C05-16 Final Report

C05-016 Final Report

“A Detector for Combined SPECT/CT”

Final Technical Report

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I. DEGREE TO WHICH PHASE I HAS DEMONSTRATED TECHNICAL FEASIBILITY

A. OVERVIEW

The goal of the Phase I research was to demonstrate the feasibility of developing a high performance SPECT/CT detector module based on a combination of microcolumnar CsI(Tl) scintillator coupled to an EMCCD readout (see **Figure 1**). We are very pleased to report that our Phase I research has demonstrated the technical feasibility of our approach with a very high degree of success. Specifically, we were able to implement a back-thinned EMCCD with a fiberoptic window which was successfully used to demonstrate the feasibility of near simultaneous radionuclide/CT using the proposed concept. Although significantly limited in imaging area ($24 \times 24 \text{ mm}^2$) and pixel resolution (512×512), this prototype has shown exceptional capabilities such as a single optical photon sensitivity, very low noise, an intrinsic resolution of $64 \mu\text{m}$ for radionuclide imaging, and a resolution in excess of 10 lp/mm for x-ray imaging. Furthermore, the combination of newly developed, thick, microcolumnar CsI and an EMCCD has shown to be capable of operating in a photon counting mode, and that the position and energy information obtained from these data can be used to improve resolution in radionuclide imaging. Finally, the prototype system has successfully been employed for near simultaneous SPECT/CT imaging using both, ^{125}I and $^{99\text{m}}\text{Tc}$ radioisotopes. The tomographic reconstruction data obtained using a mouse heart phantom and other phantoms clearly demonstrate the feasibility and efficacy of the detector in small animal research. The following were the objectives specified in the Phase I proposal:

1. In consultation with Professor Hasegawa, develop specifications for the Phase I/Phase II prototype detector;
2. Modify current vapor deposition protocols to fabricate ~2 mm thick microcolumnar CsI(Tl) scintillators with excellent columnar structure, high light yield, and high spatial resolution;
3. Perform detailed characterization of the film morphology, light output, and spatial resolution, and use these data to refine deposition protocols;
4. Develop suitable designs of a collimator to be fabricated during the Phase II;
5. Integrate thick CsI(Tl) films into the existing IGCCD camera to form a prototype dual-imaging detector module;
6. Conduct evaluation of the prototype SPECT/CT detector to determine its suitability for x-ray CT and radionuclide imaging;
7. Write the Phase I final report and prepare the Phase II research plan.

Figure 1: Conceptual design of the proposed dual-modality SPECT/CT detector.

Our work in Phase I has not only accomplished all the above stated goals, but has surpassed them in many aspects. The data presented in the report below show that the proposed combined detector will not only minimize the complexity and cost associated with conventional readouts, but will also improve system reliability necessary for the

Figure 2: SEM micrographs of microcolumnar CsI(Tl) films developed during the Phase I. (a,b) A 200 μm thick film. (c,d) A 1.5 mm thick film. Excellent columnar growth in spite of a very high thickness of the film is clearly evident.

development of a dual modality system. This is a substantial accomplishment, which brings us a step closer to our Phase II goal of developing a much larger area, higher pixel resolution detector and minimizes risk associated with implementation of the proposed design.

FABRICATION OF THICK MICROCOLUMNAR CsI(Tl) FILMS

Although microcolumnar CsI(Tl) scintillator films are commercially available, the maximum thickness of such films is $\sim 600 \mu\text{m}$, which is insufficient for providing adequate attenuation of 140 keV $^{99\text{m}}\text{Tc}$ γ -rays. The research into fabrication of the required 2 to 3 mm thick CsI(Tl) films has been going on at RMD for the past one year [i], and involved depositing high quality CsI films ranging from 200 μm to over 2.5 mm in thickness on an amorphous carbon substrate. The carbon substrates are inexpensive and minimally attenuate the incident x-rays/ γ -rays. Substrates were coated with a 1 μm thick aluminum reflector prior to CsI(Tl) vapor deposition, which enhances the light collection efficiency by $\sim 40\%$. Thinner, 200 μm to 500 μm films were fabricated for combined SPECT/CT studies using $\sim 30 \text{ keV}$ ^{125}I radioisotope and up to 70 kVp x-rays respectively.

During Phase I several hardware modifications to the existing evaporation system were made. These include enhancing the capacity of the source boat to accommodate larger quantities of CsI(Tl), the development of a specialized planetary system to hold substrates at an angle most suitable for well separated columnar growth, and re-designing the water cooled thermal shield to minimize heat transfer from the source boat to the substrates.

