Nuclear Medicine

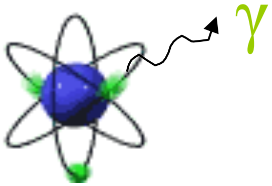
Science that contributes to the *treatment* and to the *diagnosis* of human disease (illness) using rays emitted by nucleus of radioactive atoms

Commonly used isotops

Isotop	Energy	Period
γ emitters		
Technetium 99m	140 keV *(89%)*	6,02 hours
Iodine 123	27 *(71%)* 159 keV *(83%)*	13,2 hours
Thallium 201	71 keV *(47%)*	73 hours
β+ emitters		
Oxygene 15	1738 keV	2,1 minutes
Carbon 11	960 keV	20,4 minutes
Fluor 18	634 keV	109,8 minutes
Brome 76	3980 keV	972 minutes

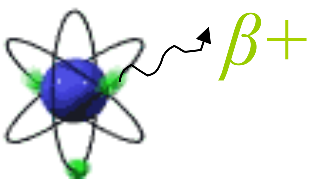
Associated imaging techniques

Emitters γ



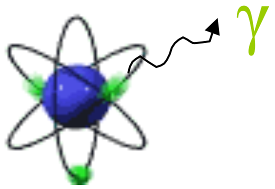
Single Photon Emission Computed Tomography (SPECT)

Emitteurs β+

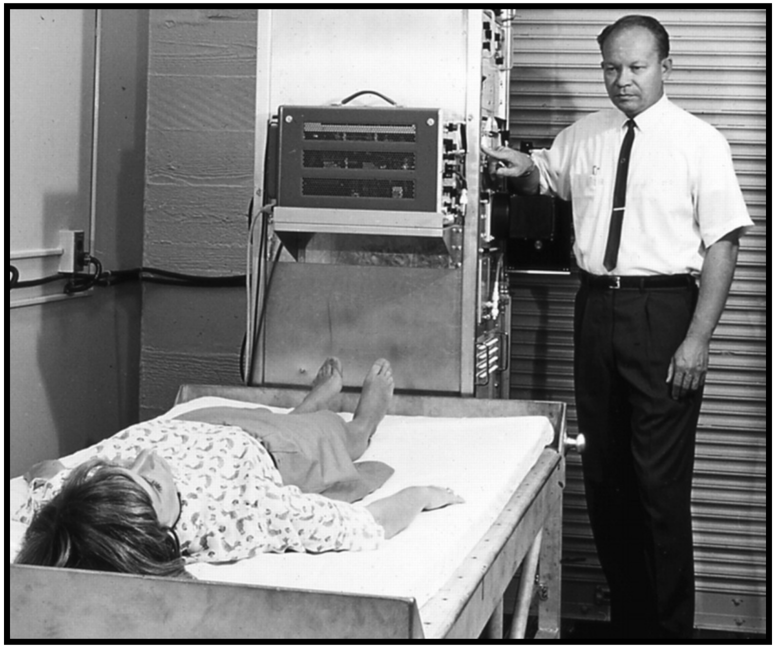


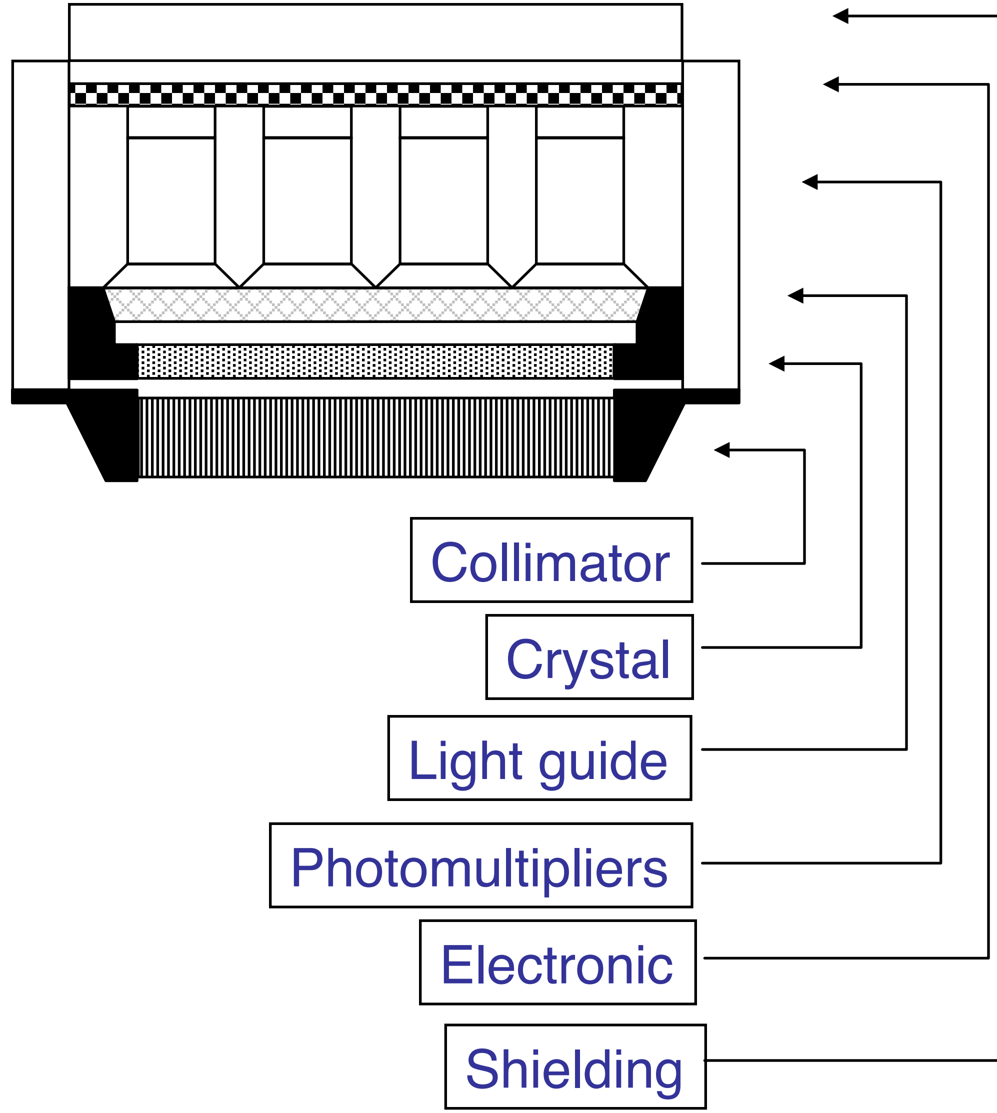
Positon Emission Tomography (PET)

Emitters γ

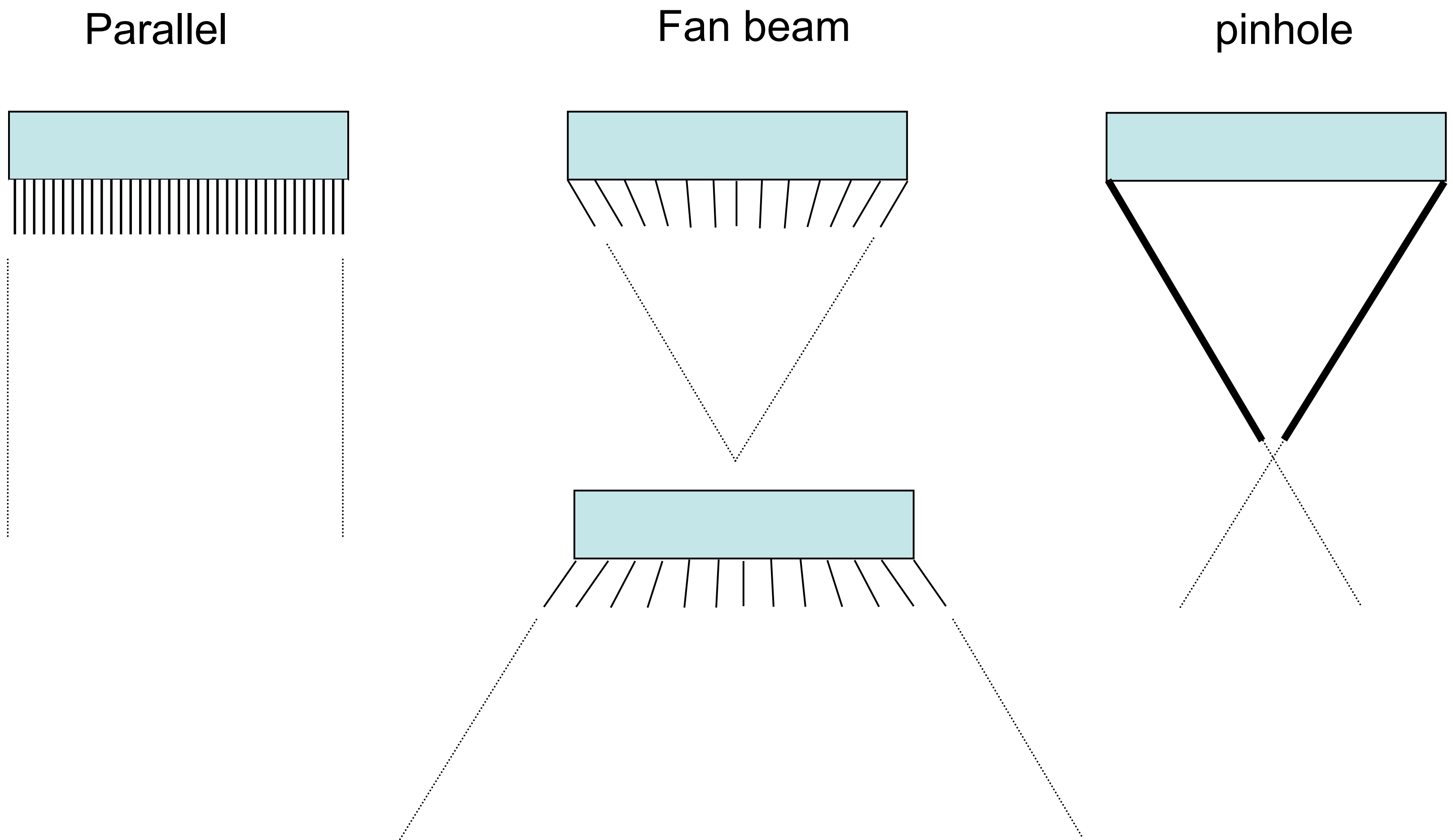


Single Photon Emission
Computed Tomography
(SPECT)



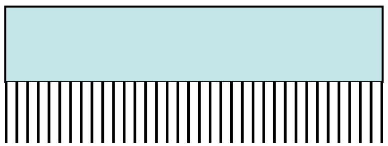

Collimator
Crystal
Light guide
Photomultipliers
Electronic
Shielding

The collimator



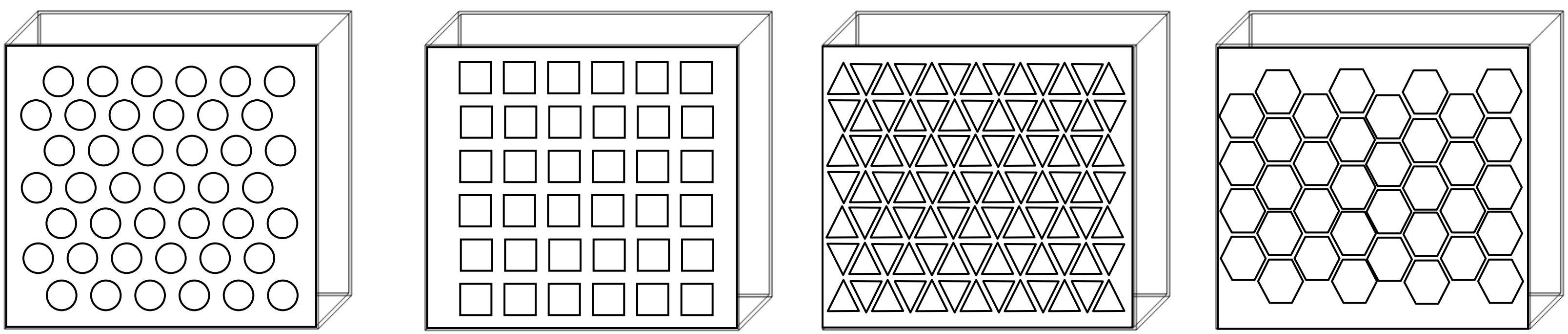
Determine the distribution of photons in the crystal

Parallel collimator



Thichness varies from 25 to 80 mm
Contains betwenn 3.10^4 and 9.10^4 holes

Different geometrial shapes of holes

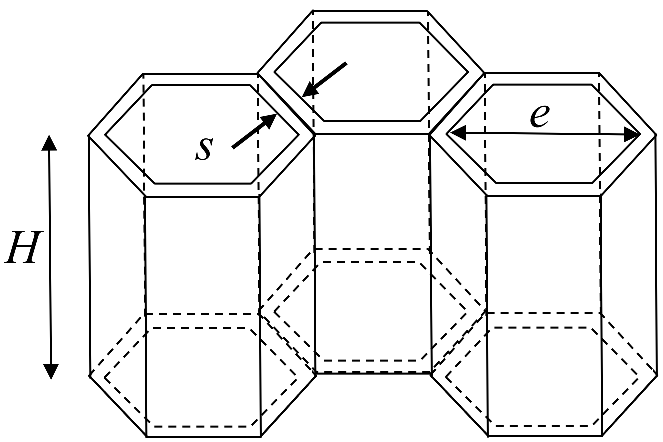


Two conception modes : « foil or cast »

Septa = Material between holes

Holes are organized in a way that optimizes the exposition of the crystal
Hexagonal arrangement presents the best compromise
Hexagone, cylindre, square, rectangle offer the same septal thickness which is not the case of the circle

Minimum septum thickness is determined by the energy of the photons



$$s = \frac{2ep}{H-p}$$ *with p* = minimum crossed distance

If we tolerate 5% of penetration,

What should be the lower limit of s ?

