

High-resolution, high sensitivity detectors for molecular imaging with radionuclides: The coded aperture option

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Abstract

Molecular imaging with radionuclides is a very sensitive technique because it allows to obtain images with nanomolar or picomolar concentrations. This has generated a rapid growth of interest in radionuclide imaging of small animals. Indeed radiolabeling of small molecules, antibodies, peptides and probes for gene expression enables molecular imaging in vivo, but only if a suitable imaging system is used. Detecting small tumors in humans is another important application of such techniques. In single gamma imaging, there is always a well known tradeoff between spatial resolution and sensitivity due to unavoidable collimation requirements. Limitation of the sensitivity due to collimation is well known and affects the performance of imaging systems, especially if only radiopharmaceuticals with limited uptake are available. In many cases coded aperture collimation can provide a solution, if the near field artifact effect can be eliminated or limited. At least this is the case for “small volumes” imaging, involving small animals. In this paper 3D-laminography simulations and preliminary measurements with coded aperture collimation are presented. Different masks have been designed for different applications showing the advantages of the technique in terms of sensitivity and spatial resolution. The limitations of the technique are also discussed. © 2006 Elsevier B.V. All rights reserved.

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1. Introduction

Molecular imaging with radionuclides can perform imaging of biological processes “in vivo”. A wide range of human diseases can be studied in animal models and early detection of small tumors with high specificity is in principle possible, provided an adequate detection system is available. In fact, simultaneous requirements in terms of

high spatial resolution and high sensitivity make the technique challenging. The limitation of the sensitivity due to collimation is well known and affects the performances of detector systems. The “electronic” collimation technique used in positron emission tomography (PET) is limited only to positron emitters with intrinsic limitations in terms of spatial resolution and is also more complicated and expensive. Another electronic collimation method applied to single gamma emissions using Compton Camera techniques is rather complicated too, expensive and not yet fully developed.

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Coded aperture collimation can be a solution in many cases, for example when imaging objects having a small thickness as compared to the object–detector distance, as it is typical in small animal imaging.

In this paper simulations performed to optimize the intrinsic performances of dedicated detectors affecting the coded aperture collimation option (essentially: intrinsic spatial resolution, dimension of scintillation pixels, and pixel identification) are presented. Different masks have been designed for different applications (small animal imaging and tumor detection). Phantom measurements have been performed to compare the technique to parallel hole collimation, showing the advantages of the technique in terms of sensitivity and spatial resolution [1].

2. Equipment and methods

We have performed quite extensive simulations, first to optimize the intrinsic performances of the detectors [2–4], then the coded aperture option for collimation has been studied [5–7].

2.1. Detectors

Different detector configurations have been studied. Essentially they are pixellated NaI(Tl) scintillators with different degree of segmentation, coupled with different photodetectors having anode pixel of different size [1–4,8] (Fig. 1).

2.2. Coded aperture collimation

The spatial resolution of single photon systems is limited to the sum in quadrature of intrinsic spatial resolution of the detector and collimator bore size if parallel hole collimator is used, but significant improvements are possible if a pinhole collimator is used. The major



Fig. 1. One of the detector systems used, based on a flat panel PSPMT. Collimation masks can be seen to the right of the detector box.

drawback is the limited sensitivity one can get with a pinhole collimator. It has been shown that it is possible to increase the collimator sensitivity, while maintaining a good spatial resolution, by using multi pinhole or coded aperture technique [9,10].

Coded aperture (CA) imaging uses multiple pinholes to improve the signal throughput of single-pinhole cameras (Fig. 2). In brief, in CA imaging each pinhole forms a copy of the projection of the object onto the detector, where copies may overlap. This superposition must be undone to form a clear image. For this reason, the acquired data are post-processed (decoded) by taking their correlation with a decoding array associated to the aperture's transmission function. If this array is chosen carefully, for a 2D object it is indeed possible, as shown below, to completely undo the overlap. The reason for going through this complication is that since more photons are collected, under conditions of uniform background [10], noise in the resulting image is reduced.

The use of multiple pinholes has a second implication, specifically that, in near-field geometry, different viewing angles for each point in space are present even in a single projection.

This is different from classic pinhole imaging, where in each projection all points are seen from a single vantage point. Single-view CA data, then, are richer than single-view pinhole data in the sense that at least some partial information is available for 3D-reconstruction. This information is actually equivalent to that obtained, in a much longer time, with a single pinhole visiting sequentially all the positions of the holes in the aperture in the case of a point source, for which no overlap can be present in CA data. A simple approach to recover 3D information relies on the property that each point in the object projects the aperture onto the detector with magnification uniquely related to its distance from the plane of the aperture. A 3D image, then, can be obtained plane by plane, each plane being the result of decoding the acquired data with the decoding array scaled to match the size of the projection of the aperture corresponding to the distance of the plane from the aperture.