Figure 2 shows SEM micrographs of a representative, 200 μm and 1.5 mm thick, microcolumnar CsI(Tl) films deposited during Phase I. As can be seen from the figure, the modified evaporation system was able to produce CsI(Tl) films of required thickness. After deposition, all the films were coated with a 1- 5 μm thin layer of Parylene which forms a hermetic sealing and protects films from the atmospheric

moisture. While the films also show excellent columnar structure, further separation in neighboring columns is necessary to enhance spatial resolution. This task will be continued at RMD and will benefit the research in Phase II of the program.

CSl(Tl) FILM CHARACTERIZATION

1. X-RAY CHARACTERIZATION

The light output, signal-to-noise ratios, and spatial resolution performance of scintillator films were evaluated by coupling them to a CCD system available at RMD. This system consist of a 1024×1024 pixel thermoelectrically cooled CCD optically bonded to a 3:1 fiberoptic taper. The effective CCD pixel size is $57 \mu\text{m}$, resulting in a Nyquist limiting frequency of 8.6 lp/mm. The x-ray source used was a Gendex Series 1000, tungsten target, 40-110 kVp continuously variable energy source. For evaluation of 200 to $500 \mu\text{m}$ films the x-ray generator was set at 70 kVp, and for thicker films it was set at the maximum of 110 kVp. The source to detector distance was maintained at 65cm.

While several screens were evaluated, the data presented below are for amorphous carbon based Csl(Tl) films measuring $500 \mu\text{m}$ to 2.7 mm in thickness, that were used in imaging experiments conducted with the help of Dr. Bruce Hasegawa at UCSF and Dr. Freek J. Beekman at the UMC Utrecht, the Netherlands. Our calculations showed that $500 \mu\text{m}$ thick Csl(Tl) should attenuate ~93% of ~30 keV ^{125}I γ -rays and ~12% of 140 keV $^{99\text{m}}\text{Tc}$ γ -rays, where as 2.7 mm thick Csl(Tl) films should attenuate approximately 68% of incident 140 keV γ flux.

LIGHT OUTPUT MEASUREMENTS

Light output measurements were made by exposing the films to a uniform flood field of 110 kVp x-rays, and averaging analog to digital unit value (ADUs) in a pre-defined region of interest (ROI). For each measurement the x-ray exposure was 4 mR. The signal to noise ratio (SNR) in each screen was computed by dividing the average ADU value by the measured standard deviation in the flood image. The results of these measurements are listed in **Table 1**. As can be clearly seen, films deposited on amorphous carbon substrate with aluminum reflector show ~40% higher light yield and better SNR performance. These films were used for further experiments.

Table 1: Representative results of light output and SNR measurements on Phase I Csl(Tl) films.

Film Thickness mm (mg/cm ²)	Substrate			
	Carbon with aluminum reflector		Carbon without aluminum reflector	
	Light Output (ADUs)	SNR	Light Output (ADUs)	SNR
2.7 mm (1.22 g/cm ²)	15,100	368	9,700	236
1 mm (450 mg/cm ²)	11,800	277	7,900	180
500 μm (225 mg/cm ²)	6,800	178	4,100	115

Table 2: Specifications of the back thinned, fiberoptic window based , EMCCD used for Phase I feasibility demonstration.

Parameter	Specification
CCD Chip	E2V CCD887 BI
Illumination	Back Illuminated
CCD Format	512 x 512 Pixels
Pixel Size	16 μm Square
Active Area (1:1 fiberoptic window)	8.2 x 8.2 mm^2
Active Area (3:1 fiberoptic window)	24.6 x 24.6 mm^2
Full well capacity	250 ke-
Gain register capacity	850 ke-
Readout	16 bits; 10MHz
Frame rate (full resolution)	32 fps
Binning	Flexible binning
Frame rate binned mode	Up to 520 fps
On-chip gain	1 to >1000x
Operating temperature	-30C
Dark current	1 e-/pixel/sec @ -30C
Read noise at 10 MHz	30 e- (Unity gain)
Read noise at 10 MHz	<1 e- (Gain of 30)

SPATIAL RESOLUTION MEASUREMENTS

To evaluate spatial resolution of Phase I scintillator screens, the pre-sampling MTF was measured according to the technique described by Fujita et al [ii] and others [iii,iv,v]. An image of a 10 μm wide tantalum slit placed at a slight angle (less than 1 degrees) to the CCD pixel matrix at the center of the detector was obtained. The exposure was adjusted by varying the mAs while maintaining a constant 110-kVp, to ensure that the tails of the resulting step function had no significant electronic noise. The finely sampled LSF was obtained and normalized to a

peak value of one. The Fourier Transform (FT) of the finely sampled LSF was performed to provide the presampling MTF. **Figure 3** shows the measured MTF as a function of spatial frequency for 200 μm to 2.7 mm thick CsI(Tl) screens.