$$\text{transmission} = e^{-\mu p} \leq 0,05$$

$$e^{-\mu p} \leq e^{-3}$$

$$s \geq \frac{6e}{\mu H - 3}$$

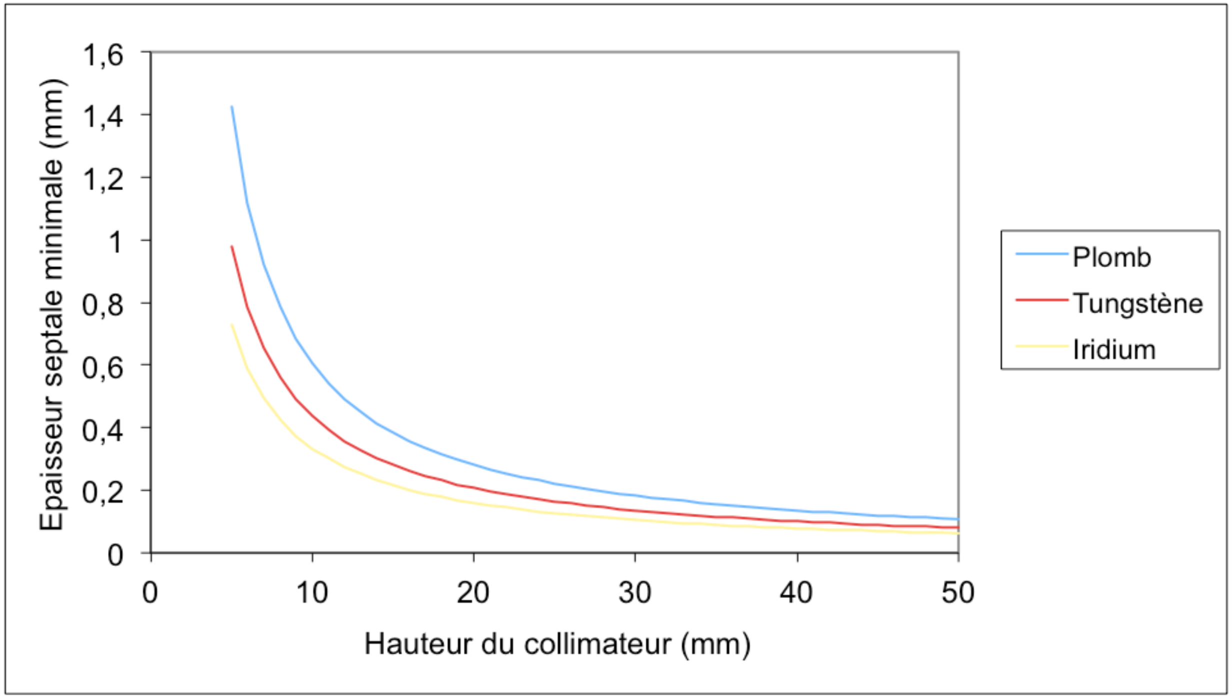
Example

Energy: 150 keV

Material: Lead
ρ = 11,35 g/cm^3
μ/ρ = 2,014 cm^2/g
μ = 22,86 cm^{-1}

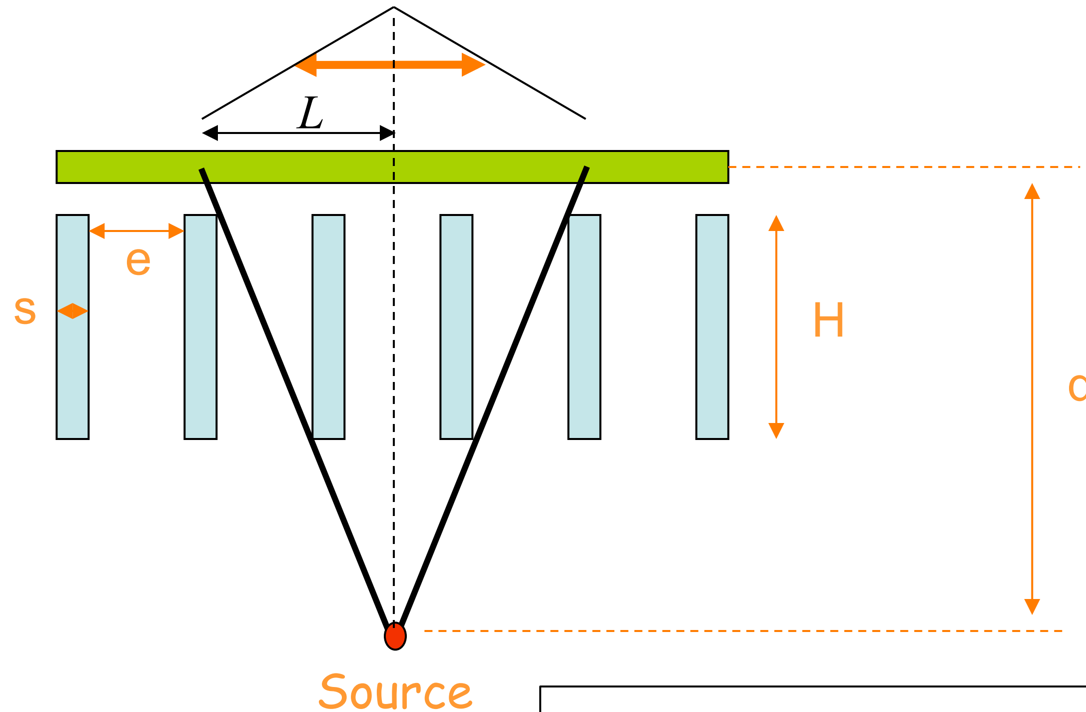
Material: Tungsten
ρ = 19,3 g/cm^3
μ/ρ = 1,581 cm^2/g
μ = 30,51 cm^{-1}

Material: Iridium
ρ = 22,42 g/cm^3
μ/ρ = 1,74 cm^2/g
μ = 39,01 cm^{-1}



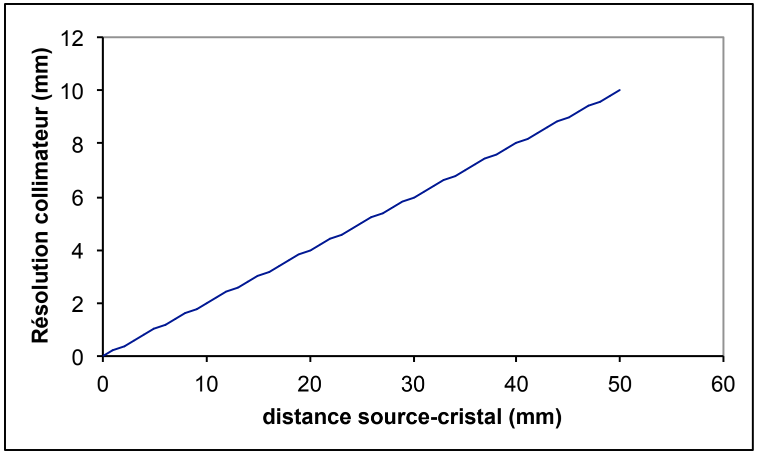
Calculate *s min* for an energy of 365 keV

Spatial resolution



Hit: $\tan\alpha = \frac{L}{d} = \frac{e}{H}$

$$R_p = \frac{d \cdot e}{H}$$



Geometrical detection efficiency

Proportion of photons emitted from a point source and
Transmitted through the collimator

$$S_p \approx k \frac{e^4}{H^2 (e+s)^2}$$

k is determined by the geometrical shape of the holes

Circulars	0,06
Hexagonals	0,07
Squares	0,08

Independant of source-collimateur distance
Two effects compensate one another:

