Universidad Complutense de Madrid
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Dpto. de Física Atómica, Molecular y Nuclear
Grupo de Física Nuclear

Programa de Doctorado de Física Nuclear

Defensa de Tesis Doctoral

SIMULATION AND IMAGE RECONSTRUCTION OF CLINICAL TOF-PET SCANNERS

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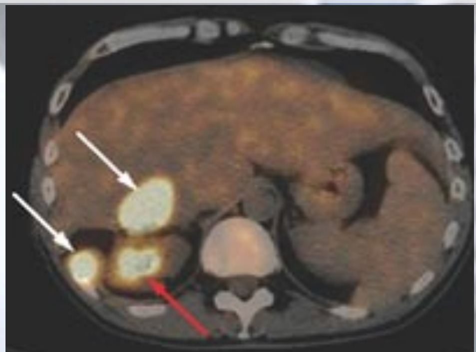
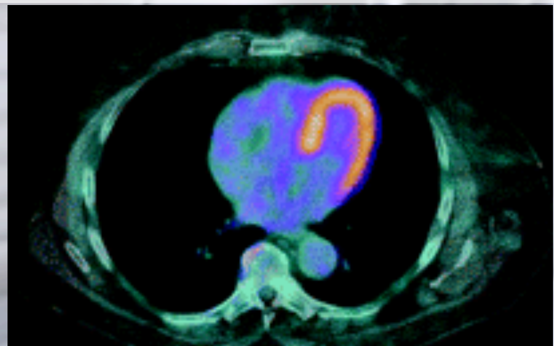
Positron Emission Tomography (PET)

- PET is a nuclear medicine imaging technique that produces a 3D image of functional processes in the body.
- It is a key diagnostic imaging modality used largely in determining the presence and severity of cancers, neurological conditions, and cardiovascular diseases.