Figure 3: Spatial resolution of Phase I CsI(Tl) films. These data demonstrate that microcolumnar structure minimizes the traditional tradeoff between detection efficiency and spatial resolution of scintillators. Microcolumnar film of required thickness can, therefore, be fabricated to achieve high detection efficiency for ~30 to 140 keV γ -rays.

As can be seen from the figure, the 10% MTF for a 200 μm film is at ~10 lp/mm, which corresponds to a resolution of 50 μm . The 10% MTF for a 2.7 mm thick film is at ~1.0 lp/mm, resulting in a limiting resolution of ~500 μm . The tails of the MTF(f) in this case extend up to 2.0 lp/mm, showing that the film will be able to resolve ~250 μm , although with reduced contrast. These data demonstrates very high spatial resolution capability of microcolumnar CsI(Tl) film, which minimizes the traditional tradeoff between detection efficiency and spatial resolution.

PHASE I EMCCD SYSTEM

Originally Phase I feasibility studies were planned to be performed using the existing, front illuminated, EMCCD and coupling it to a microcolumnar CsI(Tl) film using a fast lens. Knowing limitations of a lens coupling, we had planned to develop a system based on back thinned EMCCD bonded to a fiberoptic taper, which would enhance the system sensitivity by over an order of magnitude. We are pleased to report that in collaboration with Andor Technologies, CT, we were able to design and implement such system, which became available for the Phase I studies. Although limited in active area and pixel resolution, this system provided an ideal platform for demonstrating the feasibility of our approach. Detailed specifications of the Phase I system are given in **Table 2** and system photographs are shown in **Figure 4** respectively.

Figure 4: Photographs of the Phase I EMCCD system with the permanently attached 1:1 fiberoptic plug. Detachable 3:1 fiberoptic taper is shown on the left.

The successful development of a back thinned EMCCD camera with fiberoptic window is the first of its kind, and is a significant accomplishment. This not only boosts our confidence in the proposed design, but also allows us to refine our Phase II plans of incorporating a new, larger area, EMCCD needed for enhanced detector area and spatial resolution for SPECT/CT imaging.

EVALUATION OF THE EMCCD CAMERA

To ensure that the new EMCCD system provides very low noise, high sensitivity, and wide dynamic range, its performance was characterized during the Phase I. The system tests demonstrated excellent performance, and as such was found to be well suited for the proposed combined SPECT/CT application. Specifically, the measured dark noise at -35°C and for an internal gain of unity, was found to be $0.2\text{ e}^{-}/\text{pixel}/\text{second}$. For the maximum gain of 1000, the measured noise increased to $0.3\text{ e}^{-}/\text{pixel}/\text{second}$ which is negligible.

The effective read noise at 10 MHz readout speed (maximum possible speed) was measured to be $\sim 35\text{ e}^{-}$ for unity gain. As expected, with internal gain set to 35 or above, the effective read noise contribution was measured to be $<1\text{ e}^{-}$.

The effective dynamic range of the system for the gain of 35 was estimated as follows. The full well capacity of the e2V 887 EMCCD image pixels is 250K e^{-} and that of the gain register pixel is 850K e^{-} . Thus, when the CCD is operated at the gain of 35, the maximum usable pixel well capacity is $850,000/35$ or 24,285 electrons, or $14\frac{1}{2}$ bits. Since the dark and read noise is negligible, most of this dynamic range is useful. Thus, the "sweet point" of camera operation is the gain of 35 at which point the read noise is $<1\text{ e}^{-}$ and the camera allows a wide dynamic range of $14\frac{1}{2}$ bits.

