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A micro-machined retro-reflector for improving light yield in ultra-high-resolution gamma cameras

Jan W T Heemskerk\textsuperscript{1,2}, Marc A N Korevaar\textsuperscript{1,2}, Rob Kreuger\textsuperscript{2}, C M Ligtvoet\textsuperscript{3}, Paul Schotanus\textsuperscript{4} and Freek J Beekman\textsuperscript{1,2,5}

\textsuperscript{1} Image Sciences Institute, University Medical Center Utrecht, 3584 CG, Utrecht, The Netherlands
\textsuperscript{2} Radiation, Detection and Medical Imaging, Department of Applied Sciences, Delft University of Technology, Mekelweg 15, 2629 JB, Delft, The Netherlands
\textsuperscript{3} Department of Medical Technology and Clinical Physics, University Medical Center Utrecht, 3584 CG, Utrecht, The Netherlands
\textsuperscript{4} Scionix Radiation Detectors and Crystals, PO Box 143, 3980 CC, Bunnik, The Netherlands
\textsuperscript{5} MILABS, Universiteitsweg 100, Utrecht, The Netherlands

E-mail: j.w.t.heemskerk@tudelft.nl

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Abstract

High-resolution imaging of x-ray and gamma-ray distributions can be achieved with cameras that use charge coupled devices (CCDs) for detecting scintillation light flashes. The energy and interaction position of individual gamma photons can be determined by rapid processing of CCD images of individual flashes. Here we investigate the improvement of such a gamma camera when a micro-machined retro-reflector is used to increase the light output of a continuous scintillation crystal. At 122 keV we found that retro-reflectors improve the intrinsic energy resolution (full width at half maximum (FWHM)) by 32\% (from 50\% to 34\%) and the signal-to-noise (SNR) ratio by 18\%. The spatial resolution (FWHM) was improved by about 4\%, allowing us to obtain a resolution of 159 \(\mu\)m. The full width at tenth maximum (FWTM) improvement was 13\%. Therefore, this enhancement is a next step towards realizing compact high-resolution devices for imaging gamma emitters.

1. Introduction

Today, the majority of clinical procedures using tracers to visualize specific tissue binding sites are carried out with planar gamma camera imaging, single-photon emission computed tomography (SPECT) or positron emission tomography (PET). Imaging of single-photon-emitting radiopharmaceuticals with gamma cameras, in the planar or tomography mode, makes up the largest fraction of these molecular imaging procedures. In addition to these clinical applications, SPECT imaging of laboratory animals is currently a rapidly expanding
field since resolutions better than 0.5 mm can readily be achieved. This allows for both the visualization and the accurate quantification of ligand concentrations in small animals such as rodents with resolutions down to subcompartments of mouse organs (e.g. Beekman et al 2005, Funk et al 2006, Vastenhouw et al 2007, Van der Have et al 2009). This affects most preclinical imaging procedures since rats and mice form the majority of the experimental animal population.


For further improvement of future SPECT devices, a high intrinsic detector resolution is essential (Rogulski et al 1993, Barber 1999, Beekman and Vastenhouw 2004, Meng et al 2006, Rentmeester et al 2007). It has been shown that very high spatial resolutions (below 100 μm) can be obtained with a detector consisting of CsI(Tl) micro-columnar scintillation crystals read-out by a CCD operating at high frame rates (e.g. Beekman and De Vree 2005, De Vree et al 2005, Teo et al 2006, Meng 2006, Nagarkar et al 2006, Heemskerk et al 2007, Soesbe et al 2007, Westra et al 2009). However, due to the low capture efficiency of CsI(Tl) and the limited thickness of available micro-columnar crystals, these crystals are not well suited for small-animal imaging.

