPECT systems. Each pixel in the scintillator is cut so that it is focused at the pinhole of the collimator used in the SPECT system, as shown in Fig. 2(c) for a few scintillator pixels and in Fig. 3(a) for a complete FC scintillator, with f defined as the pinhole-to-detector distance along z , i.e., the focal length, b the pinhole-to-source distance, Δx the center position of the source in x , d the diameter of the source, t the scintillator thickness, θ the maximum ray angle, and ϕ the central incident angle, and w_s the scintillator width.

The trajectory of an incident gamma ray on the FC scintillator is confined to a single pixel, unlike in a conventional SC scintillator, thus compensating for the effect of DOI on parallax errors.

The FC scintillator only works for a particular focal length f , i.e., each scintillator pixel cut angle is dependent on f according to

$$\theta_n = \arctan \left[\frac{(n-1)w_p - w_s/2}{f} \right] \quad (3)$$

where n is the cut number, ranging from 1 to $N+1$, where N is the number of pixels, and w_p is pixel width defined at the bottom of the scintillator. Because f must remain fixed for this design, the pinhole-to-object distance b must be set to achieve the desired field-of-view (FOV) and resolution for a complete imaging system in accordance with conventional knife-edge pinhole camera design principles.

Parallax errors can still occur in FC scintillators, primarily due to scattering and penetration events, especially in the case of higher energy radionuclides [12]. In particular, photon penetration through the collimator and collimator scatter, in which the photon ray paths do not necessarily pass through a collimator pinhole, would still limit the resolution of a pinhole camera using an FC scintillator. While collimator scatter can be neglected for lower energy isotopes, photon penetration through knife-edge pinhole edges can be a strong effect, particularly for narrow, sub-mm pinholes. It is non-negligible, contributing up to a quarter of detected 140 keV photons from a hotspot phantom using a 1.0 mm pinhole collimator, and is thus worthy of further investigation [12].

III. EXPERIMENTAL SETUP

We evaluated the capability of a 3 mm thick CsI:TI FC scintillator to compensate parallax errors by comparing the FWHM of a projected source to the FWHMs for a 3 mm thick

continuous CsI:Tl scintillator and for a 1.5 mm thick CsI:Tl SC scintillator. The thinner SC scintillator is used as the gold standard with which to compare the DOI compensation effect of the FC scintillator. The FC scintillator was laser-cut to create 350 μm pixels. The angular range of the cuts was between -20° and 20° and was limited by the angular tilt range of the goniometer used to set the cut angles in the etching process. The SC scintillator was laser-cut to create 325 μm pixels. The FC scintillator was fabricated through excimer laser ablation (KrF ($\lambda = 248 \text{ nm}$)) from a continuous CsI:Tl scintillator at Resonetics Inc. The CsI:Tl crystals of thickness of 3 mm, were cut to produce structured columns, oriented towards the pinhole collimator aperture. The cut width averaged 30 μm , which is much thinner than the 325 μm pixel size and thinner than what is achievable by a wire saw. More details of the fabrication procedure are discussed elsewhere [10]. All three scintillators have an active area of $10 \times 10 \text{ mm}^2$. The experimental setup is shown in Fig. 3. The FC and SC scintillators are mounted on a fiber-optic substrate, which is then pressure-coupled to the fiber-optic plug of the EMCCD camera. Index-matching fluid is placed between the substrate and plug for each scintillator. The continuous scintillator is directly pressure-coupled to the fiber-optic plug, also with a layer of index-matching fluid between it and the plug.