To measure the sensitivity, the EMCCD camera was mounted on an optical bench and a laser beam was used to illuminate pixels through the fiberoptic window. A 540 nm collimated laser beam was made incident on the EMCCD. The camera was operated at 10 fps, and at gain of ~ 50 . The photon flux was measured with a Hamamatsu calibrated photodiode (1336-8BQ). Metallic neutral density filters (ThorLabs) were added in the path of the laser beam to attenuate the incident flux until the image could be barely seen on the monitor. The measured fluence for this setting was ~ 1 photons/pixel, indicating that camera was sensitive to ~ 1 green photons. It should be noted that conventional front illuminated CCDs cannot register a signal below ~ 30 optical photons. The significance of this result is that our prototype detector based on back illuminated

EMCCD is able to detect extremely low levels of light generated in the scintillator screens.

DETECTOR INTEGRATION AND EVALUATION USING RADIONUCLIDE SOURCES

For evaluating the feasibility of using EMCCD in photon counting mode, CsI(Tl) films selected on the basis of their performance were coupled to the fiberoptic window of the EMCCD. The goals of these studies were two fold: 1) to verify if EMCCD, with its high sensitivity and high speed, can be used in photon counting mode during

Figure 5: Image ^{99m}Tc line source and ^{125}I BrachySeeds captured in single photon counting mode with a 3 mm scintillator (left). Right column shows magnified views of single ^{99m}Tc (top) and ^{125}I (bottom) events.

radionuclide imaging, and 2) to identify pixel cluster corresponding to a single γ -ray event and use this information to localize the event with high precision. The energy and position information obtained by these measurements could then be used to improve spatial resolution of the EMCCD based γ -camera. These measurements were made in consultation with Dr. Freek Beekman, Department of Nuclear Medicine, University Medical Center Utrecht, The Netherlands. Microcolumnar CsI films of thickness varying from 500 μm and 1 mm fabricated at RMD were used for this purpose.

2. SINGLE γ -RAY PHOTON IMAGING

Initially, we recorded single events from a ^{99m}Tc source and then from a ^{125}I source in a single frame using the EMCCD camera coupled to a 3 mm thick scintillator. The relative brightness of the single events in this image (**Figure 5**) indicated that this property can be used to distinguish the photon energies of the single events when the camera is operated in an integration mode. The data also show the extent of light spread in 3 mm thick CsI(Tl).

ENERGY SPECTRA MEASUREMENTS

Figure 7: EMCCD system spatial resolution using ^{99m}Tc source. (a) Images with 1:1 Fiberoptic. (b) Images with 3:1 Fiberoptic. (c) Line profiles for integration and photon counting modes of imaging using 1:1 fiberoptic. (d) Corresponding profiles using 3:1 fiberoptic.

Figure 6: Energy spectra of ^{57}Co (122 keV) and ^{129}I (40 keV) obtained using EMCCD/columnar CsI(Tl) combination. In both cases the detector can clearly distinguish the noise. These data, for the first time, demonstrate possibility to filter some of the scattered photons using energy discrimination.

The spectral measurements shown in **Figure 6** were performed using a 500 μm thick CsI(Tl) film deposited on aluminized graphite. The detector was exposed to radioactive sources (without the collimator) and images were acquired with EMCCD operated at 30 fps. A set of 40,000 frames of data for each measurement was acquired and processed using the photon counting algorithm developed by Dr. Beekman [vi]. A set of 3000 dark images (without radioactivity) was acquired and averaged to establish the background per CCD pixel. Each CCD image with the source was background corrected by subtracting the averaged background. The corrected images were further smoothed with a 2D Gaussian kernel g (g ; FWHM of 0.15mm at the CCD) to suppress high frequency noise in the image [vi]. The resulting filtered image shows scintillation events as bright spots. If the value of a local maximum in the smoothed image lies between the lower limit (ll) and the upper limit (ul), it is assumed to be a relevant scintillation event and its position and intensity are registered in a PC. A combined histogram of events in all 40,000 frames forms the energy spectrum.

Figure 6 shows the ^{129}I (40 keV) and ^{57}Co (122 keV) energy spectra measured using 500 μm thick CsI(Tl) film, along with the background spectrum. For 122 keV and 40 keV γ -rays, the detector can clearly distinguish the noise. Also, it shows possibility to filter out some of the scattered photons using energy

Table 3: Summary of the resolution in integrating and photon counting modes of operation. These data were acquired by imaging a 30 μm wide tungsten slit with $^{99\text{m}}\text{Tc}$ and ^{125}I sources.