To increase the capture efficiency of our gamma camera, the micro-columnar crystal has been replaced by a thicker continuous (monolithic) CsI(Tl) crystal in combination with an advanced multi-scale detection algorithm (Korevaar et al 2009a, 2009b). One drawback of continuous crystals is that the spread of scintillation light is not confined and therefore significantly larger than for micro-columnar crystals. Furthermore, the light spread on the CCD will be dependent on the depth of the scintillation event in the crystal (depth of interaction, DOI). The multi-scale algorithm can incorporate information from the light spread in the estimation of scintillation position (which includes DOI) and energy, provided a sufficient number of photons is detected (Korevaar et al 2009b). With increased light output of the scintillation crystal, it is expected that the energy and position of the scintillation events can be estimated more accurately.

The light output of the scintillation crystal can be enhanced by using a reflective coating on the top of the crystal (see, e.g., Gruner et al 2002); in some cases the number of photons reaching the CCD surface will almost be doubled. However, the light spread will also increase (figure 1(a)). More improvement can be expected from the application of a retro-reflector: the reflected photons appear to arrive from the scintillation location directly; additional light spread is avoided (figure 1(b)).

Examples of the application of retro-reflectors in scintillation gamma cameras have so far been based on photo-multiplier tubes (McElroy et al 2002) and avalanche photodiodes (Fremout et al 2002). However, the retro-reflectors used in those experiments have relatively large reflective elements and are unsuited in combination with relatively thin crystals and ultra-high-resolution light sensors such as CCDs. Therefore, the goal of the present paper is to develop a retro-reflector based on microscopic, high precision reflective elements and to test it in a CCD-based gamma camera for high-resolution imaging tasks. To this end, we have first conducted ray-tracing simulations of the (optical) photon trajectories to predict the efficiency of differently structured reflective coatings. Then, the most efficient of these coatings has been
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Figure 1. In the case of the specularly reflective surface (a), photons will be reflected back from the top of the scintillation crystal to the detector at the bottom. With an ideal retro-reflector (b), the photons are reflected back through their point of origin (i.e. the location of the scintillation) onto the detector, thus maintaining the spatial resolution.

manufactured and tested experimentally by measuring the signal-to-noise ratio (SNR) and the energy and spatial resolution of a gamma camera with and without the reflector.

2. Materials and methods

2.1. EMCCD, read-out electronics and the photon-counting algorithm

The scintillation gamma camera that is used in this experiment consists of a continuous scintillation crystal being read out by an electron-multiplying (EM) CCD (Jerram et al 2001). Here we only summarize its characteristics; a comprehensive description of this gamma camera is provided elsewhere (De Vree et al 2005, Heemskerk et al 2007).

Gamma photons are captured in the scintillation crystal and the light flashes that are generated are detected by a back-illuminated EMCCD. The EMCCD that is used in these experiments is a CCD97 from E2V technologies. The quantum efficiency of the CCD97 exceeds 90% for the range of visible light from 500 to 650 nm. It has an active area of 512 lines of 512 pixels that are 16 × 16 μm² in size. To reduce the dark current to a level below 0.1 e⁻/pixel/s the EMCCD is cooled via a Peltier element and liquid cooler to a temperature of −50 °C.

Read-out of the EMCCD is performed by an in-house developed electronics board that transfers the signal to a PC. In order to improve the read-out frequency of our camera the lines are read out in pairs, which allows us to operate the camera at a rate of 50 frames per second. Through post-processing of the acquired images, the camera is operated in a photon-counting mode: each individual frame is analyzed for the presence of scintillations by a multi-scale Gaussian filter algorithm (MSA) (Korevaar et al 2009b). This algorithm estimates the center of gravity and the DOI for the separate scintillation events; the DOI is estimated through matching of the light spread with the scale of the filter. The energy of the scintillation is determined by the peak height of the signal after matched filtering.

