SUPPLEMENTARY INFORMATION

Optimization of Coded Aperture Radioscintigraphy for Sentinel Lymph Node Mapping

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**Collimator choices for image-guided surgery:** Shown in Supplementary Figure 1 are the types of collimators available for the imaging of single-photon emitting radiotracers during surgery.

![Supplementary Figure 1](image.png)

**Supplementary Figure 1 – Object, collimator, and detector relationships for conventional and coded aperture collimators:** Note overlapping projections on the detector for the coded aperture.

**Basic coded aperture theory:** In this study, we used a coded aperture (CA) system with a modified uniformly redundant array (MURA), in which four basic URA patterns are mosaically arranged as proposed by Fenimore and Cannon ([1,2]; Main Figure 1a). When the number of pixel positions (open or closed) in one mask period is \( npm \), \( npm \) divided by 2 must be a prime number and an anti-symmetric no-two-holes-touching (NTHT) MURA pattern must exist for \( npm \) [3]. The length of one mask period, \( d \), is \( npm \times Pa \), where \( Pa \) is the mask hole diameter, and the entire mask has a length of \( 2 \times d \).

The mask is positioned parallel, and centered, relative to the detector, whose smallest square dimension is \( D \). X and Y axes are in the plane of the detector, and the Z axis perpendicular to it (Main Figure 1b). If the mask thickness is ignored, when the distance between object and mask is \( a \), and the distance between mask and detector is \( b \), the mask image is \( \frac{a+b}{a} \) times magnified on the detector (magnification of mask on detector: \( M \)), and the object is magnified \( \frac{b}{a} \) times on the detector (magnification of object on detector: \( m \); Supplementary Table 1).

Gamma rays from a point source at the center of the object plane are distributed in a square with the side length of \( 2d \times \frac{a+b}{a} \) on the detector (Main Figure 1b, left, light gray square). The image is
reconstructed by decoding the data in the central \((d \times \frac{a+b}{a}) \times (d \times \frac{a+b}{a})\) region on the detector (Main Figure 1b, dark gray central square).

**Analysis of field of view (FOV):** FOV is defined as the maximal side length of the square on the object plane inside when a well-reconstructed (i.e., valid) image is available. Fenimore and Cannon [1,2] reported that when the CA described above is used, a well-reconstructed image is available by decoding the encoded images on the detector corresponding to the central \(d \times d\) region of the \(2d \times 2d\) mask. The area on the detector where the gamma rays from a point source reach through the central \(d \times d\) region of the mask is a square with the side length of \(d \times \frac{a+b}{a}\). The length on the object plane corresponding to this length is \(\frac{a}{b}\) times \(d \times \frac{a+b}{a}\) \((= d \times \frac{a+b}{b})\). This length on the object plane \(d \times \frac{a+b}{b}\) is defined as the FOV, which in turn is a function of \(a, b, npm\) and \(Pa\) (Supplementary Table 1). Acquired data are valid only when \(d \times \frac{a+b}{a} \leq D\). If \(d \times \frac{a+b}{a} > D\), some gamma rays required for the reconstruction of the object fall outside the detector (Main Figure 1b). Parameters for obtaining a valid FOV are provided in Supplementary Table 2.

The mask has finite thickness \((mt)\), so some gamma rays entering a mask hole obliquely will not be passed (Main Figure 1c). To evaluate FOV for actual masks, this geometrical effect must be taken into consideration. The central \(d \times d\) region of the mask projected onto the detector can now be expressed as a square with side length \(\frac{a+b}{a} \times d\) (Supplementary Figure 2). Projected back onto the object plane, FOV is calculated from one of two possible equations. When \(\frac{a+b}{a+\frac{mt}{2}}\times d\) is not smaller than the mask length \((2d)\), that is \(a \leq b - mt\), \(FOV = \frac{a+b}{b-\frac{mt}{2}} \times d\), and when this length is smaller than the mask length \((2d)\), that is \(a > b - mt\), \(FOV = \frac{(a+b)(a+\frac{3mt}{2})}{(a+\frac{mt}{2})(b+\frac{mt}{2})} \times d\) (Supplementary Figure 2).
Supplementary Figure 2 — The relationships among mask pattern diameter \((d)\), mask thickness \((mt)\), and FOV: Gamma rays that pass the central \(d \times d\) region of the mask distribute inside a square area on the detector with side length \(d \times \frac{a+b}{a+\frac{mt}{2}}\). When the total mask length \((2d)\) is not longer than the image on the detector \((d \times \frac{a+b}{mt})\), the margin of FOV is defined by the gamma ray that runs at the lower edge of the hole of the mask (thick arrow in left schema). When the mask length \((2d)\) is longer than the image on the detector \((d \times \frac{a+b}{mt})\), the margin of FOV is defined by the gamma ray that runs at the upper edge of the hole of the mask (thick arrow in right schema).