Mode of Operation	Tc-99m		I-125	
	1:1 Fiberoptic	3:1 Fiberoptic taper	1:1 Fiberoptic	3:1 Fiberoptic taper
	FWHM		FWHM	
Integration	342 μm	343 μm	270 μm	309 μm
Photon counting	64 μm	96 μm	66 μm	110 μm
	FWTM		FWTM	
Integration	1123 μm	983 μm	778 μm	775 μm
Photon counting	121 μm	181 μm	138 μm	221 μm

discrimination. This is an exciting result, which demonstrates the feasibility of operating EMCCD based γ -camera in photon counting mode. With refinements in thick CsI(Tl) film technology, and improved computer algorithms, the energy resolution may further be improved. This task will be pursued during the Phase II.

INTRINSIC RESOLUTION IN PHOTON COUNTING AND INTEGRATING MODES

To determine intrinsic spatial resolution of the EMCCD system for photon counting and integrating modes of operation, images of a 30 μm wide tungsten slit were obtained using $^{99\text{m}}\text{Tc}$ (37 MBq or 1 mCi) and ^{125}I (37 MBq or 1 mCi) source (**Figure 7**). A radioactive source was placed above the slit and the projection of the source through the tungsten slit was imaged. The use of a slit is a standard method for measuring intrinsic resolution, and is widely used to characterize clinical gamma cameras. These measurements were made with a 1:1 and a 3:1 fiberoptic attached to the EMCCD. In each case, a 1 mm thick microcolumnar CsI(Tl) film was optically coupled to the fiberoptic.

For photon counting mode, afore mentioned algorithm was used to detect and localize individual scintillation events in real-time (30 fps) [vi]. A simple algorithm to estimate the centroid position of the distribution of light over CCD pixels was used for precision localization of the event, which was then stored in the PC. In photon integration mode, the individual CCD images were acquired, averaged, and saved in a PC. Similarly, background images were acquired and averaged, and were used to correct the slit image.

Figure 7 show representative images and line profiles obtained using $^{99\text{m}}\text{Tc}$ source. Similar data are also acquired for ^{125}I source. The corresponding full width at half maximum (FWHM) and full width at tenth maximum (FWTM) data are outlined in **Table 3**.

The data presented here shows that a gamma camera based on the combination of a microcolumnar CsI(Tl) and an EMCCD offers an excellent intrinsic spatial resolution. Furthermore, the photon counting mode of operation significantly improves this resolution. It should be noted that no scatter correction has been applied to the above data. These data demonstrate the capability and feasibility of our approach for

SPECT imaging. With further modifications to the centroid calculation algorithm and possibly correcting for scatter, even better resolution may be obtained. These modifications/corrections will be investigated during Phase II.

COMBINED SPECT/CT DETECTOR FEASIBILITY STUDIES AT UCSF

3. PHASE I COLLIMATOR

While various collimator geometries outlined earlier were considered for the proposed application, a 0.5 mm pinhole collimator was available at Dr. Hasegawa's laboratory at UCSF and was relatively easy to implement for feasibility studies in the Phase I project. As shown in **Figure 8**, this pinhole has a 52-degree opening angle within a 1.4 cm thick lead threaded insert that can be attached to the camera housing. The figure also depicts a 1 cm reconstruction circle projected on a 2.46 cm detector field of view. Note that the red dotted lines (outer lines) define the pinhole cone angle where as the green dotted lines (inner lines) denote the detector field of view.

Table 4: Phase I 0.5 mm, 52 degree, pinhole collimator resolution and efficiency for various object distances. A reconstruction circle of 1 cm is assumed for these calculations.

Pinhole to Object Distance (cm)	Collimator to Detector Distance (cm)	Effective Magnification	Effective Collimator Resolution (cm)	Collimator Efficiency
1.0	2.13	2.13	0.076	1.67E-04
1.5	3.48	2.32	0.074	7.41E-05
2.0	4.76	2.38	0.073	4.17E-05
2.5	6.03	2.41	0.073	2.67E-05
3.0	7.28	2.43	0.073	1.85E-05
3.5	8.52	2.43	0.073	1.36E-05

Figure 8: Phase I pinhole collimator and detector geometry.

Table 4 shows the representative calculations of the collimator resolution and efficiency assuming a 1 cm reconstruction circle and 2.46 cm detector. Although intrinsic resolution of our detector is very high, the system resolution in this case is limited by the pinhole and the geometry used. In Phase II, we will design a collimator and implement a detector for a 3 cm diameter reconstruction circle, needed for imaging mice. Of course, this will affect both the spatial resolution and the geometry and efficiency of the system. Thus, designing an appropriate collimator for the Phase II detector will be a crucial task.