2.2. Scintillation crystal

An (approx.) 1.5 × 1.5 cm², 2 mm thick CsI(Tl) crystal was used, courtesy of SCIONIX Netherlands, which has an interaction probability of >50% for 140 keV Tc-99m gamma photons. The surfaces of the continuous CsI(Tl) crystal in contact with the CCD and the reflector have been polished. The crystal is proximity coupled to the CCD via a fiber-optic
window using optical grease (Bicron BC-630). As a result of the high Ti concentration of the material, the emission spectrum of the CsI(Tl) crystal (ranging from approx. 450 to 650 nm) closely coincides with the spectral response of the CCD97.

2.3. Ray-tracing simulations

The efficacy of different reflector designs was first characterized by simulating the number of reflected photons per scintillation event and their spread on the detector. These figures have been estimated for different types of reflectors with a ray-tracing code that calculates the paths of the optical photons. The reflectors that we have simulated are (i) (specular) mirror-like, (ii) a retro-reflector with square pyramids, (iii) a retro-reflector consisting of regular tetrahedra (i.e. parts of regular cubes); the geometric and material properties of the simulated crystal are consistent with our laboratory set-up (i.e. 2 mm thick CsI(Tl)). The square pyramid and tetrahedral retro-reflectors are shown in figures 2(a) and (b), respectively.

For each type of reflector we have simulated many scintillation events taking place at random depths throughout the crystal, but with a scintillation depth distribution according to Beer’s law. Approx. 7800 photons were simulated in each event which is typical for a scintillation event of Tc-99m in CsI(Tl). We assume that the generated optical photons have random directions (with an isotropic distribution) and that ideal reflections occur at the boundaries of the reflectors with a probability of 95%. Between the crystal and the reflector we simulate an optical medium with the same optical density \( n = 1.47 \) as the optical grease present in our experiment; at the boundary between the scintillator and CCD we assume complete transmission of rays within the critical angle of internal reflection. Photons with trajectories leaving the sides of the crystal are considered to be lost.

Once the individual photon traces have been determined, it is straightforward to calculate the number of photons arriving on the CCD (either directly or after reflection) and their spread. The size of the scintillation light spread on the detector of the directly detected photons is uniquely determined by the distance of the scintillation event from the detector surface and the critical angle. The center of gravity of the light spot corresponds to the \( x \)- and \( y \)-coordinates of the scintillation event.

According to the literature (scintillator.lbl.gov), CsI(Tl) generates approx. 59,000 photons per MeV of gamma radiation.
The ‘gain’ of each reflector is defined as the relative number of reflected photons versus direct photons for a large number of scintillations (>5000). Only those reflected photons that arrive at the detector within the light spread of the directly detected photons are included in this gain, since we assume (based on our MSA algorithm) that the extra photons outside this light spot do not contribute to an improvement of the spatial and energy resolution. Whether or not the calculated number of detected light photons corresponds with the actual number of experimentally detected photons is debatable, since the simulation does not include any photons losses outside the crystal or a noise model for our detector. However, as these loss factors will be equal for crystals both with and without the reflector, the detected trends of the simulations should be accurate. The results of the simulations are presented in section 3.1.

2.4. The retro-reflector

To experimentally validate our retro-reflector, we compare the gamma-ray detection capabilities of a camera with a reflector to those with an uncoated crystal. The reflector is applied to the crystal side that is not read out by the CCD (i.e. the top of the crystal) with the same optical grease as used for coupling to the CCD. To remove possible air inclusions in the reflector cavities, the crystal with the reflector was temporarily placed in vacuum.

The outcome of the ray-tracing simulations indicated that for 75 μm tetrahedral cubes a large number of photons are reflected back onto the detector, within the original photon spread. Based on this result a retro-reflector has been designed in-house for this experiment specifically. First an aluminum mold was micro-machined consisting of tetrahedral pyramids with a median of 75 μm. Subsequently, a PMMA polymer resin was cast in this mold, and a highly reflective aluminum surface coating was vapor deposited (figure 3) on the reflection cavities. Aluminum coatings have a reflectivity of >90% for the range of wavelengths of the CsI(Tl) emission spectrum (450–650 nm). The reflective tetrahedral cavities will ensure that a large fraction of the incident photons is retro-reflected in the direction of their origin.