From theory, if O is the irradiance (number of photons emitted per unit area) of the object, A is the transmission of the coded aperture (a function ranging from 0 for complete opacity to 1 for complete transparency) and R is counts recorded by the detector, we have $R = O \times A$ (\times indicates non-periodic correlation). Let G be a decoding pattern, such that $A \otimes G = \delta$ (\otimes indicates a periodic correlation).

A and G are both in the hands of the designer. The reconstructed image is $O' = R \otimes G = (O \times A) \otimes G = O^* (A \otimes G)$ where $*$ indicates correlation. $A \otimes G$ is the convolution kernel or point spread function. If $\text{PSF} = \delta$, we have perfect reconstruction, because $O = O'$.

Of course, “ideal” reconstruction is only possible after a number of approximations.

First is the far-field approximation. The second hypothesis is that detector and mask are ideal, for example

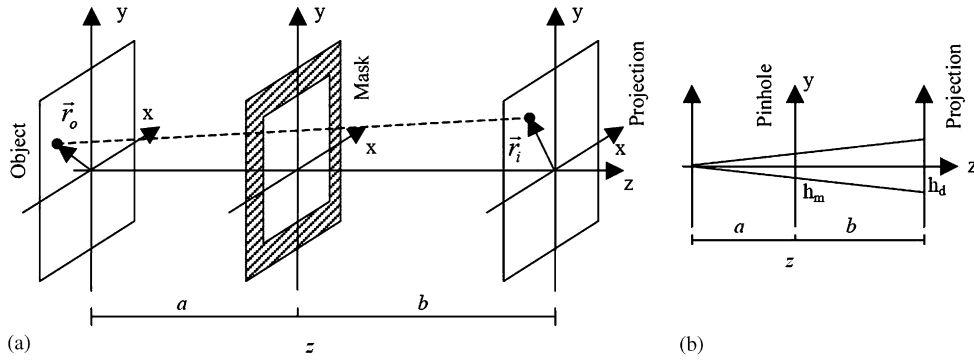


Fig. 2. Sketch of coded apertures (a) with respect to the pinhole (b).

zero-dimensional pinhole. In realistic cases resolution is slightly worse and we have blurring.

Pixel size p_d of the detector is very important because the reconstruction is well performed only when $\alpha > 2$, where α is the number of detector pixels sampling projection of a mask aperture.

If p_m is the mask pixel size, a is the distance from object to mask, and b is the mask–detector distance, the depth of field¹ (DoF) increases when p_m decreases:

$$\text{DoF} = \frac{b}{2.0(p_d/p_m) - 1} - \frac{b}{\alpha(p_d/p_m) - 1}$$

where

$$\alpha = (p_m/p_d)(a + b)/a.$$

We have studied different masks for different applications. It is evident that detecting small tumors in humans requires different mask designs than small animal imaging where better spatial resolution is required. However, in some situations sensitivity is less critical in small animal imaging than in humans where acquisition time can limit image statistics.

3. Results

We have designed essentially high-resolution and (relatively) high-field-of-view (FOV) masks.

We have simulated the performance of the high-resolution MURA-14 mask, having a pixel size of 0.69 mm, with a mask–detector distance of 45 mm and a source–mask distance of 15 mm. In this setup we measured spatial resolution as good as 0.88 mm FWHM [1], with 16 mm FOV and 9 mm DoF.

We started simulating a 2D source of different size and two possible uptake ratios within a background of 500 nCi/cm². In Fig. 3 the 2D-simulation results of tumors of different sizes (uptake ratio 6:1) are shown.

In Fig. 4, 3D-simulations (laminography) results of tumor (uptake 10:1) of 12 × 12 × 12 mm³ in size, at different positions in the depth of field (DoF) are shown.