These results are valid under the condition that all gamma rays required for the image reconstruction can pass through the holes. To verify this, we should demonstrate that the gamma ray that runs most obliquely can pass the mask. As shown in Supplementary Figure 3a, the obliquity of the gamma ray that runs most obliquely among those required for the image reconstruction is

\[
\sqrt{\frac{2}{FOV}} \times \frac{a+b}{a+\frac{mt}{2}} \quad \text{and this obliquity must be greater than } \frac{mt}{Pa} \text{ for the gamma ray to pass.}
\]
through the mask. Then, the following inequality is obtained:

\[
\frac{a + b}{\sqrt{2} \, \text{FOV} + \sqrt{2} \, d \times \frac{a + b}{a + \frac{mt}{2}}} > \frac{mt}{Pa}
\]

\((d = npm \times Pa)\). The solution of this inequality is as follows: 

\[
npm < \frac{\sqrt{2} (a + \frac{mt}{2})(b - \frac{mt}{2})}{mt(a + b)} \quad \text{when} \quad a \leq b - mt
\]

\[
npm < \frac{\sqrt{2}(a + \frac{mt}{2})(b + \frac{mt}{2})}{(2mt + a + b)mt} \quad \text{when} \quad a > b - mt.
\]

FOV was experimentally measured using a line source comprised of a 0.5 mm capillary tube filled with 3.7 MBq (100 mCi) of \(^{99m}\text{Tc}\) sodium pertechnetate. The length of the line source was 70 mm. This line source was placed diagonally on the object plane to minimize the influence of artifacts, and it was imaged after varying \(a\) from 10 to 40 cm, with an interval of 10 cm. For each image, a total of 200,000 detector counts were acquired. The reconstructed image of the line source resulted in the segment outside the FOV being improperly reconstructed and showing lower counts. Actual FOV was calculated by identifying the transition from high pixel counts to low pixel counts on the reconstructed image.

**Supplementary Figure 3 – Experimental setups for measurement of:**

a. FOV: The obliquity of the gamma ray that runs most obliquely is

\[
\frac{a + b}{\sqrt{2} \, \text{FOV} + \sqrt{2} \, d \times \frac{a + b}{a + \frac{mt}{2}}}.
\]

This obliquity must be greater than \(mt/Pa\) for all the gamma rays required for image reconstruction to pass through the mask.
b. **Sensitivity:** The ratio of detected photons to emitted photons was measured by covering the mask area outside the central \( d \times d \) region with lead plates, thus counting only those photons that contribute to image reconstruction.

c. **Resolution:** The geometrical definition of XY resolution of a coded aperture mask with finite thickness \( mt \).

**Analysis of sensitivity:** Sensitivity is defined as the ratio of the number of detected photons to that of emitted photons, and for CA masks, total sensitivity is the sum of the sensitivity for each hole. Because sensitivity is impossible to analytically calculate, we defined it as the product of the open fraction of the mask \( \rho_{ap} \), and the ratio of solid angle of the square whose side is one period of the mask \( \Omega \) to the whole of the solid angles \( 4\pi \). The solid angle subtended by a square centered on the Z axis \( \Omega \) is calculated by:

\[
\Omega = a \int_{-\frac{d}{2}}^{\frac{d}{2}} \int_{-\frac{d}{2}}^{\frac{d}{2}} \frac{dx dy}{(x^2 + y^2 + a^2)^{\frac{3}{2}}} = 4 \arctan \left( \frac{d}{2a} \right) \frac{d^2}{2} + a^2 [4]. \]

CA sensitivity must then be corrected for the PDE of the gamma camera for photons of a particular energy:

\[
g = \frac{\Omega \times \rho_{ap} \times PDE}{4\pi} = \frac{\rho_{ap}}{\pi} \times \arctan \left( \frac{d}{2a} \right) \frac{d^2}{2} + a^2 \times PDE, \]

where \( \rho_{ap} \) is defined as the open fraction of the total mask area \( (d^2) \). Hence, total area of the holes is the product of one hole area \( (\pi \times \left( \frac{Pa}{2} \right)^2) \) and the total number of holes, which is a function of \( npm \) and is defined as \( \frac{npm^2}{4} - 1 \) [3,5].