2.5. Measurements

The properties we investigate to evaluate the reflector are the spatial and energy resolution and SNR. First, the crystal with a retro-reflector is irradiated by a Co-57 (122 keV) source through a 30 μm wide slit between two tungsten plates. For the measurements without a reflector, the reflector was simply removed while leaving the crystal in place on the CCD. From the MSA list-mode data energy spectra are constructed as histograms of the intensities of the detected scintillations. The energy resolution that is determined from these spectra provides a measure for the ability of the EMCCD-based gamma camera to distinguish scintillations of different radioisotopes. It is derived as the full width at half maximum (FWHM) of the peak of the Co-57 signal in the energy spectrum.

The spectra are subsequently used to set the energy windows for event selection for the reconstruction of the projected image. For both the camera with and without the retro-reflector, this energy window ranges from 50% to 150% of the energy peak value (i.e. peak value ±50%, roughly corresponding to twice the FWHM of the photopeak for the uncoated crystal). The spatial resolution is determined from the FWHM of the projection of the slit, corrected for the width of the slit itself (Beekman and De Vree 2005).

The signal-to-noise ratio is defined as the net number of counts within the area irradiated by the slit divided by the number of false positive counts detected on an equally sized non-irradiated area of the CCD. The irradiated area is taken to be 30 columns wide, which is slightly wider than the full width at tenth maximum (FWTM) of the profile of the slit. The background is summed over the rest of the image and scaled to the same area as is irradiated.

Each of the measurements consists of a total number of 25 000 frames and the results are described in sections 3.2 and 3.3.

3. Results

3.1. Ray-tracing simulations

We present the numerical results for a CsI(Tl) scintillation crystal of 2 mm thickness irradiated by 140 keV (Tc-99m) gamma radiation. Figure 4 shows the photon spread for a crystal without a reflector (‘directly detected photons’), covered with a specular reflector, a retro-reflector with 75 μm side square pyramids and a retro-reflector with 75 μm median tetrahedra (for the reflectors the total signal of reflected and direct photons is shown). For clarity, we show the results for simulated scintillations occurring at the average scintillation depth (~900 μm). We can see that direct photons are exclusively detected with a deviation from the center of gravity smaller than ~1500 μm, as the ‘detection cone’ is cut off at the critical angle of total internal reflection at the scintillator–CCD interface. The photons that have been reflected by the reflectors, however, can have larger deviations.

For both retro-reflectors and specular reflectors, the gain was found to vary over the depth of the crystal. Figure 5 shows the variation of reflector gain with scintillation depth. This variation is the result of the fact that for a perfect retro-reflector, in general, each photon will have to reflect three times in order to reflect exactly into the direction of its origin. However, in the simulations we found that a significant number of photons will reflect only twice (or even once). For scintillations close to the top surface of the crystal, these imperfectly (retro-)reflected photons have a larger chance of arriving within the spread of the directly detected photons than for scintillations close to the detector. Therefore, the gain was found to be the largest for scintillations with a small DOI. The overall gain is largest, and its variation is
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Figure 4. Comparison of the photon spread without any coating (light gray, solid), with a specular reflector (black, dash-dot) and with retro-reflectors with square pyramids of 75 μm (dark gray, solid) and tetrahedral retro-cubes of 75 μm (dark gray, dashed) at the average scintillation depth (900 μm).

Figure 5. Comparison of the numerically calculated gain of the three different reflectors versus the depth of interaction (DOI) (only 1 in every 50 data points is shown here). For scintillations close to the crystal surface (DOI is low) the gain is highest for all three reflectors. The cubic retro-reflector has a superior performance, in particular for scintillations occurring deeper in the crystal.

smallest, for the tetrahedral retro-reflector. Table 1 lists the overall gain for the 5000 simulated events for all reflector types.
Table 1. Simulated reflection gain for different coatings.