We imaged a $\sim 100 \mu\text{Ci}$ Tc-99m (140 keV) point source, a 1.12 mm diameter resin ion exchange bead previously immersed in a NaTcO₄ solution, as it was translated across the FOV of the scintillators. A tungsten collimator with a 1 mm diameter knife-edge pinhole and a thickness of 6 mm was used. The photons emitted from a scintillator were transmitted through a 1 mm thick 1:1 fiber optic plug and collected by a cooled electron-multiplying charged-coupled device (EMCCD) camera, a back-illuminated Andor iXon DV887. The EMCCD has an $8 \times 8 \text{ mm}^2$ detector, a 16 μm pixel width, and 512×512 binning. The detector area is less than that of the scintillator area (64 mm^2 vs. 100 mm^2 , respectively) and is thus not able to capture all of the emitted scintillation light.

The values for the geometrical parameters of the experimental setup shown in Fig. 3(a) were calculated as follows. A primary constraint is that the collimated rays are properly aligned with the angled pixels of the FC scintillator. We aligned the rays by setting f so that the maximum ray angle at the edge of the scintillator, θ_{max} , is equal to 20° , the maximum pixel cut angle. We calculated the necessary values of f in order to achieve $\theta = \theta_{\text{max}}$ at the edge of scintillator ($x = -w_s/2$) from

$$f = \frac{w_s}{2 \tan \theta_{\text{max}}} \quad (4)$$

yielding $f = 13.737 \text{ mm}$. We took into account the mean DOI $\bar{v}$ for each scintillator when determining the necessary spacings between the physical components in our experimental setup in order to keep the focal length fixed at the same value for all scintillators. However, we were limited by the precision of our mechanical setup and thus set f to within $13.8 \pm 2 \text{ mm}$. The pinhole-to-object distance, b , was set to 31.6 mm, large enough so that the 1.12 mm diameter resin bead would best approximate a point source given the 2.42 mm theoretical knife-edge pinhole collimator resolution while maintaining an acceptable level of sensitivity (3.38×10^{-5}) for imaging. The resulting magnification was 0.437, yielding a FOV of 18.3 mm at a distance b from the pinhole. We adjusted the spacing between the object, collimator, and detector based on each scintillator's dimensions so that f and b were maintained approximately constant for each experimental setup.

It is important to note that the expression for the magnification of an FC-scintillator-based pinhole camera is different from that of a conventional pinhole camera ($M = f/b$). In the

case of the FC scintillator, there is additional magnification through the thickness of the scintillator, which is illustrated in Fig. 3(a). The resulting magnification of the FC scintillator setup, M_f , is thus

$$M_f = \frac{f+t}{b} \quad (5)$$

and is equal to 0.530 in this setup.

We acquired the images in “integration mode”, exposing the EMCCD for 30 s per image and measuring the number of counts accumulated in each pixel during the exposure-time. We then performed background-subtraction on each image and median filtering in order to remove dark current noise.

We measured the FWHM of the projected image along its axis of the source displacement (x in Fig. 3) using a 1D Gaussian-fitting algorithm. The FWHM of the projected spot as ϕ is varied for each scintillator is shown in Fig. 4(a) from 0° to 17° , corresponding to a change in θ of 1° to 18° . Three projections were obtained for each angle in order to obtain mean and standard deviation values for each measurement. In addition, the theoretical collimator resolution for the knife-edge pinhole collimator used in experiment, 2.42 mm, [13] is plotted in Fig. 4(a) for sake of reference. The FWHM values were actually scaled from the measured profiles to object space, i.e., they were divided by the camera magnification M in order to provide a common reference plane for comparison [13]. The continuous and SC FWHM values were thus divided by $M = 0.437$. The “uncorrected” FWHM values were divided by with $M = 0.437$ while the “corrected” FWHM values were divided by the corrected magnification, $M_f = 0.530$.