Therefore, \( \rho_{ap} \) is \( \pi \times \left( \frac{npm^2}{4} - 1 \right) \). Sensitivity is a function of \( a, b, npm, Pa \) and PDE, as shown in Supplementary Table 1.

To account for finite mask thickness, sensitivity can be expressed as a function of the distance from the mask center \( (l) \), the distance between the center of the mask and the object \( (a) \) and the mask thickness \( (mt) \). The length of the hole covered by the geometrical effect \( (c) \) is \( \frac{mt}{a - \frac{mt}{2}} \times l \) (Main Figure...
1c) and the area of the hole through which gamma rays can pass is

$$\frac{Pa^2}{2} \left[ \arccos \left( \frac{c}{Pa} \right) - \frac{c}{Pa} \sqrt{1 - \left( \frac{c}{Pa} \right)^2} \right].$$

When the center of the mask is set to the origin and the point in the mask is expressed using Cartesian coordinates, both $x$ and $y$ are distributed between $-d/2$ and $+d/2$, and $c$ can be expressed as

$$\frac{mt}{a} \sqrt{x^2 + y^2}.\] Therefore, under the condition that the holes are uniformly distributed, sensitivity corrected for mask thickness is expressed using the following expression:

$$\rho_{ap} \frac{d/2}{8\pi} \int_{-d/2}^{d/2} \int_{-d/2}^{d/2} \frac{A}{d^2} \left[ \arccos \left( \frac{mt}{APa} \sqrt{x^2 + y^2} \right) - \frac{mt}{APa} \sqrt{x^2 + y^2} \sqrt{1 - \left( \frac{mt}{APa} \right)^2 \left(x^2 + y^2\right)} \right] dxdy \times PDE,$$

where $A = a - \frac{mt}{2}$. This integral can be rewritten as follows by replacing $x = Pa \times X$ and $y = Pa \times Y$ because $d = npm \times Pa$:

$$\rho_{ap} \frac{npm/2}{8\pi} \int_{npm/2}^{npm/2} \int_{npm/2}^{npm/2} \frac{Pa^2 A}{\left(Pa^2 X^2 + Pa^2 Y^2 + A^2\right)^{3/2}} \left[ \arccos \left( \frac{mt}{A} \sqrt{X^2 + Y^2} \right) - \frac{mt}{A} \sqrt{X^2 + Y^2} \sqrt{1 - \left( \frac{mt}{A} \right)^2 \left(X^2 + Y^2\right)} \right] dXdY \times PDE,$$

where $A = a - \frac{mt}{2}$ (Main Table 1). Interestingly, the term inside the square brackets, which corrects for the geometrical effect of mask thickness, is independent of $Pa$.

Sensitivity was measured experimentally using a 75 µm diameter point source [6] containing 7.4 MBq (200 mCi) of $^{99m}$Tc. To count only gamma rays that pass through the central $d \times d$ region of the mask, the area outside this region was covered with lead as shown in Supplementary Figure 3b. A total of 200,000 counts were acquired with the point source at the specified distance from the mask.

**Analysis of XY resolution and Z resolution:** The system’s spatial resolution ($SR$) on the transverse plane parallel to the detector (XY resolution) can be calculated from the intrinsic resolution of the detector ($IR$) and the resolution of the collimator ($CR$) in the same way as in a conventional pinhole camera: $SR = \sqrt{IR^2 + CR^2}$ [7]. For a CA, $IR$ can be estimated as $\frac{a}{b}$ times as long as the original $IR$ of the gamma camera because the object is $\frac{b}{a}$ times magnified or reduced on the detector, and $CR$ corresponds to that of a pinhole, which can be expressed as $Pa \times (\frac{a+b}{b})$ [8]. Therefore, XY resolution is
expressed as: $\sqrt{(IR \times \frac{a}{b})^2 + \left[Pa \times (1 + \frac{a}{b})\right]^2}$, which in turn is a function of $a$, $b$, $Pa$ and $IR$ (Supplementary Table 1).