<table>
<thead>
<tr>
<th>Retro-reflector</th>
<th>No of direct photons</th>
<th>No of reflected photons</th>
<th>Gain (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirror</td>
<td>9037066</td>
<td>3329131</td>
<td>36.8</td>
</tr>
<tr>
<td>Square 75 μm</td>
<td>9037534</td>
<td>4372173</td>
<td>48.4</td>
</tr>
<tr>
<td>Tetrahedral 25 μm</td>
<td>9039292</td>
<td>5382168</td>
<td>59.9</td>
</tr>
<tr>
<td>Tetrahedral 75 μm</td>
<td>9035540</td>
<td>5360889</td>
<td>59.3</td>
</tr>
<tr>
<td>Tetrahedral 125 μm</td>
<td>9036769</td>
<td>5328560</td>
<td>59.0</td>
</tr>
</tbody>
</table>

Because the multi-scale photon-count algorithm provides an estimation of the DOI, we can correct for the variation of the gain in the determination of the energy values using the calculated gain factors from figure 5 (see section 3.2).

From our simulations we conclude that the tetrahedral retro-reflector (retro-cubes) has an efficiency that is >20% higher than the retro-reflector constructed from square pyramids and >1.5 times as high as a normal mirror. Therefore, we expect that the application of this new retro-reflector will lead to a significant improvement of the light output of our scintillator and a subsequent improvement of the spatial and energy resolution of our EMCCD-based gamma camera.

In principle, smaller retro-cubes will enhance the ability to reflect light back into the original direction. In our simulations we have found that below a size of ~75 μm the improvement is only small, whereas for retro-cubes of 125 μm a large variation in gain values for scintillations with small DOI arises. This indicates the influence of the lateral position of the individual scintillations (with respect to the retro-reflector) on the gain. We have therefore decided to fabricate a retro-reflector with a median of 75 μm.

The experimental validation of the application of this retro-reflector in comparison with an uncoated crystal is presented in the following two sections.

3.2. Measured energy spectrum and SNR

Figure 6(a) shows the experimentally obtained energy spectra for the crystal with and without the retro-reflector, accumulated in the entire crystal thickness.

For the spectrum with the retro-reflector, the estimated energy values of the scintillation events have been corrected for the DOI-dependent gain due to the retro-reflector. According to the simulations (figure 5), for scintillations occurring close to the top of the scintillation crystal almost twice the number of photons will be detected compared to scintillations close to the detector. The position of the photopeak is therefore dependent on the DOI. To correct for this, the DOI information of the individual scintillations from the MSA algorithm (Korevaar et al 2009b) is used to scale the energy as a function of the DOI. The scaling factors have been derived directly from the calculated gain values of figure 5. With this correction a single narrow photopeak is obtained (figure 6(a)), showing that there is good agreement between simulations and the experiment.

From these spectra the energy window for SNR and spatial resolution comparison of the different optical coatings was determined as explained before (i.e. ranging from 12.5 to 37.5 au). Table 2 shows the overall energy resolution and SNR for the coated and uncoated crystal, showing an improvement of the energy resolution as well as the SNR when the retro-

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8 25 μm tetrahedral structures could also have been constructed, but the limited advantage in gain would not compensate for the extra expense and expected mechanical difficulties in fabrication.
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Figure 6. (a) Energy spectrum for the 2 mm thick CsI(Tl) crystal, for the case of no coating (dashed, left y-axis) and the specially designed retro-reflector (solid, right y-axis). The energy window for the SNR and spatial resolution measurements runs from 12.5 to 37.5 au on the x-axis for both cameras. (b) Profiles of the images of the slit for the crystal with a retro-reflector and without.