IV. EXPERIMENTAL RESULTS AND DISCUSSION

Representative images of the translated source are shown Fig. 4(b)–(d) for the SC, FC, and continuous scintillators, respectively. We see in Fig. 4(a) that the FC scintillator, despite being twice times as thick as the 1.5 mm thick SC scintillator, has a comparable FWHM over the ray angle range shown in the figure, indicating that the focusing effect of the FC scintillator is indeed compensating the DOI effects. Also, it can be seen that the FWHM for the continuous scintillator monotonically increases with ray angle. However, in the case of the FC and SC scintillators, the FWHM remains fairly constant as ray angle increases and then begins drop as the ray angle exceeds 12° . Also, Figs. 4(b)–(d) show that the projections seem to become smaller in diameter at steeper angles for the SC and FC scintillators, but not for the continuous scintillator. What is happening is that at steeper angles, the gamma rays emitted from the source towards the pinhole collimator effectively see a narrower pinhole than at shallower angles because the septa penetration is being reduced in the knife-edge pinhole geometry; thus the FWHM of the point-spread-function becomes narrower [11]. Of course, DOI causes the FWHM to widen at steeper angles, so these two effects compete. DOI appears dominant in the case of the continuous scintillator, but in the case of the FC and SC scintillators, the reduction of the septa penetration dominates.

In addition, although a relatively minor effect, the longer pixels at the edge of the FC scintillator relative to the pixels near the center of the FC scintillator lead to increased visible light absorption and scatter of visible photons and thus increased attenuation near the edges of the crystal. Using the following expression for FC pixel length,

$$l_\theta = T \sec \theta \quad (6)$$

where l_θ is the pixel length at a cut angle of θ , it can be shown that the pixel length at the edge of the scintillator is about 0.19 mm, or 6.3% of the scintillator thickness of 3 mm. At steeper angles, such as at 45° , the pixel length would increase by 1.25 mm, a 40% increase over the nominal value, and would become non-negligible in processing data from a FC scintillator.

Fig. 5 shows line profiles of the images depicted in Fig. 4(c), with a count level of “0” indicating the background level. The line profiles were not magnification-scaled as were the FWHM values in Fig. 4 (a). The point-spread-function peak monotonically decreases with increasing angle as expected due to the well-known $\cos^3 \theta$ dependence of geometric sensitivity on incidence angle for a pinhole collimator [13].

V. CONCLUSION

We demonstrated DOI compensation using a laser-pixelated focused-cut (FC) CsI:Tl scintillator. The pixels of an FC scintillator were laser-cut so that each pixel was focused towards the pinhole aperture. Thus, each collimated gamma ray passing through the scintillator can only interact within a single pixel. An experimental comparison of the FWHM of a projected Tc-99m source using three different scintillators showed that the FC scintillator had comparable resolution compared with a thinner SC scintillator. This result demonstrates the potential of using FC scintillators to achieve ultra high sub-mm resolution preclinical imaging and thus warrants investigating the performance of a full preclinical SPECT imaging system using an FC scintillator.

This technique can be potentially adapted to fabricate large area detectors with steeper cut angles by using the appropriate goniometer. The advantage of having a large area detector is that you can get better magnification and thus perform higher resolution pinhole gamma camera imaging.

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REFERENCES

1. Franc BL, Acton PD, Mari C, Hasegawa BH. Small-animal SPECT and SPECT/CT: important tools for preclinical investigation. *Journal of Nuclear Medicine*. 2008 Oct 1.vol. 49:1651–1663. [PubMed: 18794275]
2. Jaszczak RJ, Li J, Wang H, Zalutsky MR, Coleman RE. Pinhole collimation for ultra-high-resolution, small-field-of-view SPECT. *Physics in Medicine and Biology*. 1994 Mar 1.vol. 39:425–437. [PubMed: 15551591]
3. Funk T, Després P, Barber WC, Shah KS, Hasegawa BH. A multipinhole small animal SPECT system with submillimeter spatial resolution. *Med Phys*. 2006 May 1.vol. 33:1259–1268. [PubMed: 16752560]
4. van der Have F, Vastenhout B, Ramakers RM, Branderhorst W, Krah JO, Ji C, Staelens SG, Beekman FJ. U-SPECT-II: An Ultra-High-Resolution Device for Molecular Small-Animal Imaging. *Journal of Nuclear Medicine*. 2009 Mar 16.vol. 50:599–605. [PubMed: 19289425]
5. Korevaar MAN, Heemskerk JWT, Beekman FJ. A pinhole gamma camera with optical depth-of-interaction elimination. *Physics in Medicine and Biology*. 2009 Jul 7.vol. 54:N267–N272. [PubMed: 19521006]
6. Korevaar MAN, Heemskerk JWT, Goorden MC, Beekman FJ. Multi-scale algorithm for improved scintillation detection in a CCD-based gamma camera. *Physics in Medicine and Biology*. 2009 Feb 21.vol. 54:831–842. [PubMed: 19141886]