- Hole efficiency decreases as $1/d^2$
- Number of holes is proportional to d^2

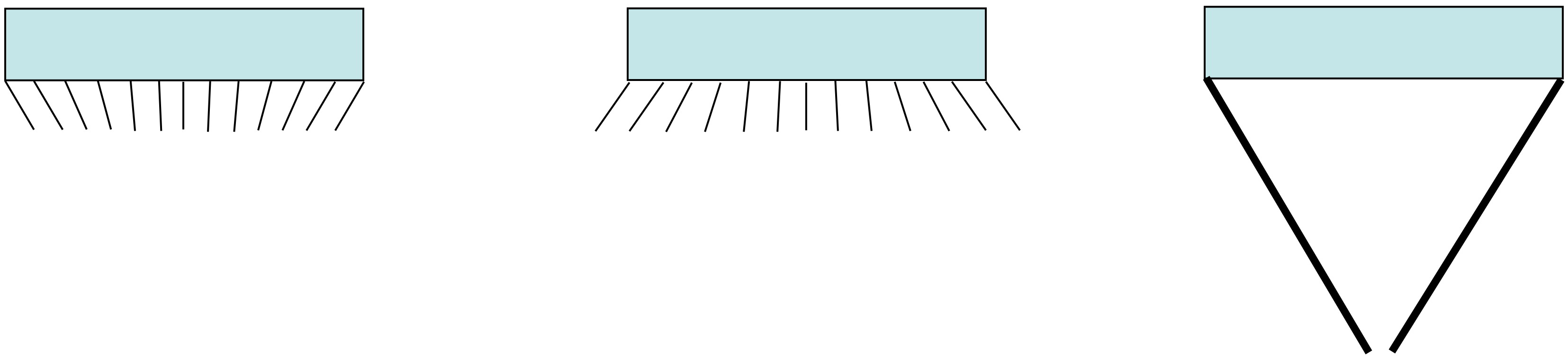
Hole effective height

Modification due to septal penetration

$$H = H_r - \frac{2}{\mu}$$

Real height

Non parallel collimator



The field of view varies as function of the magnification factor

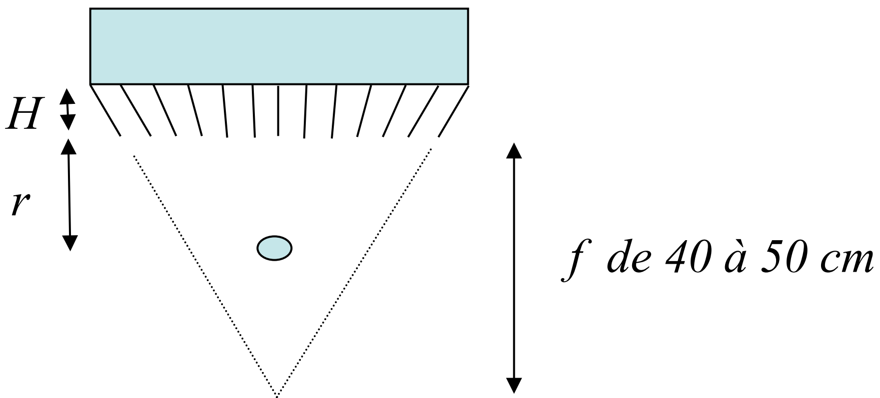
$$F_M = \frac{F}{M}$$

Total field of view of the camera

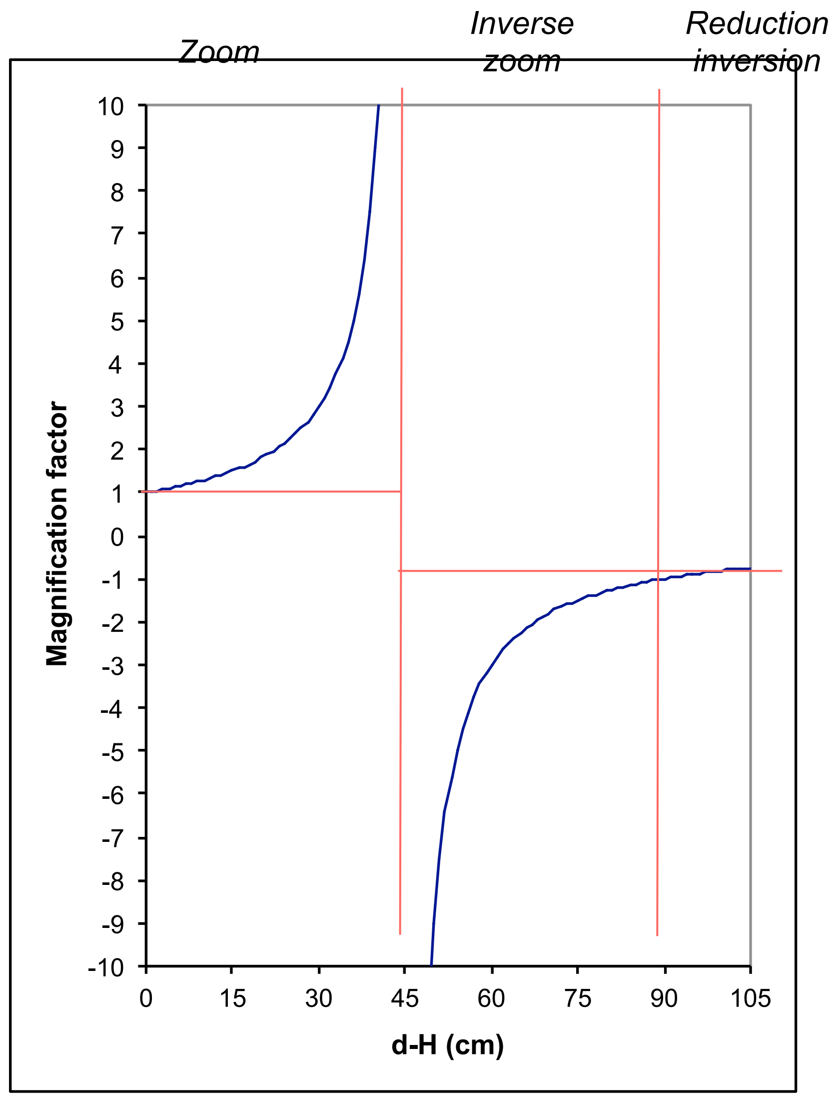
Magnification factor

$$R_s = \sqrt{R_c^2 + \left(\frac{R_i}{M}\right)^2}$$

Collimateur convergent

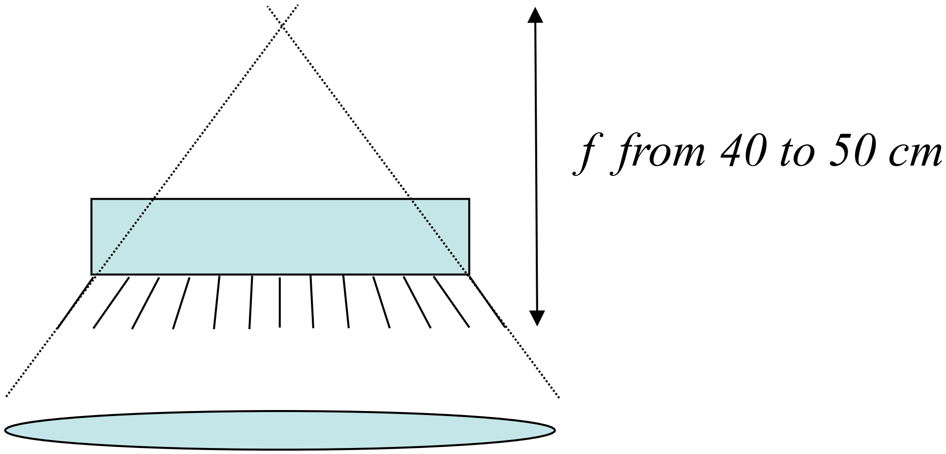


$$M = \frac{H+f}{H+f-r}$$

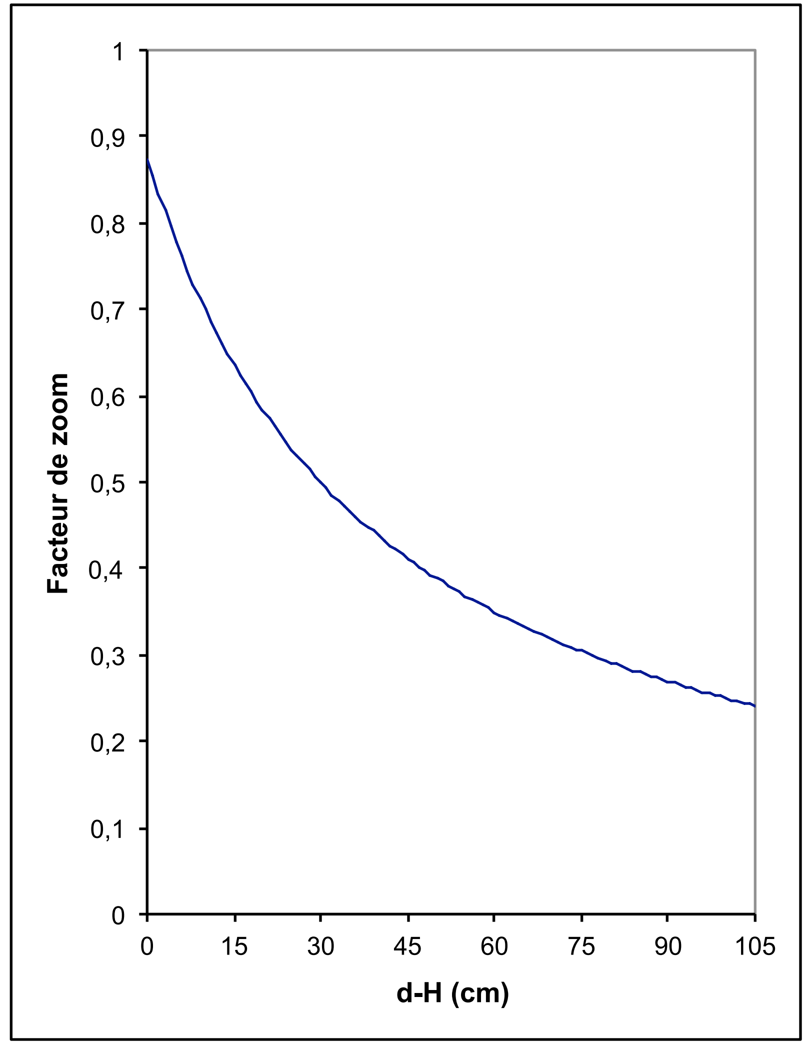


Special case: *fan beam*

Fan beam collimator

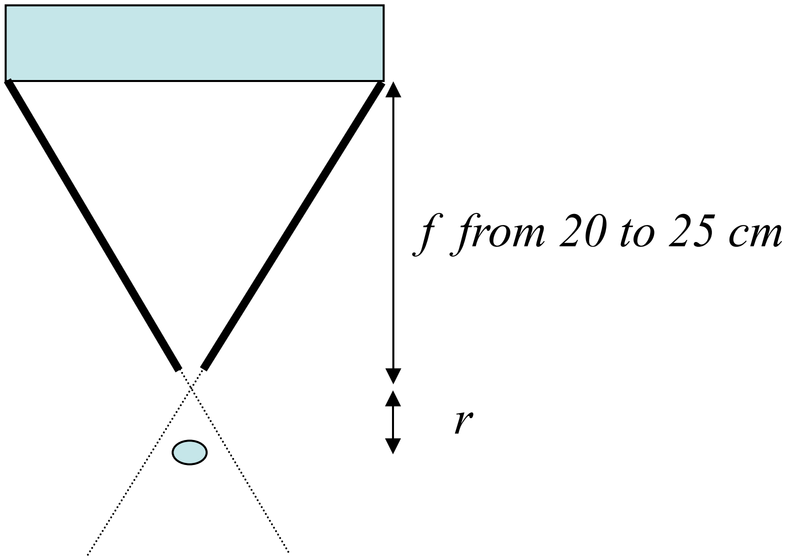


$$M = \frac{f - H}{f + r}$$

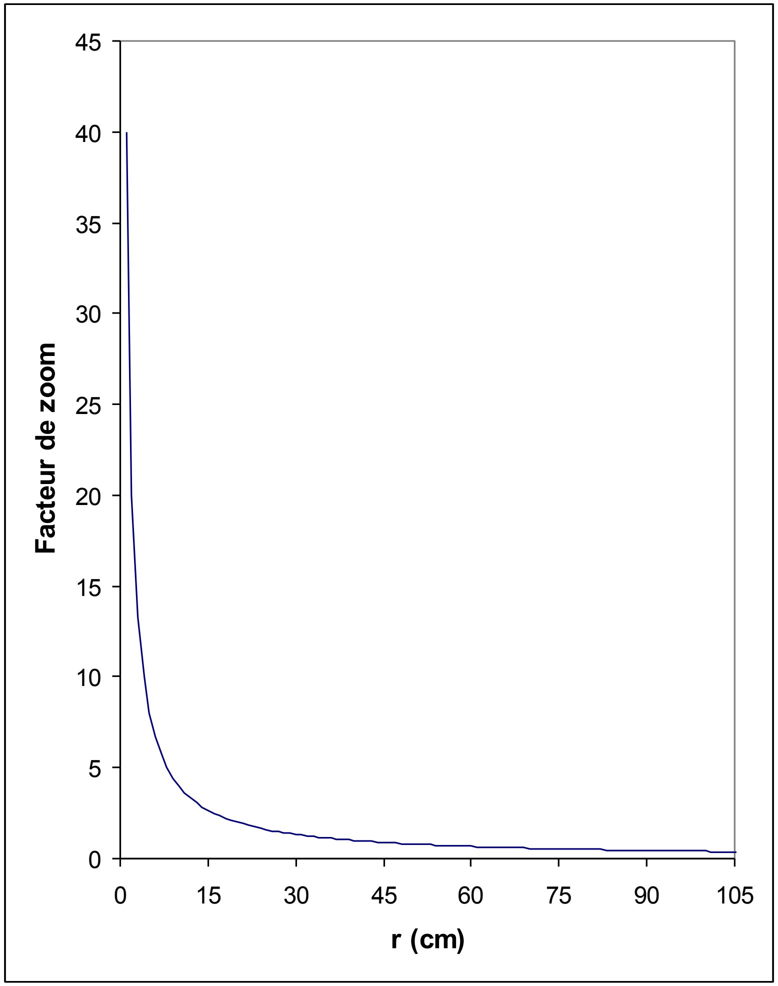


Special case: *fishtail*

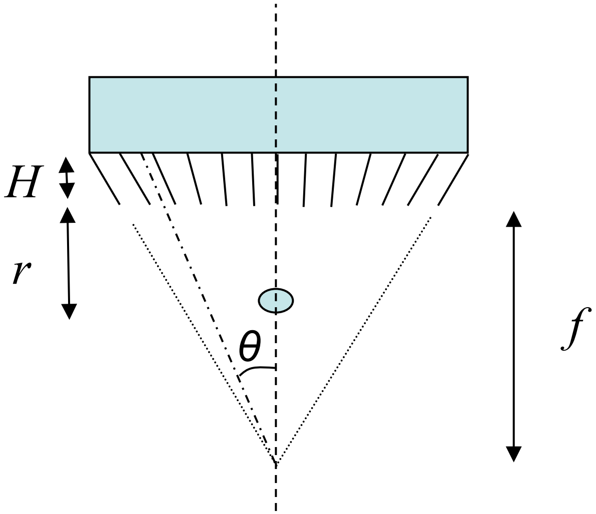
Pinhole collimator



$$M = \frac{f}{r}$$

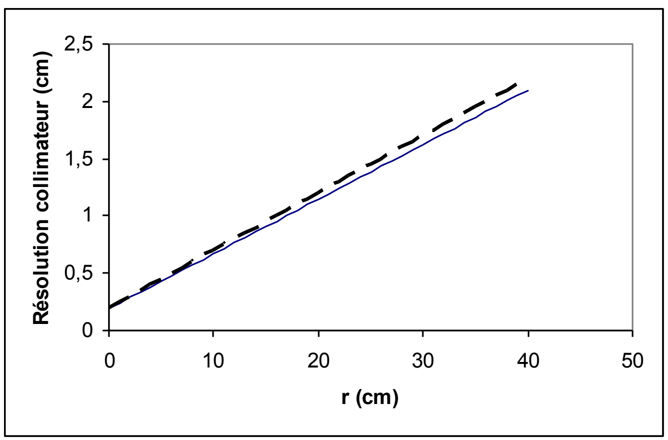


Spatial resolution
Detection efficiency

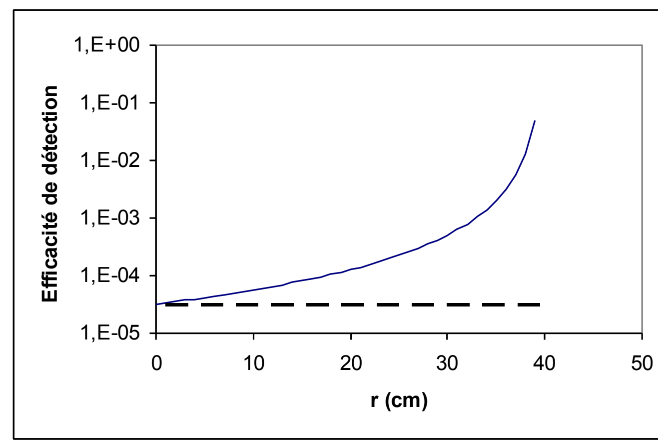


Convergent collimator

$$R_c \approx \frac{R_p}{\cos\theta}\left(1 - \frac{H}{2(f+H)}\right) \qquad S_g \approx S_p \cos^2\theta \frac{f^2}{(f-r)^2}$$

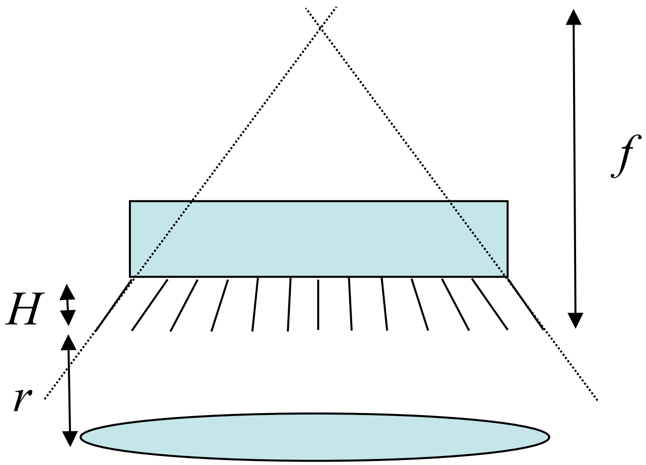


$H = 4\ cm$
$f = 40\ cm$
$e = 0{,}2\ cm$
$s = 0{,}02\ cm$
$\theta = 0°$



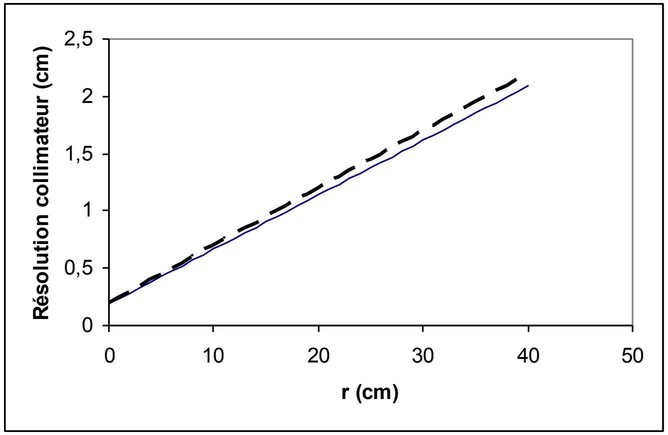
Spatial resolution and detection efficieny vary in the field of view
Maximum for $\theta=0$

Spatial resolution
Detection efficiency

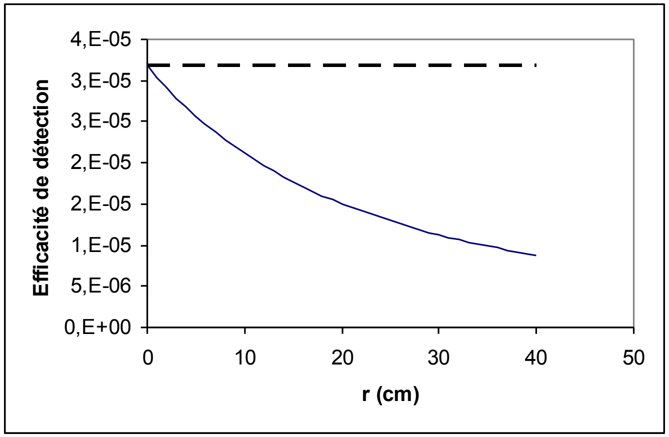


Divergent Collimator

$$R_c \approx \frac{R_p}{\cos\theta}\left(1+\frac{H}{2f}\right) \quad S_g \approx S_p \cos^2\theta \, \frac{(f+H)^2}{(f+H+r)^2}$$