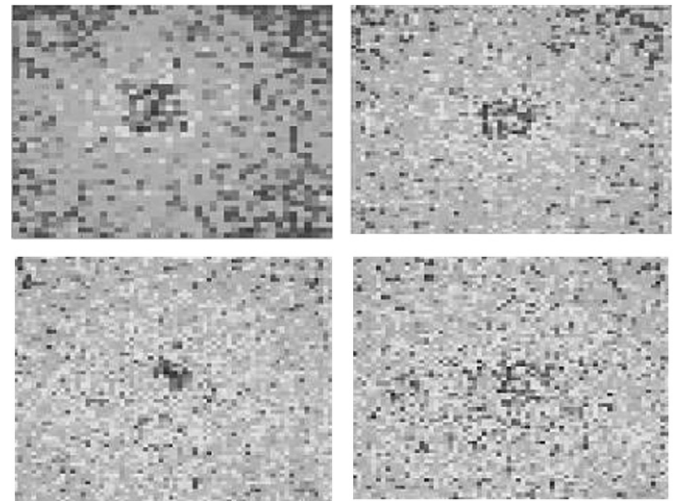


Fig. 3. Simulation of 12, 9, 6 and 3 mm square source, respectively, corresponding to 6:1 uptake ratio with respect to a background of 500 nCi/cm², simulating 6 cm thick surrounding tissue.

We have used the mask–antimask technique [10] to reduce near-field artifacts. In the 3D-case artifacts are still present because of the activity out of the focus and out of the FOV. Measurements have been performed according to the specifications of the previous paragraph with a 50 × 50 mm² imaging detector. We have used a phantom for breast tumor detection with 8 mm diameter “lesion” source at different “depths” (detector to tumor distances: 15, and 0 mm) and different absolute uptakes with 12:1 uptake ratio relatively to a background as thick as the DoF (30 mm).

The measurements show an agreement with the simulation, but the residual artifacts are slightly different, probably due to the different amount of background activity out of the FOV. The problem is under investigation (Fig. 5).

4. Conclusions

We have performed simulations and measurements to study the coded aperture option for radionuclide imaging of a spot inside a background volume with thickness comparable with the DoF of the mask. This is the case for

¹Depth of Field is the axial range where the image reconstruction can be performed correctly performed.

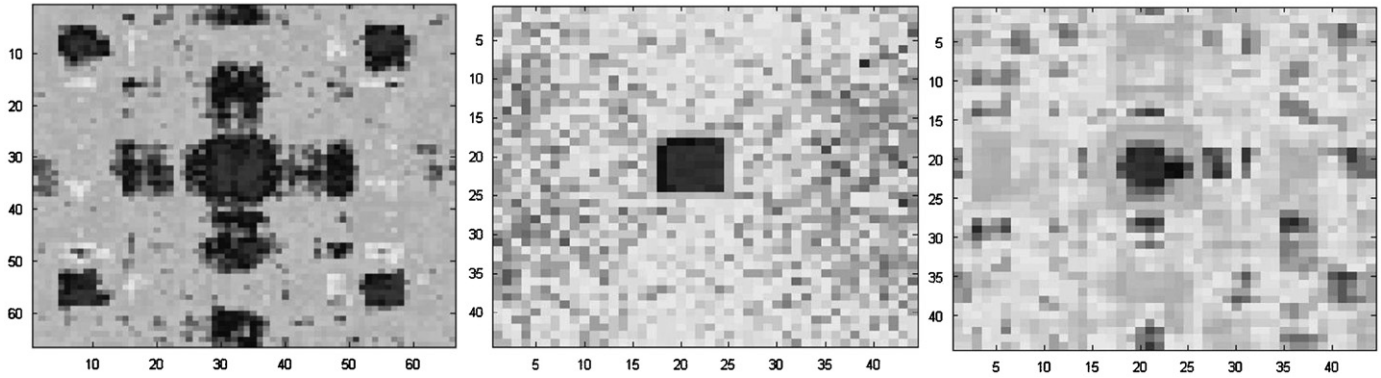


Fig. 4. Simulation of 8 mm tumor in different positions in a phantom as thick as the depth of field of 30 mm (uptake ratio 12:1).

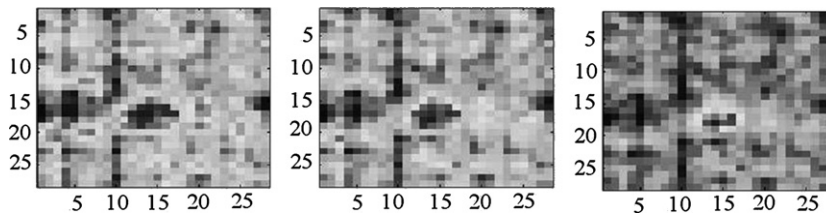


Fig. 5. Measurements corresponding to the same conditions of Fig. 4 for 8 mm diameter spherical source.

example for detecting small tumors in humans. Preliminary results are promising, they show that reasonable DoF (few cm) may be feasible. Nevertheless the issue of artifact elimination requires careful studies to show that the technique is really applicable when the volume detection is relatively big. The problem of artifacts due to activity present out of FOV and out of focus is under study. Moreover the small FOV shows to be a limitation for the cost of large area high-resolution detectors.

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