DETECTOR ASSEMBLY & EXPERIMENTAL SETUP

To properly position the detector and

collimator, a special housing was designed and fabricated during Phase I. The housing is lined with a 7 mm thick lead to effectively shield the detector from background and scattered radiation. The EMCCD camera is mounted on rails so that the collimator-to-detector distance can be easily adjusted. The front of the box is machined to mate with the threaded pinhole insert described above (**Figure 8**). Care has been taken to ensure that the incident x-rays are not attenuated by the lead housing when the collimator is removed for CT imaging.

As shown in **Figure 9** the experimental setup consisted of the detector housing, the x-ray generator, and a high precision rotation stage mounted on an optical bench. Both the x-ray generator and the rotation stage are computer controlled, and their operation synchronized with image acquisition by the EMCCD detector. The x-ray source used was an Oxford Instruments XRF-5011, 75 Watt, tungsten anode x-ray generator with a 70 μm focal spot [vii] having an operational range of 20-50 kVp with a maximum anode current of 1.0 mA. A 0.4 mm thick Al sheet was used to filter the low energy x-ray component from the emerging beam. For experiments

Figure 9: Phase I experimental setup showing the detector housing, the collimator, the rotation stage, and the x-ray generator.

reported here, the source was operated at 40 kVp, 0.4 mA. Unless otherwise stated, the EMCCD detector was operated with a 3:1 fiberoptic taper and a 500 μm CsI(Tl) screen for the following experiments.

LINE SOURCE IMAGING

The spatial resolution of the system was measured by imaging a capillary tube with a 0.58 mm bore (i.d.) filled with a 460 μCi aqueous solution of $^{99\text{m}}\text{Tc}$. The capillary tube was placed 1.25 cm from the pinhole collimator and was imaged with a pinhole-to-detector distance of 2.5 cm. The expected collimator resolution for 0.5 mm pinhole and the specified geometry is 0.75 mm.

FWHM = 0.93

Figure 10: A 60 Second image of a 0.65 mm internal diameter capillary filled with 460 μCi aqueous $^{99\text{m}}\text{Tc}$ source obtained using the Phase I detector. The effective fwhm resolution is 0.93 mm is slightly worse than the expected resolution of 0.75 mm. This may be due to the parallax error arising from γ -penetration through the lead pinhole edges.

Figure 10 shows a 60 s image of the capillary tube and the corresponding line profile through the image. As can be seen, the capillary is well resolved which demonstrates that the Phase I detector could produce high quality images of sources with activity comparable

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to that used in small animal imaging, within a reasonable time of 60 seconds. The measured FWHM resolution is 0.93 mm, which is dominated by the pinhole collimator and the specific geometry used. The slight broadening beyond the expected 0.75 mm resolution may be due to parallax error arising from the penetration of 140 keV ^{99m}Tc gamma rays through thin pinhole edges.

FLOOD IMAGES

Flood field images using the collimated EMCCD-CsI(Tl) detector were recorded by imaging a flood tank phantom having a cross sectional area of $\sim 7 \times 7 \text{ cm}^2$ and filled with a uniform aqueous 5 mCi solution of ^{99m}Tc -pertechnetate. The flood source was positioned 25 cm away from the pinhole and imaged through a 0.5 mm pinhole over a period of 10 min to ensure count density. We note that this image was

Figure 11: Flood histogram using 5 mCi aqueous ^{99m}Tc source showing response uniformity of the Phase I detector.

recorded using the integration mode of the detector. Therefore, the uniformity image is similar to one that would be recorded using an x-ray source without a collimator. For this study, we also recorded a 10 minute “dark image” (without the radioactivity) which was subtracted pixel-by-pixel from the flood tank image. In addition, an image having a similar count density was recorded using the same flood source, was background-subtracted, and was used to normalize the first flood-image image for systematic

Figure 12: Simultaneous ^{99m}Tc line source (0.6 mm capillary) and ^{125}I BrachySeeds (2 vertical capsules) imaging using 3 mm (left) and 0.5 mm (right) thick CsI(Tl) scintillators.

uniformities. The resulting image is shown in **Figure 11 (a)** and the corresponding line profile through the image is shown in **Figure 11 (b)**. These data demonstrate the excellent uniformity of the detector response over its entire area. Since the CCD response is uniform, the data essentially reflects the uniformity of CsI(Tl) film response to 140 keV ^{99m}Tc γ -rays.