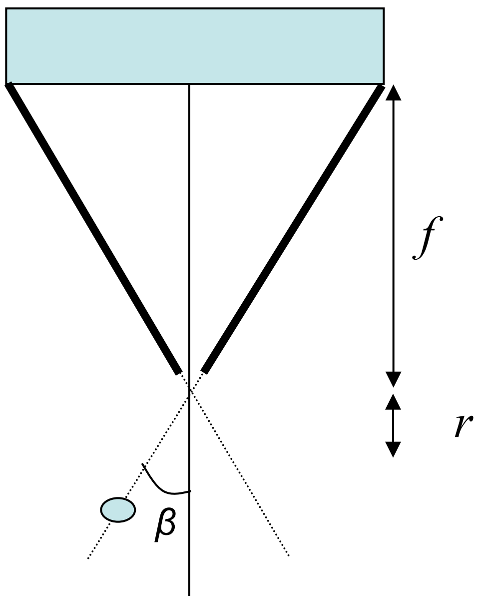


$H = 4$ cm
$f = 40$ cm
$e = 0{,}2$ cm
$s = 0{,}02$ cm
$\theta = 0°$



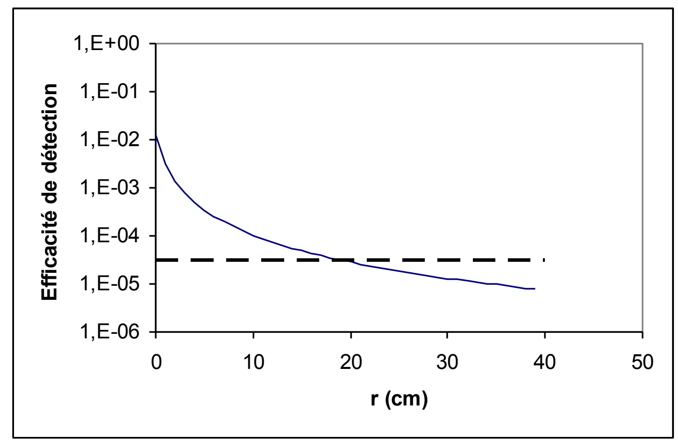
Spatial resolution
Detection efficiency

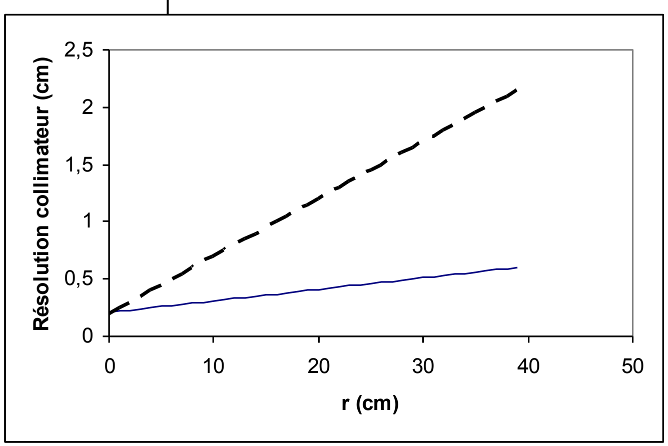
Pinhole collimator



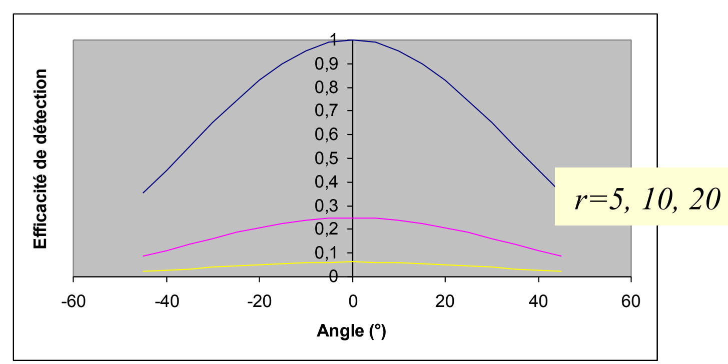
$$R_c = e + e\frac{r}{f}$$

$$S_g \approx \frac{e^2 \cos^3 \beta}{16 r^2}$$



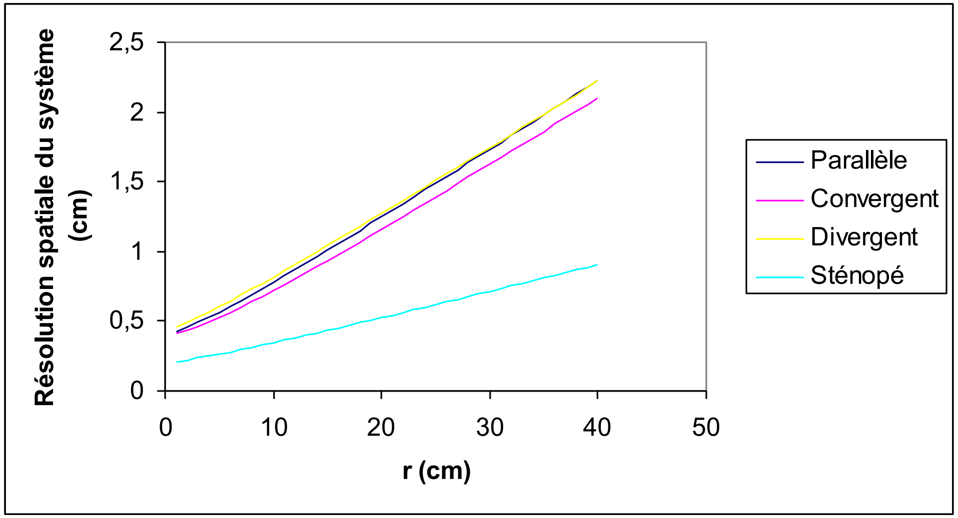


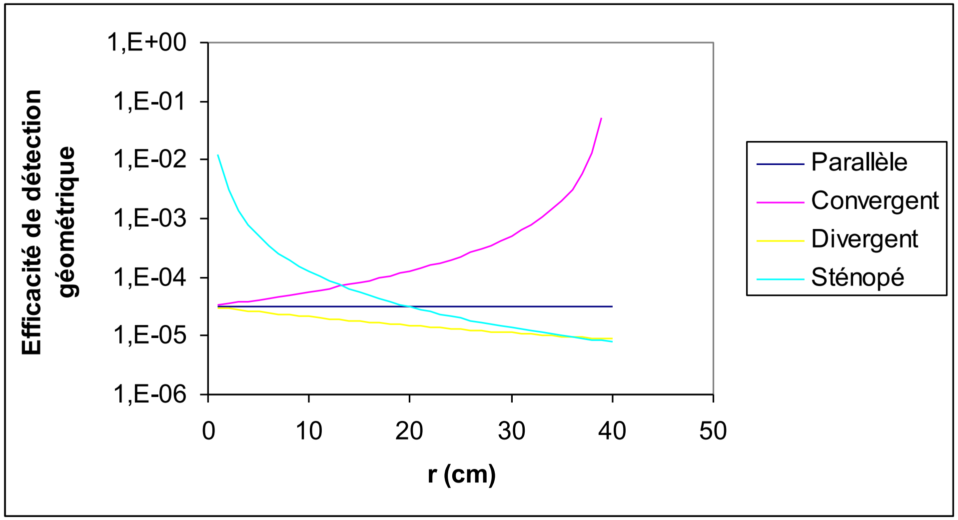
f = 20 *cm*
e = 0,2 *cm*
β =0°



Comparison

Ri = 0,34 cm
H = 4 cm
f = 40 cm
e = 0,2 cm
s = 0,02 cm
$\theta = 0°$





Paper study

D Lowe et al, ’’Optimisation of the design of round-hole parallel collimators for ultra-compact nuclear medicine imaging,’’ NIM A488 (2002) 428-440.

Scintillating crystal

The crystal dimension determines the geometrical field of view of the camera

At the beginning,
The field of view was circular with small diameter
Actually,
Rectangular going to 590 x 390 mm²
Requiring crystal dimension of 600 x 450 mm²

Its thickness determines the detection efficiency
As ^{99m}Tc is the main used isotope
Crystal thickness was optimized for 140 keV
Generally, NaI(Tl) 9,5 mm (84% @140 keV)

Luminescence effect by fluorescence

incidents $\gamma \rightarrow N_0^*$ excited states $$N^*(t) = N_0^* e^{-t/\tau_0}$$

Number of optical photons:

Energy deposit in the crystal

Fluorescence decay constant

$$N_{h\nu} = \frac{\Delta E}{h\nu}\varepsilon = N_0^* - N^*(t) = N_0^*\left(1 - e^{-t/\tau_0}\right)$$

Efficiency of the crystal

Crystals characteristics

	YAP:Ce	$LaBr_3$:Ce	$LaCl_3$:Ce	NaI:Tl
Density($g.cm^{-3}$)	5.35	5.29	3,9	3,7
$1/\mu$ (mm) [à 140keV]	6,7	3,6	4,5	4,9
Yield (ph/MeV)	18000	63000	50000	38000
λ_{max} (nm)	370	380	350	415
Refraction index	1.93	1.9	1,9	1,85
Resolution (%) [@ 140keV]	20	6	10	9
Photoelectric proportion (%) [@ 140keV]	50	79	80	84
Decay time (ns)	27	25	20	230
Hygroscopic	Non	Oui	Oui	Oui

Limit on the decay time

Depends on the free electrons/holes velocity from the ionisation band to the luminescence center

Depends on the life-time of the emission state of the activators

Limit on the light yield

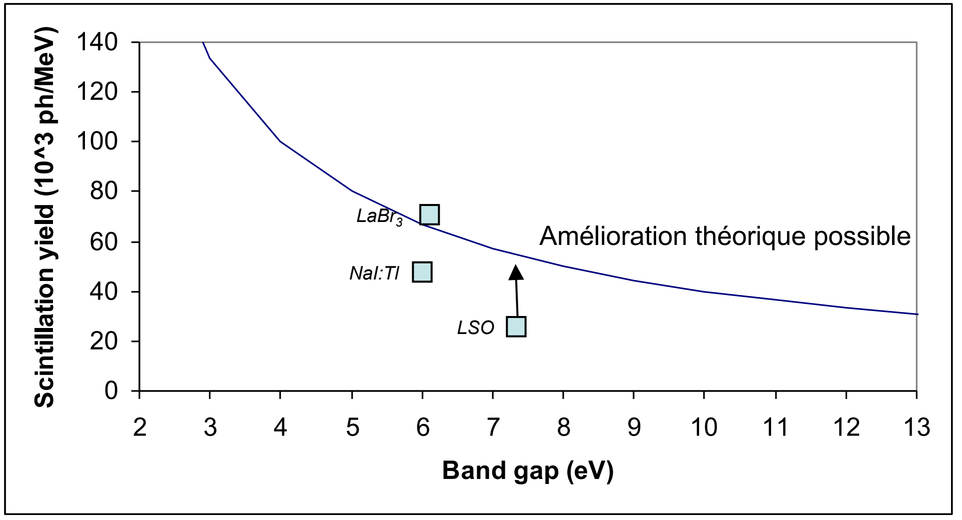
Determined by the number of electrons/holes pairs created in the ionization band

Photon energy

$$n_{ph} = \frac{E_\gamma}{\beta E_g}$$

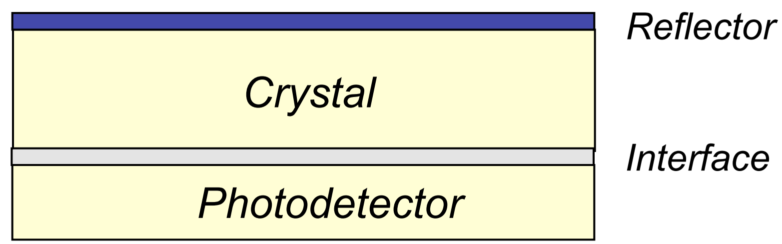
About 2,5

Energy gap of the media



Coupling: optimization

Optimize surface treatment



The choice of the reflector:

Specular reflector:

reflexion angle = incidence angle -> not ideal

Lambertian reflector:

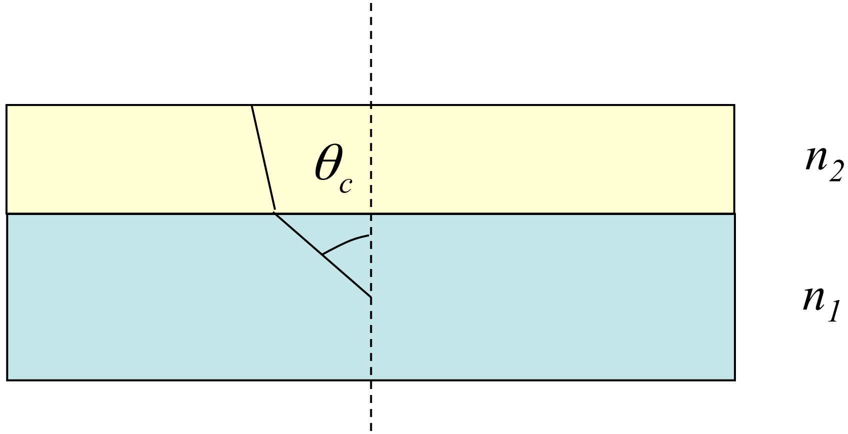
$R(\theta_r)=\cos\theta_i$, almost normal to the crystal reflexion -> better

Reduces the light spread

Treatment surfaces:
Avoid/Reduce total reflexion

Total reflexion critical angle :

$$\theta_c = \sin^{-1}\left(\frac{n_2}{n_1}\right)$$



Example:
NaI:Tl n=1,85
Optical diffusor: n=1,5

$$\theta_c = 54°$$

Intrinsic resolution

Crystal / PMT coupling

Barycenter approach

Valid for a uniform crystal coupled to several cells of the photodetector

Number of photoelectrons

$$R_i = 2{,}35\left(\frac{\left(\sum s_i^2 n_i\right)^{1/2}}{\sum s_i\left(dn_i/dx\right)}\right)$$