However, the above equation is not valid for a mask of finite thickness. The resolution of a pinhole, $Pa \times \left(\frac{a + b}{b}\right)$, was defined by Brownell [9] as the separation distance of two point sources that gives touching image circles on the detector. According to this definition, the resolution of a CA mask with thickness $mt$ can be calculated geometrically. A point source on the object plane is imaged as a circle with diameter $Pa \times \frac{a + b}{a + \frac{mt}{2}}$ on the detector plane. When the image of another point source is touching this circular image, the distance between both point sources is the geometrical resolution of the mask. This geometrical resolution, $R_{col}$, can be calculated by the following equation (Supplementary Figure 3c):

$$\frac{Pa}{2} \left(\frac{a + b}{a + \frac{mt}{2}}\right) + \frac{Pa}{2} \left(\frac{a + b}{a + \frac{mt}{2}}\right) = R_{col}$$

Therefore, SR for a CA mask of finite thickness $mt$ is:

$$\sqrt{(IR \times \frac{a}{b})^2 + \left[\frac{Pa \times a(a + b)}{\left(a + \frac{mt}{2}\right)\left(b + \frac{mt}{2}\right)}\right]^2}.$$ 

Experimentally, XY resolution was measured using a 75 µm point source [6] labeled with 740 kBq (20 µCi) of $^{99m}$Tc. For each image $10^6$ counts were acquired, and the PSFs were obtained from the reconstructed images, and XY resolution calculated as the full-width at half-maximum (FWHM) of the PSF.

One of the unique features of coded aperture radioscintigraphy is the reconstruction of 3-D objects from 2-D data sets. Although Z resolution cannot be obtained by the geometrical method described for XY resolution, an analytical solution of its PSF has recently been described [10]. The longitudinal profile of the Z PSF is obtained by reconstructing multiple object planes at various distances from the detector. This profile has the shape of a peak centered in correspondence to the true depth of the source, and Z resolution is defined as the FWHM of this peak. Z resolution is a function of
where $\sigma$ is the standard deviation of the Gaussian representing the intrinsic PSF of the detector and $X_c$ is the positive solution of the equation described in the footnotes of Main Table 1. This equation cannot be solved analytically; instead, it was solved numerically by the successive approximation method.

**Signal-to-noise ratio of NTHT MURA masks:** When an image resolution element is defined as the area of a source that can be seen through one opening by one point on the detector, as previously proposed by Fenimore [1,2], SNR of NTHT MURA at the element $(i, j)$ can be calculated by the following formula [3]:

$$
SNR_{ij} = \frac{N_T I_T \sqrt{\rho/2(1-t)\Psi_{ij}}}{\sqrt{(1-t)\Psi_{ij} + t + \xi}}
$$

where $N_T$ is the total number of pixels in the mask, $I_T$ is the total number of counts of the single hole due to the source, $\rho$ is the open fraction of the pattern, $t$ the transparency of the mask, $\Psi_{ij}$ the fraction of total counts due to the source present at the $ij$th element, $\xi$ the ratio of the uncoded background to $I_T$. $N_T$ can be calculated by the square of $npm$. When the target is cube-shaped, $\Psi_{ij}$ can be calculated using the number of the elements covered by the target material. As the size of the resolution element can be calculated by dividing the size of FOV by $npm$, the number of pixels covered by the target material is the square of the number obtained by dividing the object size by the size of the element [1,2]. FOV can be calculated by $d \times \frac{a+b}{b}$. When the object size is smaller than the size of the resolution element, $\Psi_{ij}$ was set to 1. $\rho$ was defined by $npm$ using the formula $\left(\frac{npm^2}{4} - 1\right)$, which was assumed to be 0 to be consistent with very low background activity, such as sentinel lymph node biopsy.