LINE AND POINT SOURCE IMAGING USING ^{99m}Tc AND ^{125}I

These data were acquired with the EMCCD camera coupled to a 3 mm thick CsI(Tl) scintillator and then with the camera coupled to a 0.5 mm thick scintillator. The goal of this study was to compare the relative performance of the detector using a thin scintillator more suitable for imaging low-energy photons (e.g., ^{125}I) vs. one that is more suitable for imaging higher energy photons (e.g., from ^{99m}Tc). These

measurements were obtained by imaging a 0.58 mm (i.d.) capillary tube filled with ^{99m}Tc simultaneously with two adjacent BrachySeeds as ^{125}I point sources. The resulting radionuclide images (**Figure 12**, left) were obtained with the 3 mm CsI(Tl) scintillator using a 20 sec exposure, and shows the ^{99m}Tc -filled line source next to 2 vertical BrachySeed capsules (^{125}I). In this image, the intensities of the ^{125m}Tc and ^{125}I sources on the image are comparable. A similar image (**Figure 12**, right) recorded with a 30 s exposure using the 0.5 mm CsI (same activity levels) illustrates, as expected, the higher fraction of 35 keV relative to 140 keV photons recorded with the thin scintillator. Spatial resolution loss of the line source image is also evident in image acquired with the 3 mm scintillator (**Figure 12**, left) caused by parallax error and light spread in the thicker scintillator.

Figure 13: I-125 SPECT projection image (top left), reconstructed image (top right), line profile (bottom left) and dimensions of BrachySeed (bottom right).

FWHM = 0.7mm

SPECT IMAGING USING ^{125}I

For SPECT imaging using ^{125}I source, the 500 μm thick CsI(Tl) screen was coupled to the EMCCD. For ^{125}I ~ 30 keV γ -rays, a mean attenuation length in CsI is 100 μm . While a thinner scintillator, in principle, will produce better spatial resolution for 30 keV γ -rays, we evaluated the EMCCD with the 500 μm scintillator so that the performance can be compared against that obtained with the 140 keV γ -rays.

A sealed source of ^{125}I used for brachytherapy implant ("BrachySeed") was used in the evaluation. Each BrachySeed (400 μCi) consists of two 0.5 mm diameter ceramic beads infused with ^{125}I and housed within a sealed titanium capsule

having a 0.05 mm thick wall. Since the size of the ceramic beads is slightly smaller than the effective diameter of the pinhole, these BrachySeed sources can be considered "point" sources. The BrachySeed was mounted on the rotating platform for SPECT imaging and 72 projection images were obtained. The CCD integration time for each projection was 10 s. A count profile through the image of one ^{125}I seed from the projection image as well as the reconstructed tomogram are shown in **Figure 13**. The measured spatial resolution through the center of one bead is 0.7 ± 0.1 mm FWHM and compares well with the 0.75 mm theoretical resolution of the pinhole system.

COMBINED SPECT/CT IMAGING AT THE UCSF

The performance of the EMCCD detector with a 500 μ m CsI scintillator for X-ray and SPECT imaging of ^{99m}Tc -pertechnetate (140 keV) was evaluated using a mouse heart phantom. The mouse heart phantom is configured as an outer polyethylene rod 9.6 mm outer diameter, with a 5.0 mm cylindrical hole drilled through it with a plug on one end to form a “well”. The phantom also included an acrylic rod insert mounted on one end having a thread that allowed it be inserted into the well of the outer polyethylene container. A small 1 mm thick, 3 mm diameter cylindrical disc was attached to the opposite end (**Figure 14**). When inserted into the cylindrical well of the polyethylene rod, the insert formed a fillable cylindrical chamber having an annular cross-section, with the small disc simulating a regional perfusion “defect” of the mouse

Figure 14: Disassembled mouse heart phantom photograph (left) and cross sectional view of the assembled mouse heart phantom (right) through the defect region.

myocardium. The dimensions of the myocardial phantom approximated the size of a mouse heart, with a 5 mm diameter chamber and a 1.75 mm annular chamber. However, the size of the outer “body” of the phantom (9.6 mm) was smaller than the thoracic diameter of a normal adult mouse but was limited by the active area of the Phase I EMCCD detector.

CT data were acquired by mounting the phantom on the rotating stage of the imaging apparatus, with the phantom placed 4 cm from the detector and 360 projection images were taken with an X-ray tube (40 kVp, 0.4 mA) located 29 cm from the detector. Each projection accumulates photons for 0.5 s and was flood-field corrected. Tomographic images, reconstructed using a filtered back projection algorithm with representative slices (**Figure 15**) clearly show the “normal” and “defective” regions of the ventricular chamber.