Linear coordinates

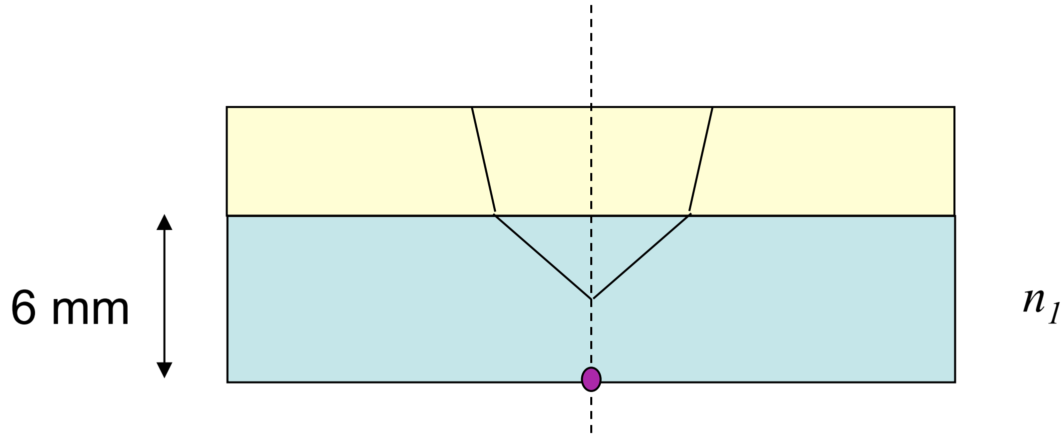
PMT weight factor

Limit resolution research
Minimize R with respect to s

Reducing the dimension of the photodetector cell

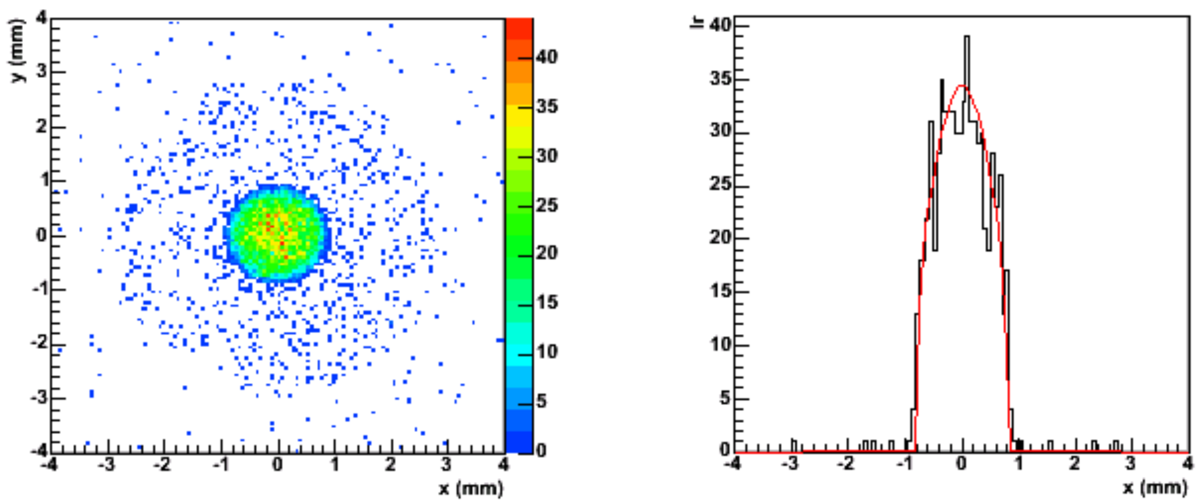
$$R_i = 2{,}35\left(\sum \frac{\left(dn_i / dx\right)^2}{n_i}\right)^{1/2}$$

Resolution improvement due to a high number of photoelectrons

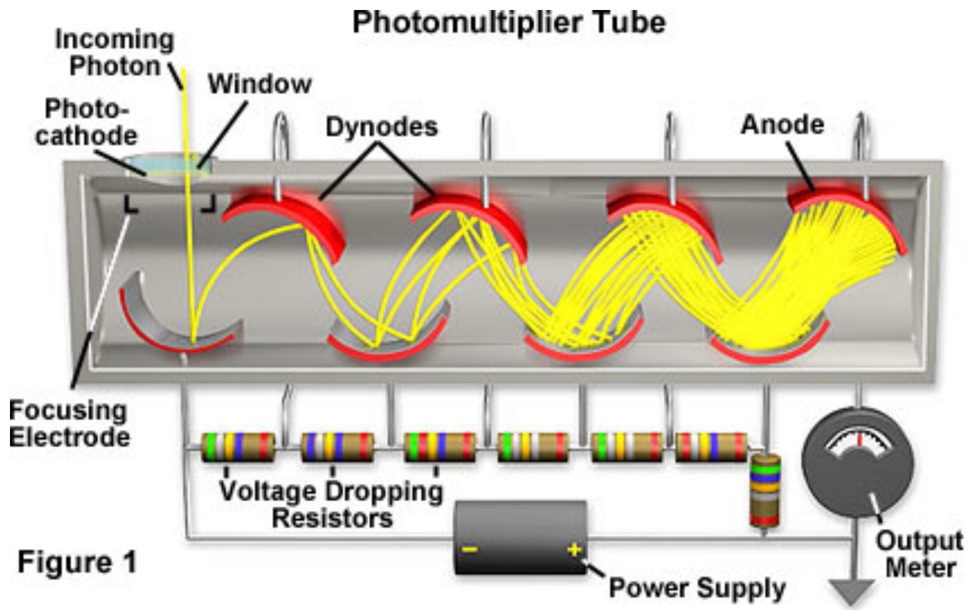


For NaI:Tl, If the scintillation occured at the edge, the light spot spread is 16 mm
If scintillation occurs in the center, the light spot spread is 8 mm
If the diffusion media is « AIR », the light spot spread will be 4 mm

Geant4 simulation
Crystal YAP (n=1,93)
Thickness 3mm
Scintillation in the center



Photomultiplier Tube



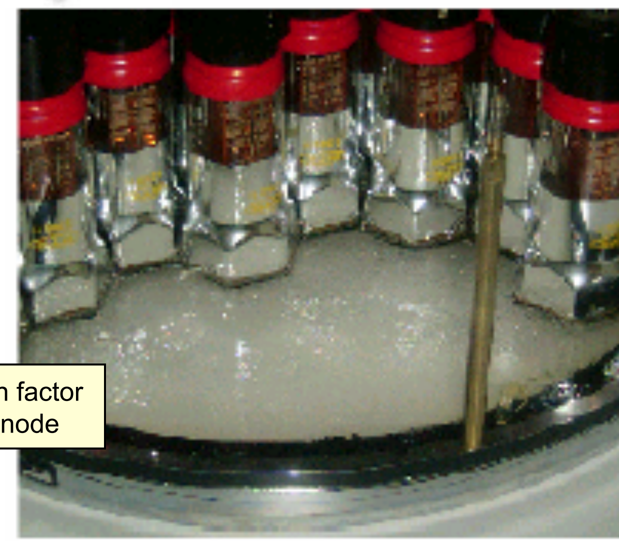
Nb of e⁻ collected at the anode

Nb of primary e⁻

$$n_a = n_k \prod_N g_i$$

Amplification factor
Of each anode

Nb ofdynodes



http://www.olympusmicro.com/primer/digitalimaging/concepts/photomultipliers.html

La charge $Q = Ne$

N
$=$

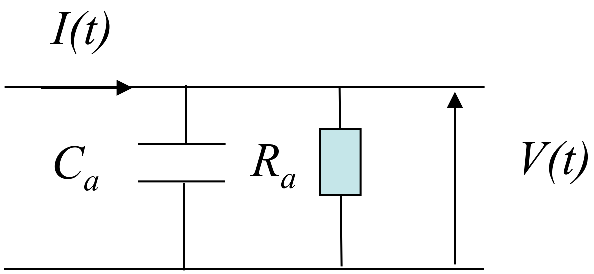
$N_{h\nu}$	Number of optical photons emitted by the scintillator
$\Omega(\lambda)$	Optical yield of the photocathode
$\sigma(\lambda)$	Quantum yield of the photocathode
C	Collection yield of the optical entry
G	Global gain of the PM

$$N_{h\nu} = \frac{\Delta E}{h\nu}\varepsilon$$ et $$\Gamma = \frac{\varepsilon}{h\nu}\Omega(\lambda)\sigma(\lambda)C$$ Total conversion coefficient

$$Q = \Gamma \Delta E G e$$

with $G = K \times HT^{\alpha d}$

Output Voltage



$$I(t) = \frac{dQ}{dt} \propto \frac{Q}{\tau_0} e^{-\frac{t}{\tau_0}}$$

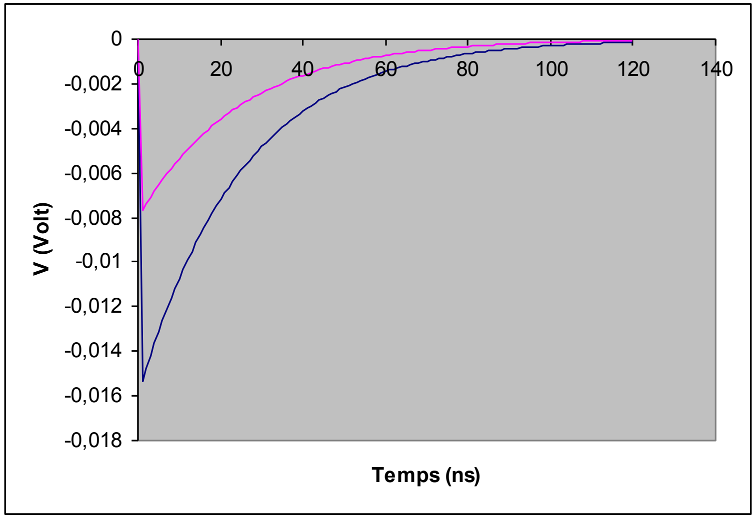
$$I(t) = C_a \frac{dV(t)}{dt} + \frac{V(t)}{R_a} = \frac{dQ}{dt}$$

$$\frac{dV(t)}{dt} + \frac{1}{R_a C_a} V(t) = \frac{Q}{C_a \tau_0} e^{-\frac{t}{\tau_0}}$$

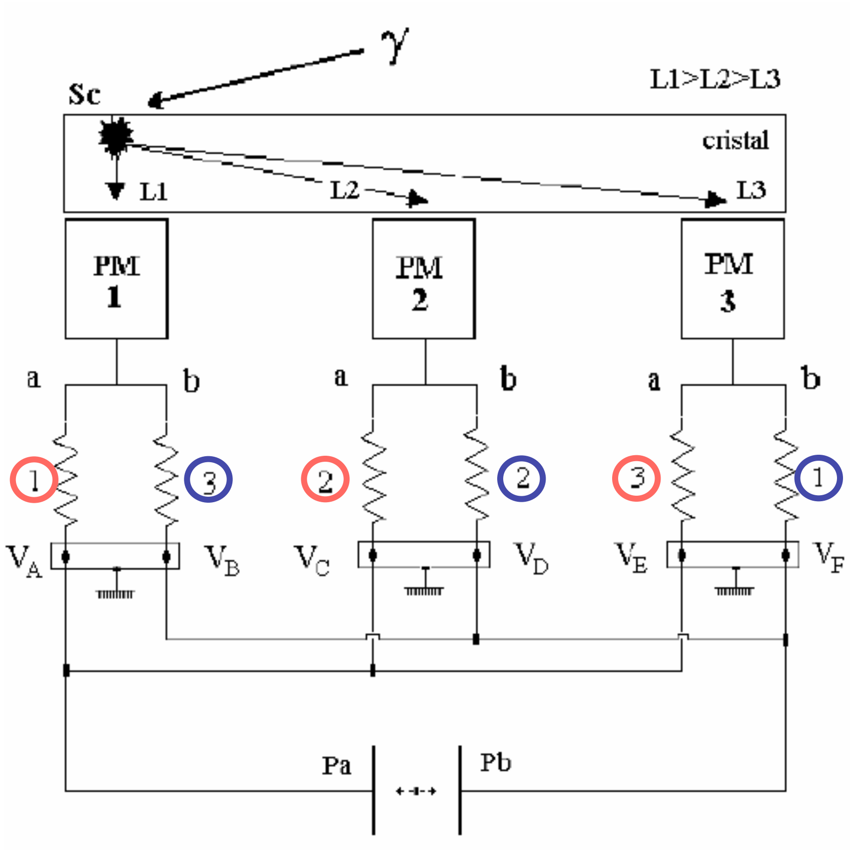
with $\tau_a = R_a C_a$

$$V(t) = \frac{Q}{C_a} \frac{\tau_0}{\tau_0 - \tau_a} \left(e^{-\frac{t}{\tau_0}} - e^{-\frac{t}{\tau_a}} \right)$$

R_a= 50 Ω
C_a=10 pF
τ_0=25 ns
Q_1=1,6 10-13 C
Q_2=0.8 10-13 C



Scintillation localization

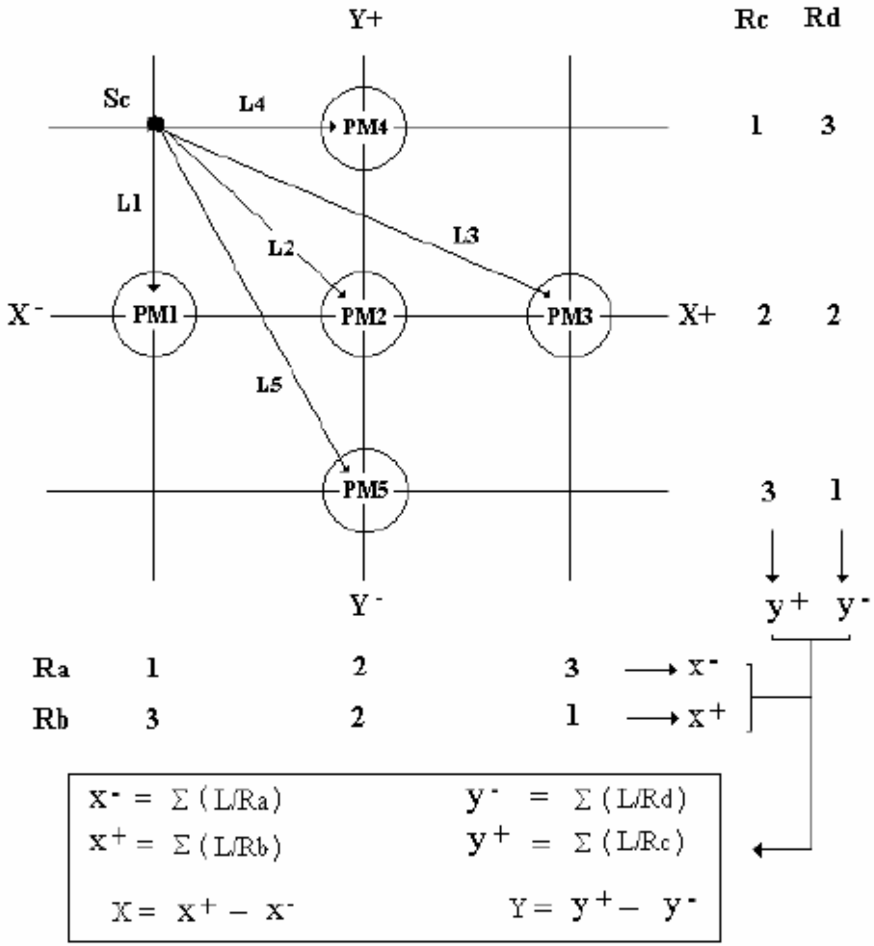


Each PM anode is connected to two separated circuits (« a » and « b ») yielding to vertical layers (Layers of horizontal deviation) of an oscilloscope « Pa » et « Pb ».