7. Maas MC, Schaart DR, van der Laan DJJ, Bruyndonckx P, Lemaître C, Beekman FJ, van Eijk CWE. Monolithic scintillator PET detectors with intrinsic depth-of-interaction correction. *Physics in Medicine and Biology*. 2009 Apr 7.vol. 54:1893–1908. [PubMed: 19265203]
8. Du H, Yang Y, Cherry S. Comparison of four depth-encoding PET detector modules with wavelength shifting (WLS) and optical fiber read-out. *Physics in Medicine and Biology*. 2008 Apr 7.vol. 53:1829. [PubMed: 18364541]
9. Orita N, Murayama H, Kawai H, Inadama N, Tsuda T. Three-dimensional array of scintillation crystals with proper reflector arrangement for a depth of interaction detector. *Nuclear Science, IEEE Transactions on*. 2005; vol. 52:8–14.
10. Nagarkar, VV.; Kudrolli, H.; Singh, B. Focused Scintillator Array for High Resolution Gamma Ray Imaging; *IEEE Medical Imaging Conference*, 2010; 2010. p. M14-M98.
11. Metzler SD, Greer KL, Jaszczak RJ. Determination of mechanical and electronic shifts for pinhole SPECT using a single point source. *Medical Imaging, IEEE Transactions on DOI -* 10.1109/42.97591. 2005; vol. 24:361–370.
12. Deloar HM, Watabe H, Aoi T, Iida H. Evaluation of penetration and scattering components in conventional pinhole SPECT: phantom studies using Monte Carlo simulation. *Physics in Medicine and Biology*. 2003 Apr 21.vol. 48:995–1008. [PubMed: 12741497]
13. Cherry, SR.; Sorenson, JA.; Phelps, ME. *Physics in Nuclear Medicine*. 3rd edition. Philadelphia: Saunders; 2003.

Fig. 1.
Mean centroid offset vs. ray angle in a CsI scintillator for a 140 keV gamma ray.

Fig. 2.

(a) Geometrical illustration of the DOI and resulting parallax error occurring when a gamma ray passes through a continuous scintillator, (b) a SC scintillator, and (c) DOI compensation by a FC scintillator.

Fig. 3.
 (a) Schematic diagram of the experimental setup with the FC scintillator. The red lines indicate the boundaries of the emitted gamma rays from the source and the yellow shading indicates light emitted from scintillation events; (b) a photograph of the actual experimental setup.

(a)

(b)

(c)

(d)

Fig. 4.

(a) FWHM, including the magnification corrections, of the projected image vs. central ray angle, ϕ , for the continuous, straight-cut, and focused-cut scintillators (with and without magnification correction) along with the theoretical collimator resolution without DOI taken into account. Error bars indicate the standard deviation obtained from three sets of measurements; (b) an overlay of spot images from the SC scintillator with $\phi = 0^\circ, 10^\circ, 17^\circ$ and a blue line indicating the range of pixels used to determine the FWHM of the 0° spot; (c) and (d) show similar images for the FC scintillator and for the continuous scintillator, respectively. The line profiles used to calculate the FWHM values in (a) are indicated by black lines, with arrows pointing in the direction of increasing ϕ .

Fig. 5.
Line profiles of the FC scintillator images shown in Fig. 4(c) taken along the x axis indicated in the figure.