**The effect of independent variables on SNR:** We evaluated the effects of independent variables such as $a$, $b$, $npm$, $Pa$, $\sigma$, and $X_c$ and object size on SNR by changing a single variable while others remained constant. The default values of these independent variables were determined by initial optimization using sensitivity/(XY resolution)$^2$ as the figure of merit and included: $a = 25$ cm, $b = 35$ cm, $npm = 62$, and $Pa = 1.44$ mm. $D$ varied from 10 cm to 40 cm. Because the camera must be under the table in intraoperative scintigraphy, minimal $a$ (min $a$) must be larger than the table thickness, which is usually $\approx$ 10 cm. As typical torso thickness is $\leq$ 30 cm, so the upper limit of $a$ was set to min $a + 30 = 40$ cm. $b$ was varied from 10 cm to 50 cm because the operating table height is about 70 cm and the height of the
camera is about 20 cm. $npm$ divided by 2 must be a prime number and an anti-symmetric MURA pattern must exist for this number. $Pa$ varied between 0.5 mm and 2.5 mm. $I_T$ was set to 2,000 counts at $a = 1$ cm and decreased at the inverse square of $a$.

Object size was set to 0 (point source), 2 mm, 5 mm, and 10 mm. The maximal size of micrometastasis in the lymph node in breast cancer is 2 mm [11]; 5 mm is the mean size of a non-pathological axillary lymph node; and 10 mm is the border size of a non-pathological lymph node [12].

**The relationship between SNR and object size:** We evaluated the relationship between SNR and the object size while changing the value of each independent variable: $a$ varied from 10 cm to 40 cm with an interval of 10 cm. $b$ varied from 10 cm to 50 cm with an interval of 10 cm. $npm$ varied as 14, 38, 62, and 94. $Pa$ varied from 1 mm to 2.5 mm with an interval of 0.5 mm. These complex relationships are highlighted in Supplementary Figures 4 and 5.

![Supplementary Figure 4](image)

**Supplementary Figure 4 – The effect of variation in independent variables $a$, $b$, $npm$, and $Pa$ on SNR for objects of specified diameter.**
Supplementary Figure 5 – The effect of variation of object diameter on SNR for independent variables $a$, $b$, $npm$, and $Pa$ of specified values.

**The effect of mask size on SNR:** Not all desired mask sizes can be constructed due to the limited availability of high-density alloys in large sheets. In Supplementary Figure 6, we explored the relationships among mask size, object size, and SNR, where $d$ is the length of one mask period ($d = npm \times Pa$), and the detector size $D$ is held constant at 40 cm. As can be seen, SNR is improved with larger mask size for all objects except a point source.

Supplementary Figure 6 – The effect of variation of $npm$ on SNR as a function of object diameter.
**Effect of object size on CA mask performance:** In the above analysis, we assumed a point source. However, during image-guided surgery, objects to be imaged would vary over a wide range from a small collection of malignant cells (i.e., point source-like) to 1 cm lymph nodes. As described in detail in Supplementary Figures 4-6, we explored the relationship between object size, the figure of merit used for CA mask optimization (SNR vs. sensitivity/(XY resolution)$^2$, and various object-to-detector ($a + b$) distances. The results, summarized in Supplementary Figure 7, suggest a troubling trend where SNR falls off dramatically as object size increases (i.e., becomes more distributed), and even more so as $a + b$ increases. CA masks optimized for SNR are more tolerant of object size variations compared to masks optimized for sensitivity/(XY resolution)$^2$, however, overall performance is better for the latter if object size is small (Supplementary Figure 6a and Supplementary Table 3).

![Graph showing the effect of object size on SNR](Graph.png)

**Supplementary Figure 7 - The effect of object size on SNR:** The effect of object size (mm) on SNR, at a distance of $a + b = 45$ or $a + b = 60$ cm, using coded aperture masks optimized for SNR (solid curves) or those optimized for the ratio sensitivity/(XY resolution)$^2$ (dashed curves).

**Optimization of coded aperture masks:** Although, in general, SNR provides an attractive figure of merit to optimize CA masks, image-guided surgery requires balancing of sensitivity with resolution. For this reason, we compared masks optimized using SNR to those optimized using the metric sensitivity/(XY resolution)$^2$, which is essentially a normalization of sensitivity over area. As shown in Supplementary Table 3, each figure or merit had advantages and disadvantages, with SNR-optimized masks having a lower overall SNR but less susceptibility to object size, and ratio-optimized masks having improved performance for small objects and rapidly degrading performance at the object size increased. However, when considering the vastly improved resolution with ratio-optimized masks, we chose sensitivity/(XY resolution)$^2$ as the figure or merit for designing CA masks for image-guided
surgery. Fortunately, the LabVIEW software written for parameter optimization permits any desired figure of merit to be used for such analysis.