Arbitrary:
L1=12
L2=10
L3=6
with V~L/R

Pb-Pa=(Vb+Vd+Vf)-(Va+Vc+Ve)=(12/3+10/2+6/1) – (12/1+10/2+6/3) = 15-19 = -4

Displacement to the left of the light spot !!



$$X = \frac{X^+ - X^-}{X^+ + X^-} \qquad Y = \frac{Y^+ - Y^-}{Y^+ + Y^-}$$

$$W = X^+ + X^- + Y^+ + Y^-$$

New approaches

Crystals segmentation

Advantages:

Light confinement
The spatial resolution is given by the crystal size: choice of the resolution
Almost-independent count rate
Possible rejection of scattered

Drawbacks:

Dead zone due to segmentation
Increase of pixel numbers
Degradation of light collection with thin crystals
Adaptation of the collimator holes shape
Pixellization artifcats
Price

Photodetectors

PM multi anodes / sensitive to the position
Solid detector

Performances' evaluation

Characterized by 6 parameters

Energy resolution

Spatial linearity

Uniformity

Spatial resolution

Detection efficiency

Count rate

Usually, these parameters are correlated

Performances very in the field of view

Three regions:

FFOV: Full field of view

UFOV: Useful field of view 95% de FFOV

CFOV: Central field of view 75% de FFOV

Energy resolution

coupling with a PMT

N =	
$N_{h\nu}$	Number of optical photons emitted by the scintillator
$\Omega(\lambda)$	Optical yield of the photocathode
$\sigma(\lambda)$	Quantum yield of the photocathode
C	Collection yield of the optical entry
G	Global gain of the PM

$$\overline{N} = \overline{N_{h\upsilon}}\,\overline{\Omega}\,\overline{\sigma}\,\overline{C}\,\overline{G}$$

with $\upsilon_x = \dfrac{\sigma_x^2}{\overline{x}^2}$ Relative variance

$$\upsilon_N = \upsilon_{N_{h\upsilon}} + \frac{\upsilon_\Omega}{\overline{N}_{h\upsilon}} + \frac{\upsilon_\sigma}{\overline{N}_{h\upsilon}\overline{\Omega}} + \frac{\upsilon_C}{\overline{N}_{h\upsilon}\overline{\Omega}\,\overline{\sigma}} + \frac{\upsilon_G}{\overline{N}_{h\upsilon}\overline{\Omega}\,\overline{\sigma}\,\overline{C}}$$

Random variable	Distribution law	Relative variance
$N_{h\upsilon}$	poissonienne	$\upsilon_{N_{h\upsilon}} = \dfrac{1}{\overline{N}_{h\upsilon}}$
Ω	binomiale	$\upsilon_\Omega = \dfrac{1-\overline{\Omega}}{\overline{\Omega}}$
σ	binomiale	$\upsilon_\sigma = \dfrac{1-\overline{\sigma}}{\overline{\sigma}}$
C	binomiale	$\upsilon_C = \dfrac{1-\overline{C}}{\overline{C}}$

$$\upsilon_N = \frac{1+\upsilon_G}{\overline{\Omega}\,\overline{\sigma}\,\overline{C}\,\overline{N}_{h\upsilon}}$$

To this, we add the Noise Equivalent Count (NEC)

NEC : *Required input signal so that the output signal has an amplitude equal to the effective value of the output signal generated by the electronic noise*

Entre 0,1 et 0,2

$$R_e = \frac{\Delta E}{E_\gamma} = 2{,}35\sqrt{\frac{1+\upsilon_G}{\overline{\Omega}\,\overline{\sigma}\,\overline{C}\,\overline{N}_{ph}} + \left(\frac{NEC}{\overline{\Omega}\,\overline{\sigma}\,\overline{C}\,\overline{N}_{ph}\overline{G}}\right)^2}$$

To this we add,

Crystal homogeneities

Light transport with the crystal

Spatial linearity

Capability of an imaging instrument to provide an image consistent with the object, without geometric distorsion

The spatial linearity of a gamma camera is determined by analyzing the induced distorsions in the scintigraphic image of radioactive source with a know geometry

A distorsion can be corrected at the scintillations positionning matrix

Uniformity

A camera response to small object of a given acitivity is more or less independent of the object position in the field of view

This quality is to be examined in two cases:

There is no collimator
Intrinsic uniformity
because it is a property of base of the γ camera

There is a collimator
System uniformity
because this property is related to particular use cases

Case of uniform irradiation

Integrale uniformity Ui

within a large ROI (Region Of Interest)

that limits the studied field (UFOV ou CFOV)

$$Ui = (Cmax – Cmin) / (Cmax + Cmin) \text{ en } \%$$

Differential uniformity Ud

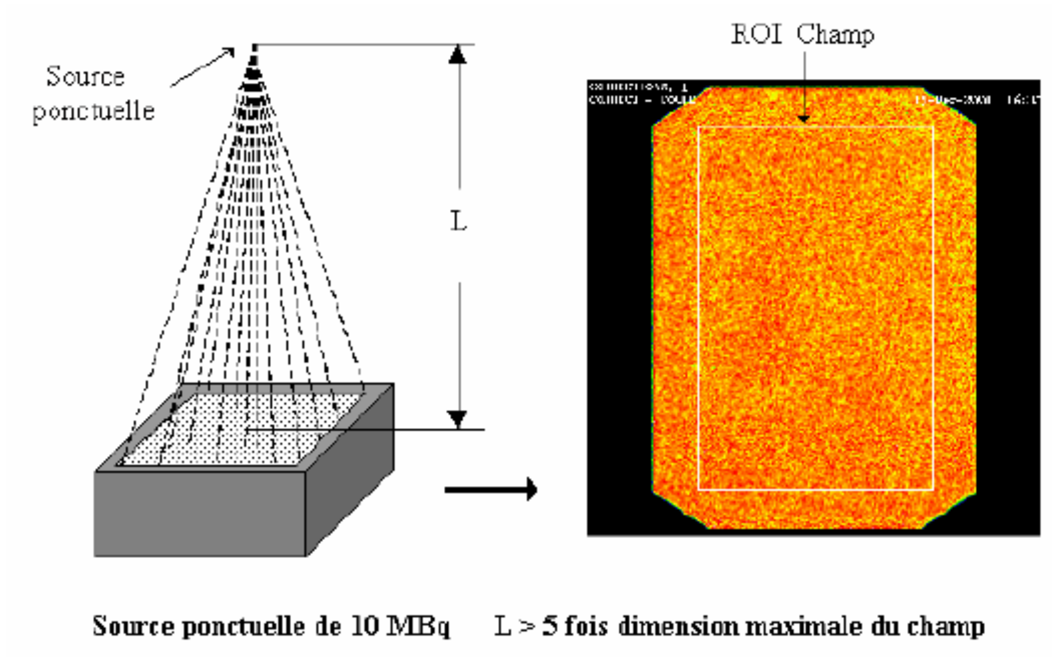
largest local variation between two pixels,

in the ROI limiting the studied field

The localization is arbitrary defined by a group of 25 pixels centered around a non zero pixel

$$Ud = (C_{hi} – C_{low}) / (C_{hi} + C_{low}) \text{ en } \%$$

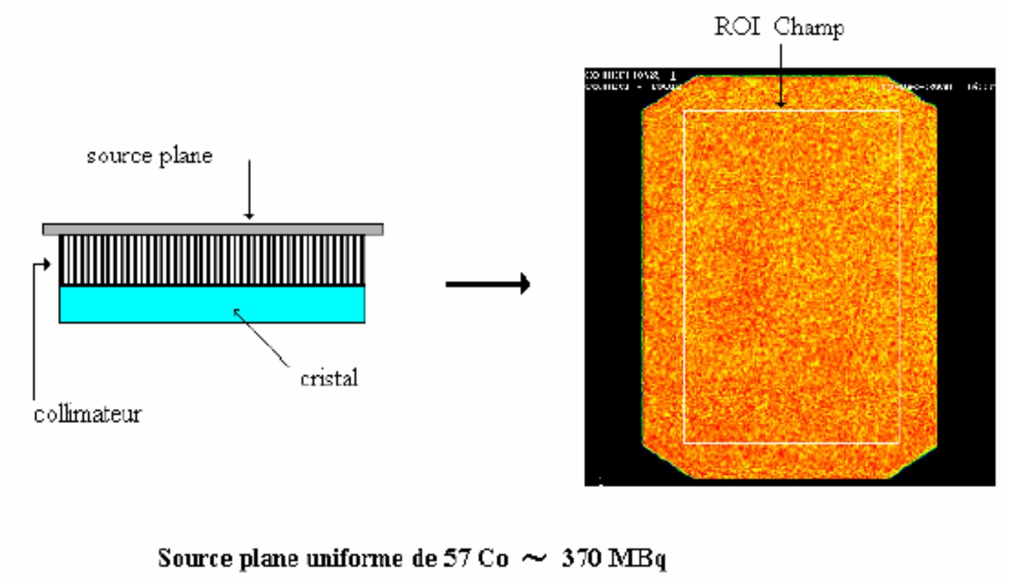
Intrinsic uniformity



Integral uniformity		Differential uniformity	
CFOV	UFOV	CFOV	UFOV
2,5	3,0	1,5	2,0

^{99m}Tc

System uniformity

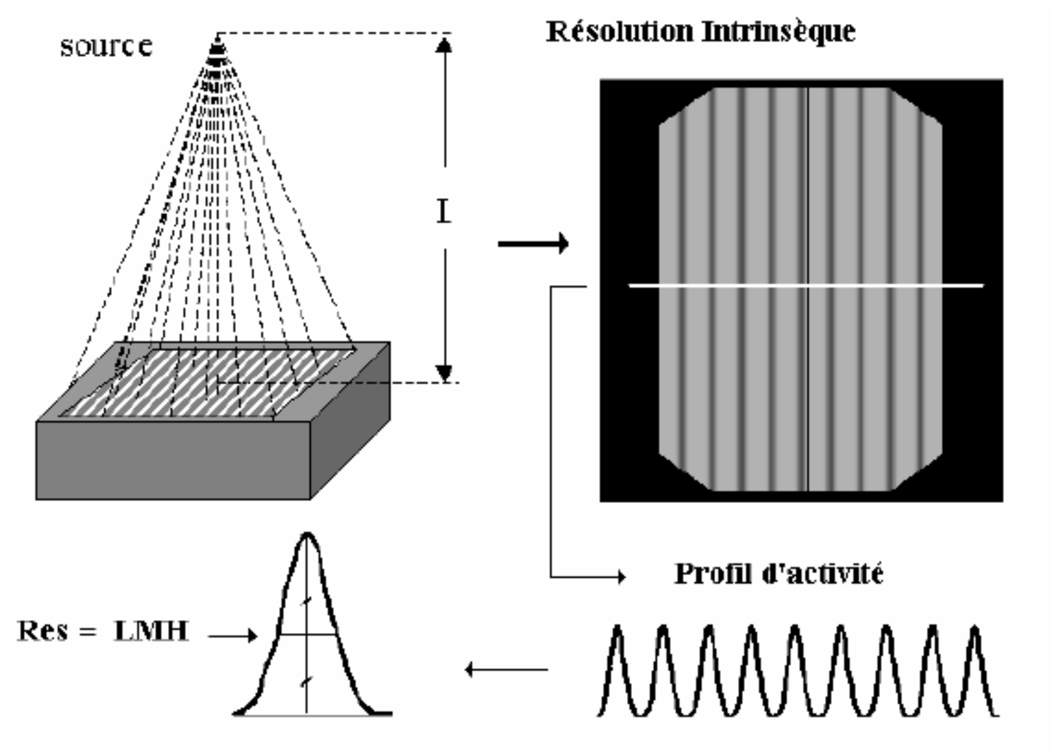


Integral uniformity		Differential uniformity	
CFOV	UFOV	CFOV	UFOV
4,0	5,1	2,5	3,0