SPECT images were then obtained with the phantom filled with 10 mCi of ^{99m}Tc -pertechnetate. Seventy-two SPECT projections over 360° were obtained with a 30 s/projection exposure time through a 0.5 mm pinhole. The images were reconstructed with 24 iterations of a ML-EM algorithm in a 128x128x72 matrix. The slice through the “normal” region (**Figure 16**) shows good contrast between the regions with and without radioactivity. The outline of the 1 mm x 3 mm disc “defect” is clearly identifiable even with the EMCCD camera operating in integration mode, *i.e.*, without energy discrimination of individual γ rays to reject the scattered rays from the direct signal.

The mean attenuation length through the CsI(Tl) scintillator for 140 keV γ -rays is

Figure 15: X-ray CT projection of mouse heart phantom (left) and the reconstructed slices (right) through the normal and defective regions.

2.6 mm. While using a thicker scintillator will result in a higher conversion efficiency of the γ -rays to optical photons, it results in a larger lateral spreading of the optical photons. In addition, the use of a thick scintillator is associated with a parallax error when γ -rays penetrate the scintillator at an angle and convert into optical photons at different depths and lateral positions along the ray-path. A trade-off between detection efficiency and these effects therefore was taken so that we could evaluate the EMCCD camera at a higher spatial resolution. Nevertheless, these SPECT and CT images of the mouse heart phantom are very encouraging in that they clearly demonstrate the feasibility of using a single EMCCD detector for combined SPECT/CT imaging with radionuclides at 140 keV even under non-ideal conditions.

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Figure 16: ^{99m}Tc SPECT images (top row) of the mouse heart phantom through the normal and defective regions reconstructed using a ML-EM algorithm. (Bottom) Line profile through center of phantom.

SUMMARY

Overall, these tests of the EMCCD camera demonstrate the capabilities and versatility for use in X-ray CT and SPECT imaging with ^{99m}Tc and ^{125}I . The tests with the mouse heart phantom demonstrate that the same camera can be used for SPECT and CT imaging almost simultaneously with the insertion and removal of the pinhole. Even with the lower efficiency scintillator for 140 keV, high quality SPECT images can be taken. Further work in designing a high resolution converging hole collimator will enable the system to operate for both SPECT and CT

without the need to remove the collimator.

[i] V.V. Nagarkar, V.Gaysinskiy, I. Shestakova, S. Taylor, H. Barrett, G. Entine, Thick Microcolumnar CsI(Tl) Films for Small Animal SPECT, submitted (accepted) to IEEE 2004, Rome, Italy October 16-22 2004.

- [ii] Fujita, H., D.Y. Tsai, T. Itoh, K. Doi, J. Morishita, K. Ueda and A. Ohtsuka. (1992). "A simple method for determining the modulation transfer function in digital radiography." *IEEE Trans. Med. Imaging* MI-11: 34-39
- [iii] Vedantham, S., A. Karellas, S. Suryanarayanan, D. Albagli, S. Han, E. Tkaczyk, C. Landberg, B. Opsahl-Ong, P. Granfors, I. Levis, C.J. D'Orsi and R.E. Hendrick. (2000). "Full Breast Digital Mammographic Imaging with an Amorphous Silicon-based Flat Panel Detector: Physical Characteristics of a Clinical Prototype." *Med. Phys.* 27: 558-567.
- [iv] Vedantham, S., A. Karellas, S. Suryanarayanan, M. Sayag, R. Kleehammer, R. Heidsieck and C.J. D'Orsi. (2000). "Mammographic imaging with a small format CCD-based digital cassette: Physical characteristics of a clinical system." *Med. Phys.* 27(8): 1832-1840.
- [v] Dobbins, J.T., D.L. Ergun, L. Rutz, D.A. Hinshaw, H. Blume and D.C. Clark. (1995). "DQE(f) of four generations of computed tomography acquisition devices." *Med. Phys.* 22(10): 1581-1593.
- [vi] Gerralt A. de Vree, Frans van der Have, Freek J. Beekman, EMCCD-based Photon Counting Minim Gamma Camera With a Spatial Resolution of <100 μm , Presented at the IEEE 2004, Rome, Italy, October (2004).
- [vii] SourceBlock Product Family, SB-80-500, Source-Ray, Inc, 167 Keyland CT. Bohemia, NY 11716, 631-244-8200.