99mTc-methylene Diphosphonate (MDP) Bone Scanning in Mice: CD-1 mice (Charles River Laboratories, Wilmington, MA) weighing 25 g were used under the supervision of an approved institutional protocol. Mice were injected intravenously with 12.95 MBq (350 µCi) 99mTc-MDP 4 h prior to coded aperture and micro-computed tomographic (microCT) imaging. MicroCT imaging was performed on an eXplore Locus micro-computed tomography system (GE Healthcare Biosciences, Waukesha, WI) using an isotropic resolution of 90 µm. Coded aperture imaging was performed using the optimized mask described above, collection of $10^7$ total counts, and laminographic reconstruction.

Supplementary Figure 8 – The effect of object size on image interpretation: Micro CT (left), coded aperture reconstruction (middle), and a merge of the two (right), 4 h after intravenous injection of 12.95 MBq (350 µCi) of 99mTc-MDP into a 25 g CD-1 mouse. Shown are coded aperture reconstructions at $Z = 11.15$ cm (bottom) and $Z = 11.85$ cm (top). Results are representative of $n = 3$ independent experiments.
Supplementary Table 1 - Key Independent and Dependent Variables in Coded Aperture Imaging Assuming an Infinitesimally Thin Mask.

### Independent Variables

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>$a$</td>
<td>Mask to object distance</td>
</tr>
<tr>
<td>$b$</td>
<td>Mask to detector distance</td>
</tr>
<tr>
<td>$d$</td>
<td>Length of one period of mask ($= npm \times P_a$)</td>
</tr>
<tr>
<td>$D$</td>
<td>The smaller dimension of the rectangular FOV of the detector</td>
</tr>
<tr>
<td>$f$</td>
<td>Form factor ($f=\frac{1}{\sqrt{2}}$ for round holes, $f=1$ for square holes)</td>
</tr>
<tr>
<td>$IR$</td>
<td>Intrinsic resolution (FWHM) of camera ($= 3$ mm for the camera used in this study)</td>
</tr>
<tr>
<td>$k$</td>
<td>Resolution index (for FWHM, $k=\frac{1}{2}$)</td>
</tr>
<tr>
<td>$npm$</td>
<td>Number of pixel positions (open or closed) in one mask period</td>
</tr>
<tr>
<td>$P_a$</td>
<td>Diameter of mask holes</td>
</tr>
<tr>
<td>$PDE$</td>
<td>Photopeak detection efficiency of detector</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>Standard deviation of the Gaussian representing the intrinsic PSF of the camera ($=\frac{IR}{2\sqrt{2} \times \ln 2}$ = 1.274 mm for the camera used in this study). Note that $\frac{1}{2\sqrt{2} \times \ln 2}$ is the classic conversion factor from FWHM to standard deviation.</td>
</tr>
</tbody>
</table>

### Dependent Variable

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Formula</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnification of object on detector ($m$)</td>
<td>$\frac{b}{a}$</td>
<td></td>
</tr>
<tr>
<td>Magnification of mask on detector ($M$)</td>
<td>$1 + \frac{b}{a} = 1 + m$</td>
<td></td>
</tr>
</tbody>
</table>
FOV

\[ d \times (1 + \frac{a}{b}) \]

Only valid if \( d \times \frac{a+b}{a} \leq D \)

XY Resolution

\[ \sqrt{(IR \times \frac{a}{b})^2 + \left( P_a \times (1 + \frac{a}{b}) \right)^2} \]

Z Resolution

\[
\frac{4 \times (npm - 1) \times a \times \left( \frac{a}{b} \times \frac{X_c}{P_a} \right)}{(npm - 1)^2 - 4 \times \left( \frac{a}{b} \times \frac{X_c}{P_a} \right)^2}
\]

\( X_c \) is the positive solution of equation 1 described in the footnotes.