^{57}Co

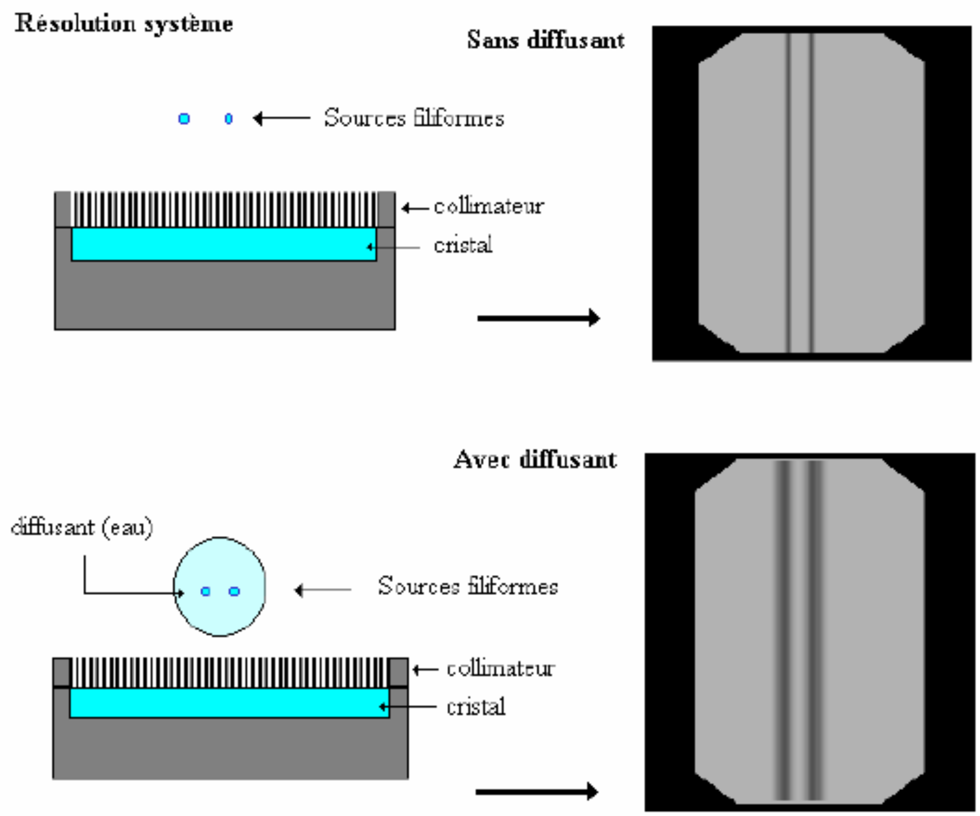
Spatial resolution

Intrinsic spatial resolution



Spatial resolution

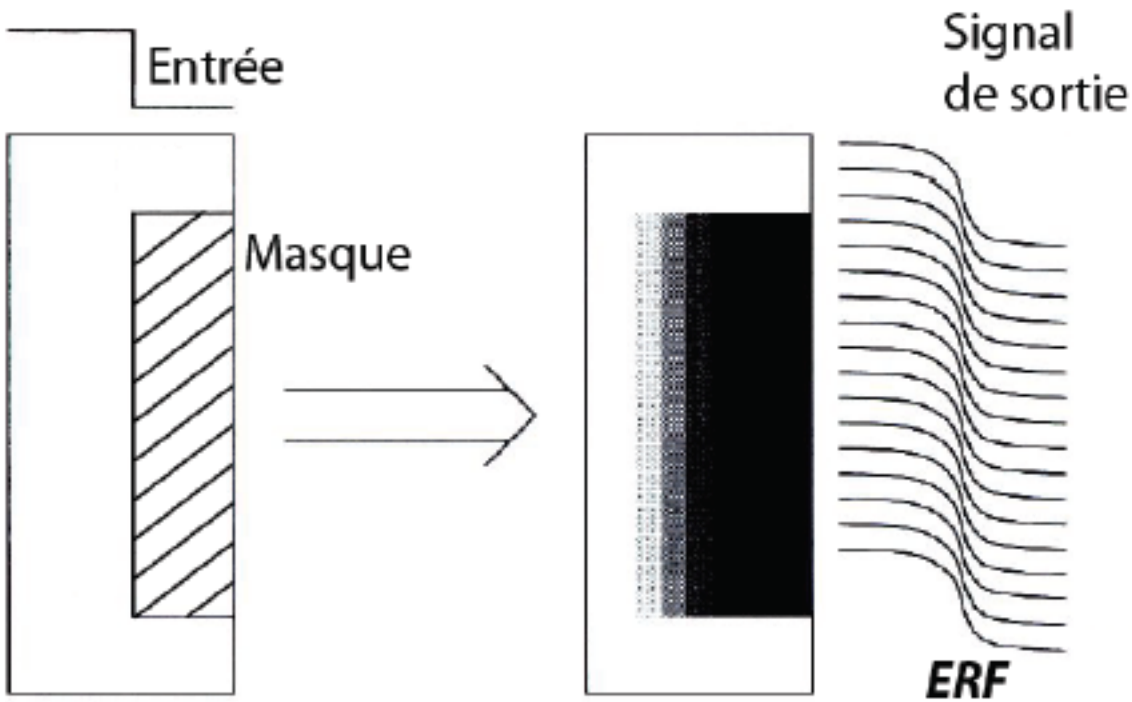
Spatial resolution of the system



Other method: calculate the FTM (Full Width tenth measurement)

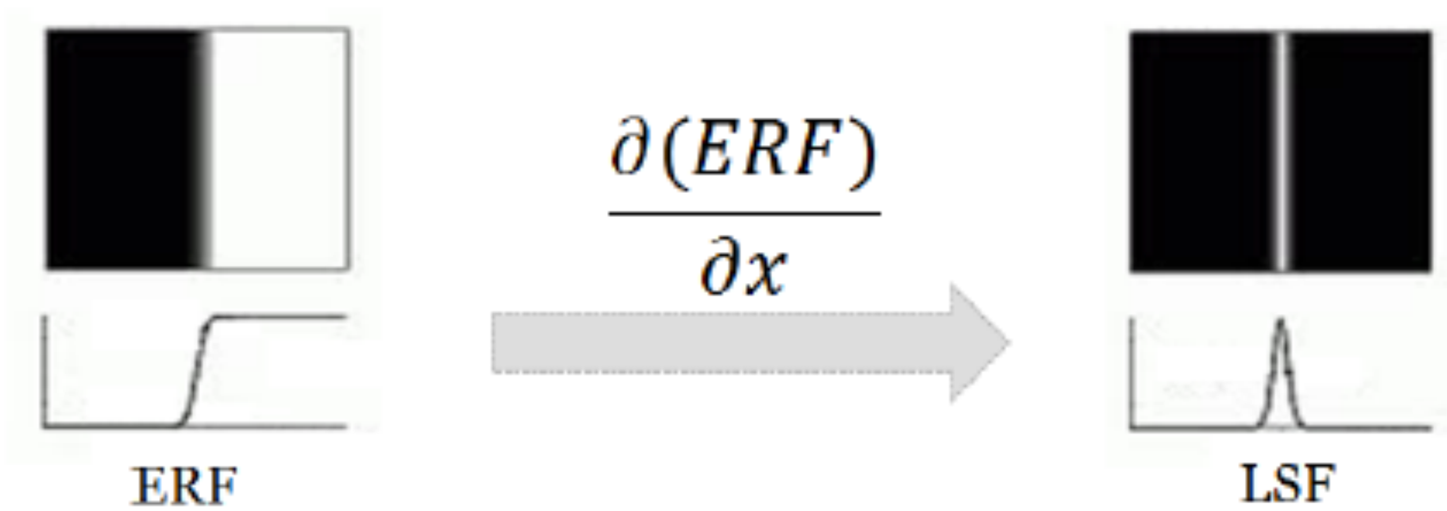
Spatial resolution measurement

- Edge Response Function « ERF »

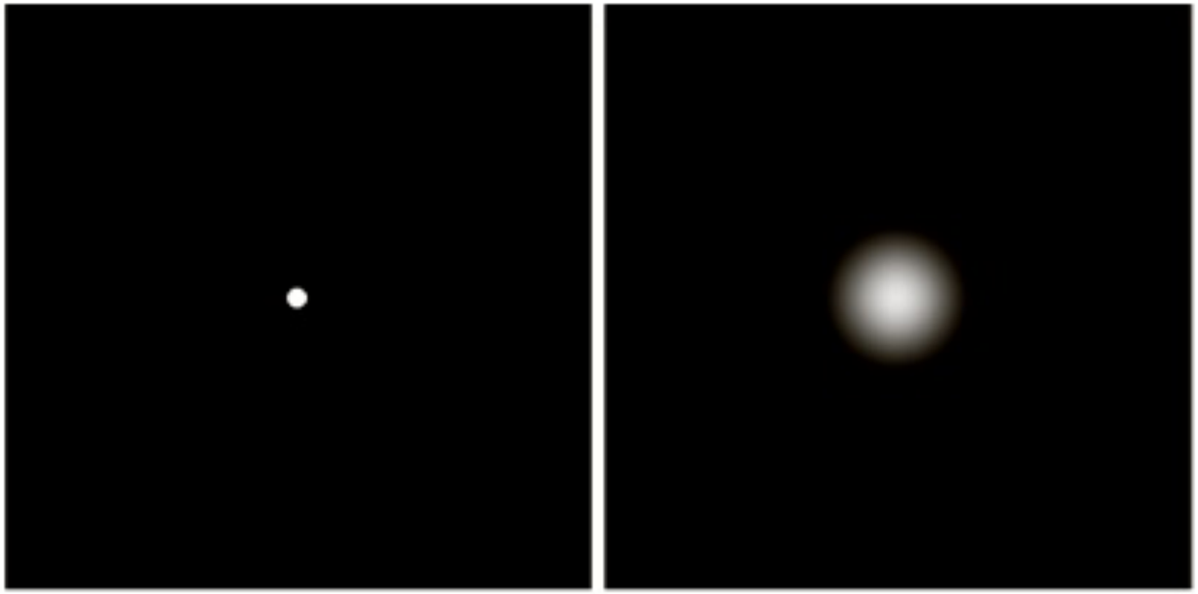


Mesure de la résolution spatiale d'un système

- Mesure de la Edge Response Function « ERF »

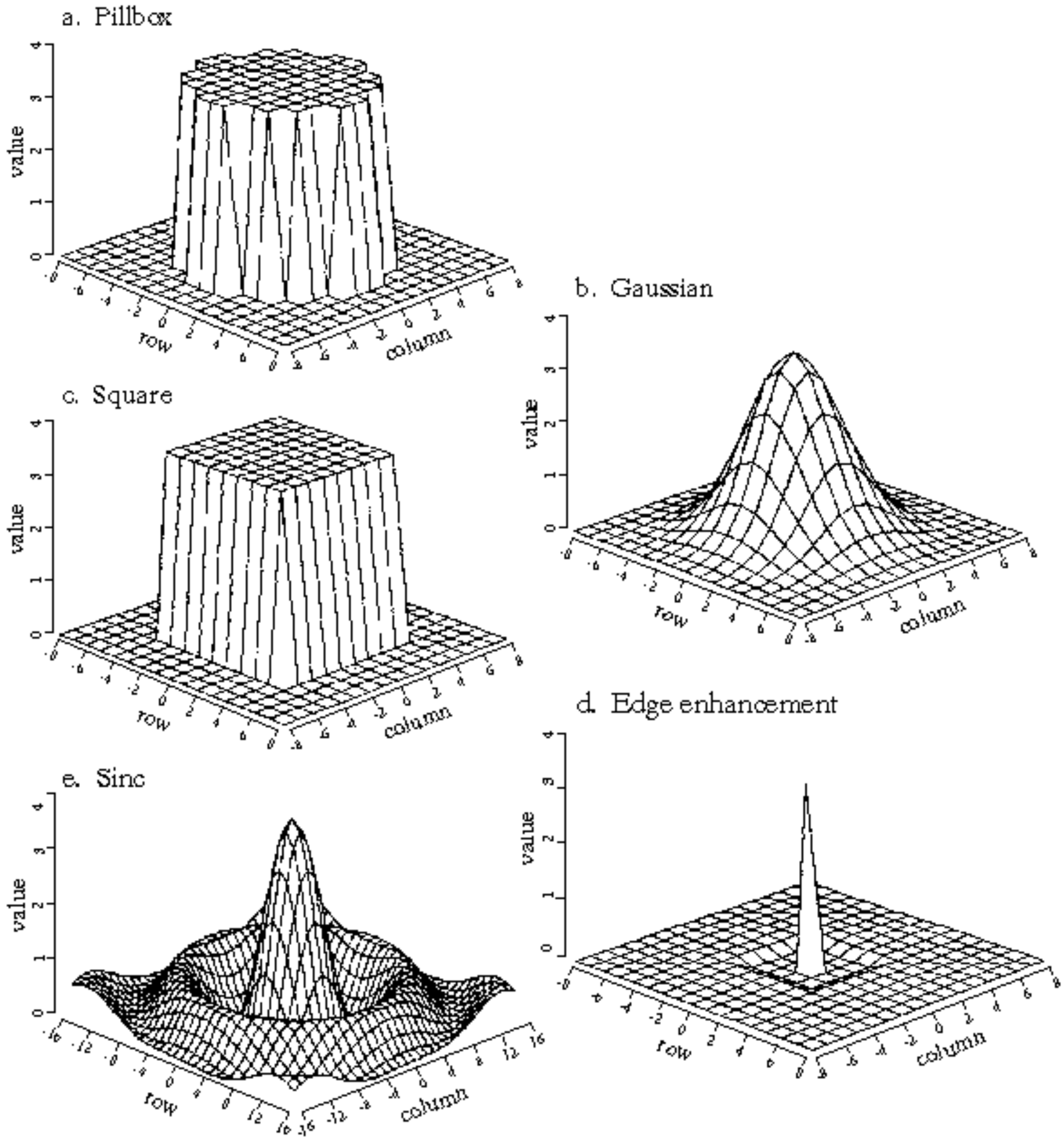


Point-Spread Function (PSF)

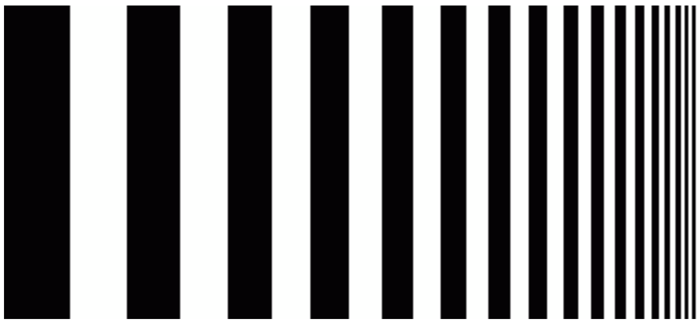


a b

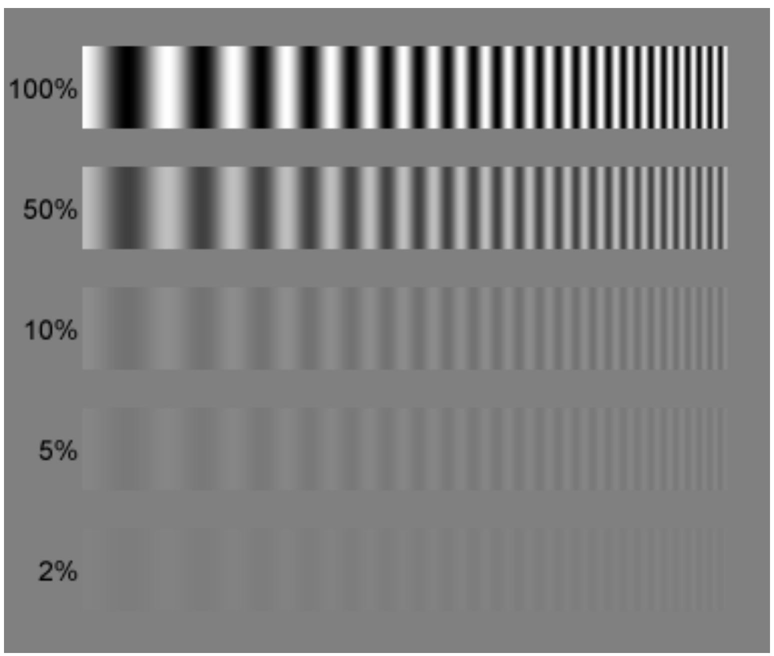
FIGURE 5.24 Degradation estimation by impulse characterization. (a) An impulse of light (shown magnified). (b) Imaged (degraded) impulse.