Table 2. Energy and spatial resolution and SNR for the CsI(Tl) crystal with and without a retro-reflector.

<table>
<thead>
<tr>
<th></th>
<th>Without reflector</th>
<th>With retro-reflector</th>
<th>Improvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy resolution (%)</td>
<td>50</td>
<td>34</td>
<td>32</td>
</tr>
<tr>
<td>Spatial resolution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FWHM (mm)</td>
<td>165</td>
<td>159</td>
<td>3.6</td>
</tr>
<tr>
<td>FWTM (μm)</td>
<td>424</td>
<td>370</td>
<td>12.6</td>
</tr>
<tr>
<td>Signal/true-positive counts</td>
<td>4125/251</td>
<td>4444/230</td>
<td></td>
</tr>
<tr>
<td>SNR</td>
<td>16.4</td>
<td>19.3</td>
<td>17.5</td>
</tr>
</tbody>
</table>

The improvement of the SNR is the result of the inclusion of more true positive counts as well as a reduced background level due to the better energy resolution.

3.3. Spatial resolution

Figure 6(b) shows the accumulated profiles of the images of the slit for the camera with a retro-reflector and without. Figure 7 shows the variation of the spatial resolution (in μm FWHM) for events at different DOIs. In figure 7 the improvement of the spatial resolution through the application of the retro-reflector is clearly visible, although limited to scintillations occurring in the top of the crystal (small DOI).

The spatial resolution is listed in table 2, for both FWHM and FWTM, showing a significant improvement of the FWTM by using the retro-reflector. However, the improved spatial resolution (FWHM) for small DOIs shown in figure 7 does not directly translate into an improvement of the FWHM of the reconstructed profile of the line source (figure 6(b)). This is because the width of the accumulated profile is dominated by the FWHM of the smallest profiles (for large DOIs) which show almost no improvement in figure 7. Nonetheless, for applications where the DOI information is taken into account in the image reconstruction
Figure 7. Variation of the spatial resolution (FWHM) of the continuous CsI(Tl) crystal with the estimated depth of interaction, measured with and without a retro-reflector.

(e.g. pinhole gamma imaging) the retro-reflector will present a clear improvement as shown in figure 7.

4. Discussion and conclusions

We have shown that the use of micro-machined retro-reflectors greatly improves both energy resolution and SNR of CCD-based gamma cameras, by 32% and 17.5%, respectively. In agreement with the outcome of the ray-tracing simulations the retro-reflector significantly improves the light output, in particular, for scintillations occurring close to the top of the scintillator. Furthermore, because the multi-scale algorithm allows for a depth-of-interaction separated analysis, we have found that the spatial resolution also significantly improves for scintillation events occurring further from the CCD surface, even up to 50% for scintillations in the top of the crystal; the overall FWTM resolution improved by 12.6%.

The application of the retro-reflector in our CCD-based gamma camera presents a further step in improving the camera’s performance and bringing its energy resolution up to par with that of PMT-based gamma cameras. In SPECT, sufficient energy resolution is essential to discriminate scattered photons from primary photons. However, in small-animal SPECT, the number of scattered photons is relatively low due to the small sizes of the objects under investigation. Furthermore, the amount of scatter in pinhole apertures is quite low and does not give rise to strong contamination of projection data, even without energy discrimination (Van der Have and Beekman 2004). The energy spectra presented in this work clearly indicate that the current prototype camera may be able to perform sufficient scatter rejection for applications such as small-animal SPECT.

For further development of EMCCD-based gamma cameras, we are searching for scintillators giving excellent energy and spatial resolution in combination with a high capture
efficiency. All three factors will depend on the light yield and thickness of the scintillation crystal. The degrading effects of having a thick crystal (for high detection efficiency) on spatial and energy resolution might be alleviated by using a retro-reflector. Retro-reflectors thus provide an important tool for combining good spatial and energy resolution with a high detection efficiency.

Acknowledgment

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