Sensitivity

\[
\frac{\rho_{op}}{\pi} \times \arctan \frac{1}{\left( \frac{2 \times a}{d} \right)^2 + 2 \times \frac{d}{2 \times a}} \times PDE
\]

\( \rho_{op} = \pi \times \left( \frac{npm^2 - 1}{8 \times npm^2} \right) \)

(Open area fraction of aperture for round mask holes)

(1)

\[
\frac{\sigma^2}{2X_c^2} \left[ E_+ \times \text{erf}(E_+) - E_- \times \text{erf}(E_-) + \frac{1}{\sqrt{\pi}} \exp(-E_+^2) - \frac{1}{\sqrt{\pi}} \exp(-E_-^2) \right]^2 = k \times \text{erf}^2 \left[ \frac{M \times P_a \times f}{2 \times \sqrt{2} \times \sigma} \right]
\]

where:

\[
E_+ = \frac{\left( \frac{M \times P_a \times f}{2} + X_c \right)}{\sqrt{2} \times \sigma}, \quad E_- = \frac{\left( \frac{M \times P_a \times f}{2} - X_c \right)}{\sqrt{2} \times \sigma}
\]

and \( \text{erf} (x) = \frac{2}{\sqrt{\pi}} \int_0^x \exp(-t^2)dt \)

Open area fraction for round mask holes derived from:

\[
\left( \pi \times \left( \frac{Pa}{2} \right)^2 \right) \times \left( \frac{npm^2 - 1}{4} \right) \div (npm \times Pa) = \pi \times \left( \frac{npm^2}{8 \times npm^2} \right)
\]
Supplementary Table 2 - The Requirements for Each Independent Variable to Obtain a Valid FOV, Taking into Account Mask Thickness (\(mt\)).

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original inequality</td>
<td>(d \times \frac{a + b}{a + \frac{mt}{2}} \leq D)</td>
</tr>
<tr>
<td>(a) (object to mask distance)</td>
<td>(a \geq \frac{2b \times npm \times Pa - D \times mt}{2(D - npm \times Pa)})</td>
</tr>
<tr>
<td>(b) (mask to detector distance)</td>
<td>(b \leq \frac{2a \times (D - npm \times Pa) + D \times mt}{2npm \times Pa})</td>
</tr>
<tr>
<td>(npm) (number of pixel positions, open or closed, in one mask period (d))</td>
<td>(npm \leq D \times \frac{2a + mt}{2Pa \times (a + b)})</td>
</tr>
<tr>
<td>(Pa) (diameter of holes of mask)</td>
<td>(Pa \leq D \times \frac{2a + mt}{2npm \times (a + b)})</td>
</tr>
</tbody>
</table>
**Supplementary Table 3 – Comparison of SNR-Optimized and Sensitivity/(XY Resolution)^2-Optimized Coded Aperture Masks.**

<table>
<thead>
<tr>
<th>Object Size</th>
<th>Optimization Method</th>
<th>a+b (cm)</th>
<th>a (cm)</th>
<th>b (cm)</th>
<th>npm</th>
<th>XY Resolution (mm)</th>
<th>Sensitivity (%)</th>
<th>SNR</th>
<th>Sens/XY^2</th>
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<tbody>
<tr>
<td>0 (point source)</td>
<td>SNR</td>
<td>45</td>
<td>10</td>
<td>35</td>
<td>62</td>
<td>1.44</td>
<td>2.03</td>
<td>0.344</td>
<td>151</td>
</tr>
<tr>
<td>Sens/XY^2</td>
<td>45</td>
<td>10</td>
<td>35</td>
<td>62</td>
<td>1.44</td>
<td>2.03</td>
<td>0.344</td>
<td>151</td>
<td>0.0836</td>
</tr>
<tr>
<td>2 mm</td>
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<td>45</td>
<td>10</td>
<td>34</td>
<td>62</td>
<td>1.47</td>
<td>2.17</td>
<td>0.315</td>
<td>131</td>
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<tr>
<td>Sens/XY^2</td>
<td>45</td>
<td>10</td>
<td>35</td>
<td>62</td>
<td>1.44</td>
<td>2.03</td>
<td>0.344</td>
<td>130</td>
<td>0.0836</td>
</tr>
<tr>
<td>5 mm</td>
<td>SNR</td>
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<td>10</td>
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<td>62</td>
<td>1.44</td>
<td>2.03</td>
<td>0.344</td>
<td>20.8</td>
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<tr>
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<td>0.317</td>
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REFERENCES