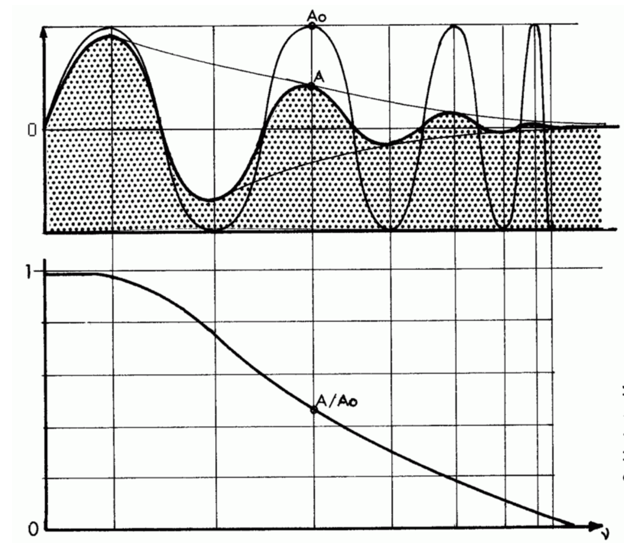

a. Pillbox
value
row
column
b. Gaussian
value
row
column
c. Square
value
row
column
d. Edge enhancement
value
row
column
e. Sinc
value
row
column

Modulation transfer function



Mire

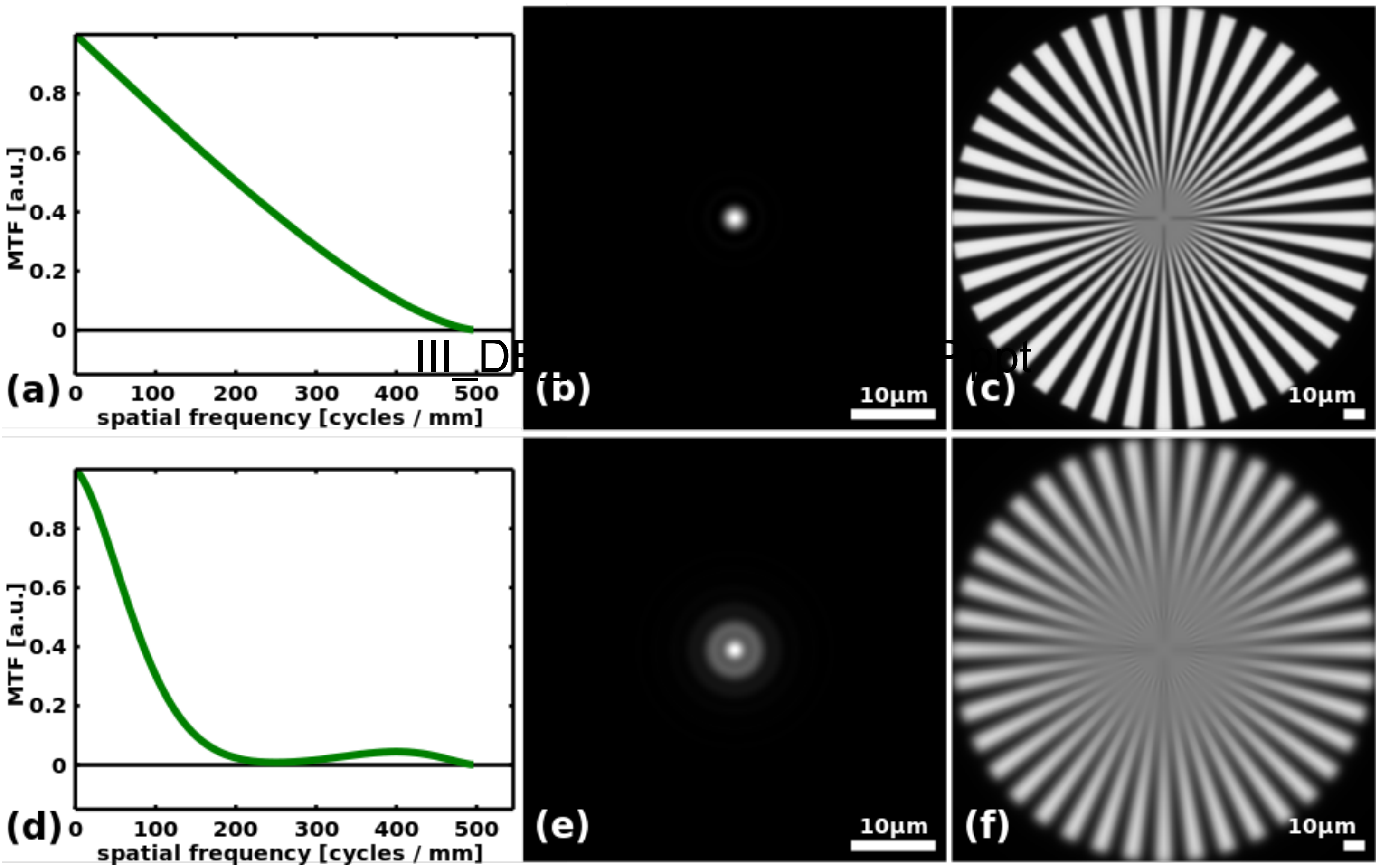




Contrast variation as function of frequency

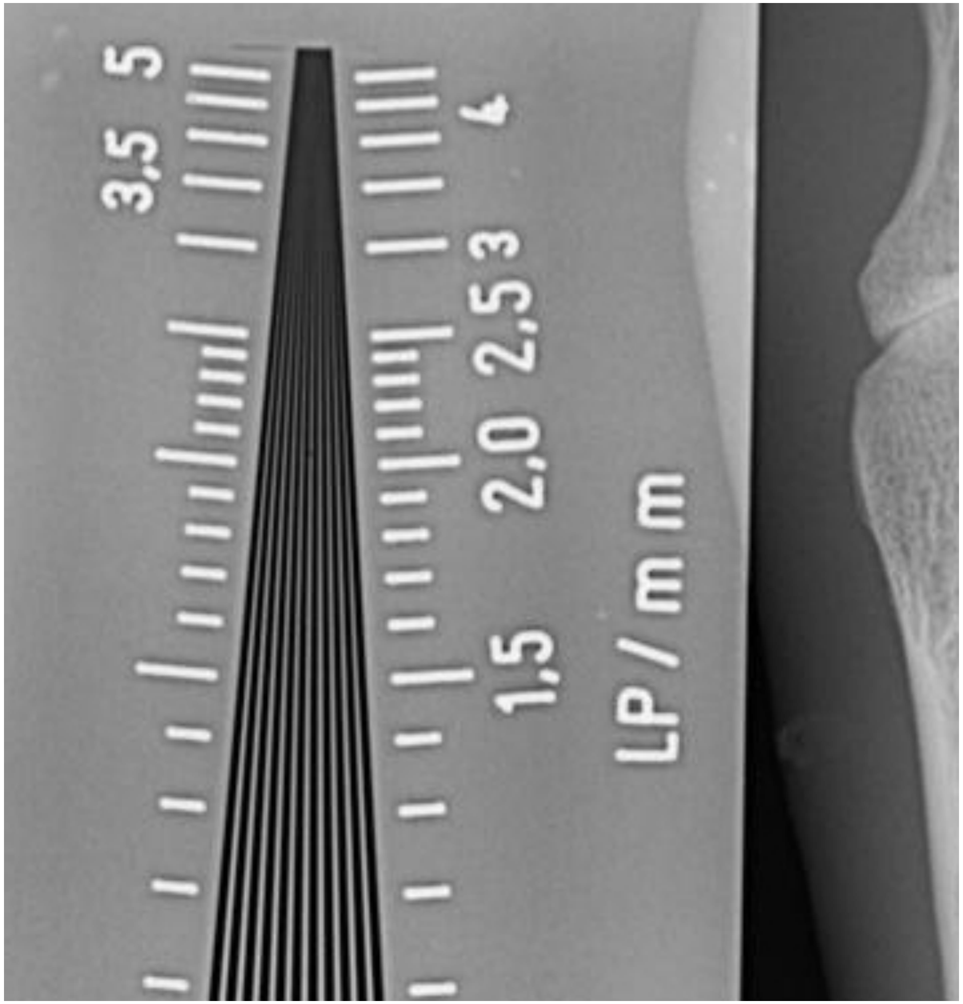
https://fr.wikipedia.org/wiki/Fonction_de_transfert_de_modulation

Modulation transfer function
Fourier Transform of PSF (or LSF)



https://commons.wikimedia.org/wiki/
File:Illustration_of_the_optical_transfer_function_and_its_relation_to_image_quality..svg

Spatial frequency unit : Line pair per mm



Detection efficiency or *sensitivity*

Probability of detecting an incident photon
Quantified as the count rate with a planar source

System = intrinsic (S_i)+ collimator (S_c)
With $S_i >> S_c$

S_i crystal dependent
S_c collimator dependent

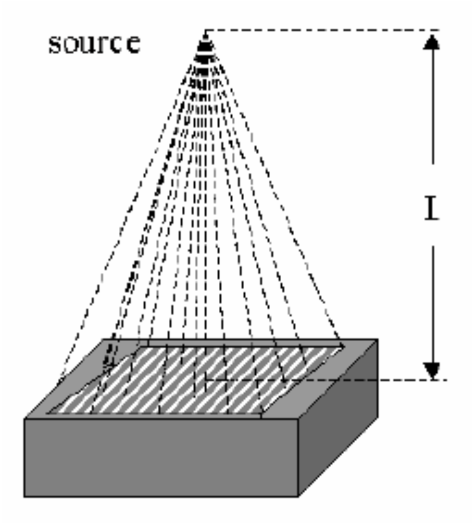
Current value, collimator LEHR: 130 cps/MBq

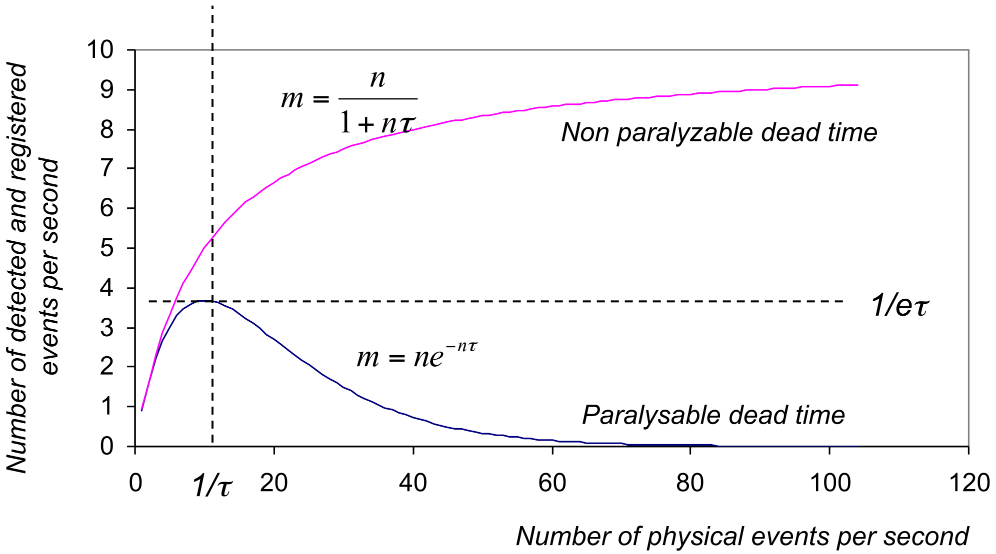
Count rate

With the increase of the activity,
the count rate has two components:

The linearity of the observed count rate
The accuracy of the positionning of the registered event

Source activity variation





Clinical procedures

The power of nuclear medicine is that it offers the possibility of acquiring images of a physiological function

Planar imaging : integration of a volume

One big advantage is the capability of the activity follow-up upon time

Installation

Image optimization requires a well controlled envionment

Variation of ambient temperature: 3-5°C / hour with collimator
-> 1°C/ hour at crystal level

Conclusion: The collimator protects the crystal

Knowing of background noise

Acquisition consideration

Patient movement

« Macroscopic and microscopic »

Choice of the collimator

resolution, efficiency, energy…

Size of the image matrix

pixel = LTMH/3, Magnification usage

Partial volume effect

Object size < 2xLTMH

Energy window

Compromise between contrast and efficiency

Typically: 20% around the peak of interest

Count rate

Injected activity in order to reduce the loss in counts (<10%)

Contrast in the image

Object contrast

$$C_O = \frac{A_a - A_n}{A_n} \qquad C_O = \frac{A_a - A_n}{A_a + A_n}$$

Normal activity *Abnormal activity*

n = background count
n+Δn = counting in the ROI
Δn > 10% of n (for 2σ)

$$\sigma_n = \sqrt{n}$$

$$\sigma_a = \sqrt{n + \Delta n}$$

$$\sigma = \sqrt{\sigma_n^2 + \sigma_a^2}$$

$$\text{si } \Delta n << n, \quad \sigma \approx \sqrt{2n}$$

$$2\sigma = 95{,}5\% = 2\sqrt{2n}$$

$$2\sqrt{2n} \geq 0{,}1n$$

Different types of acquisitions

Static

Radiopharmaceutical distribution should remain unchanged during all the acquisition period

Dynamic

Set of static images (time)
Stop point: count rate or measurement time

Hole body

Set of static images (space)

Synchronized

Set of static images (time) synchronized with a physiological rythm

List mode

Quality control

Tedious procedure: Standardization

Satisfy two requirements:

Perfomances comparison before the purchase
Detect performances « degradation » during the utilization

Constructors' dedicated procedures
NEMA and IEC

Users' dedicated procedures
AAPM, IAEA, IPSM, IPEM

Quality control

Installation

Control of the stability of the high voltage delivered to the instrument (24h)
Electric protection: inverter
Control of the temperature and humidity
Protection against magnetic field

Acquisition condition

Follow the constructor instruction
Check the photoelectric peak position
Adjust the energy window
The count rate should be less than ~$2x10^4$ cps (< 10% of loss)
No magnification acquisition
The position of the camera should be well known
In case of a multi-head camera, the measurements should be performed on each detector
Protect the detector from leakage and schock

Quality control

Source

If possible, realize the test with ^{99m}Tc
Optimize the point source located at 5xFOV
Check the uniformity of planar source

Phantom

The phantom size should correspond to the system resolution
The LTMH = 1,75 x size of the smallest object

Mechanical system

Collimator (lead…)
Collimator charging
System rotation
Check there is no eventual collision

Quality control

Different tests proposed for the procedures:

Energy calibration: find the photoelectric peak and center the energy window
Perform a background couting: test contamination
Unifomity
Detection efficiency
Energy resolution
Spatial linearity
Spatial resolution
Collimator: Holes' orientation
Count rate