Fenskeet al., (2008) *Nat Clin Prac Oncol* 5, 677-681

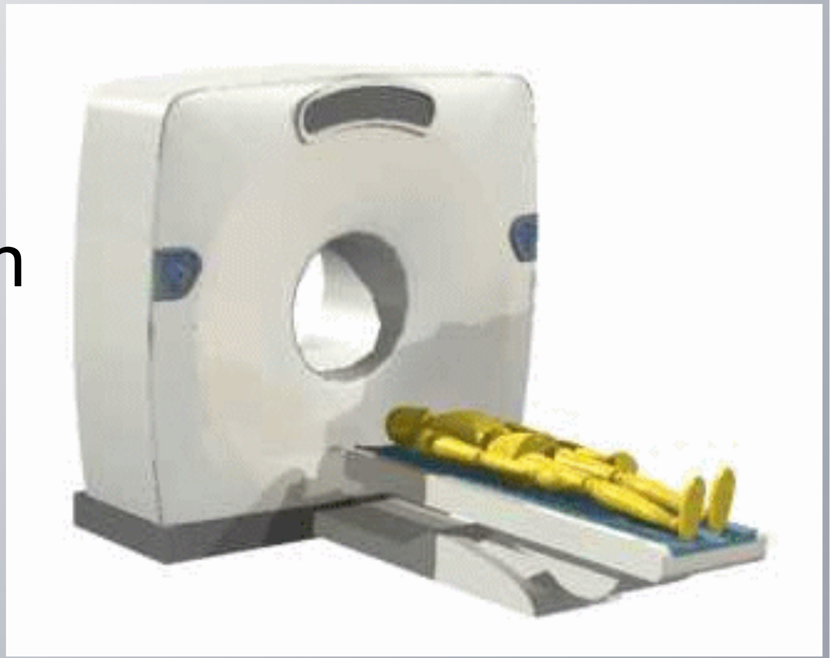


Gould et al., (2007) J Nucl Med 48, 1112–1121

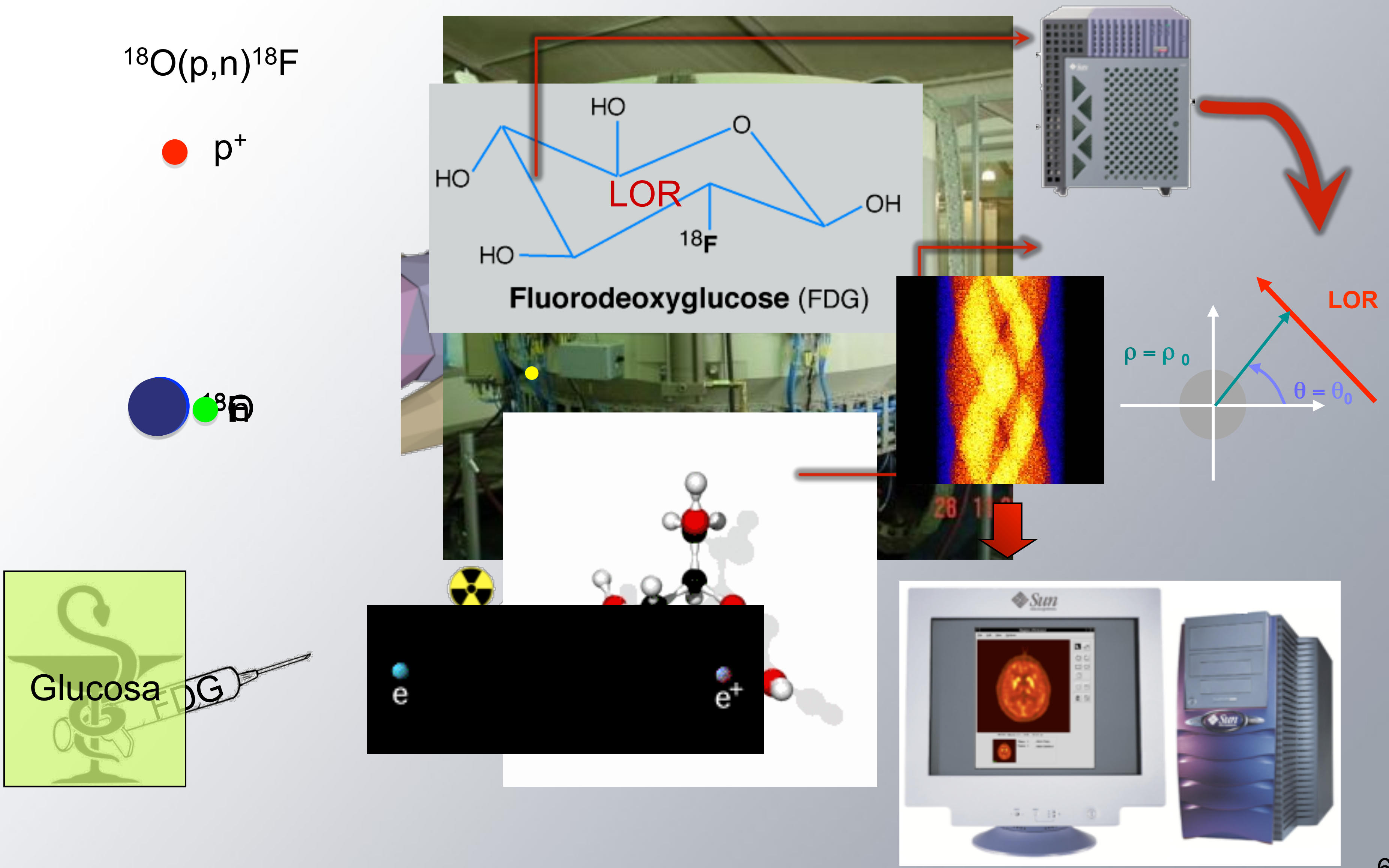
Hicks et al., (2012) *Nat Rev Clin Oncol* 9, 712-720

PET Scanners

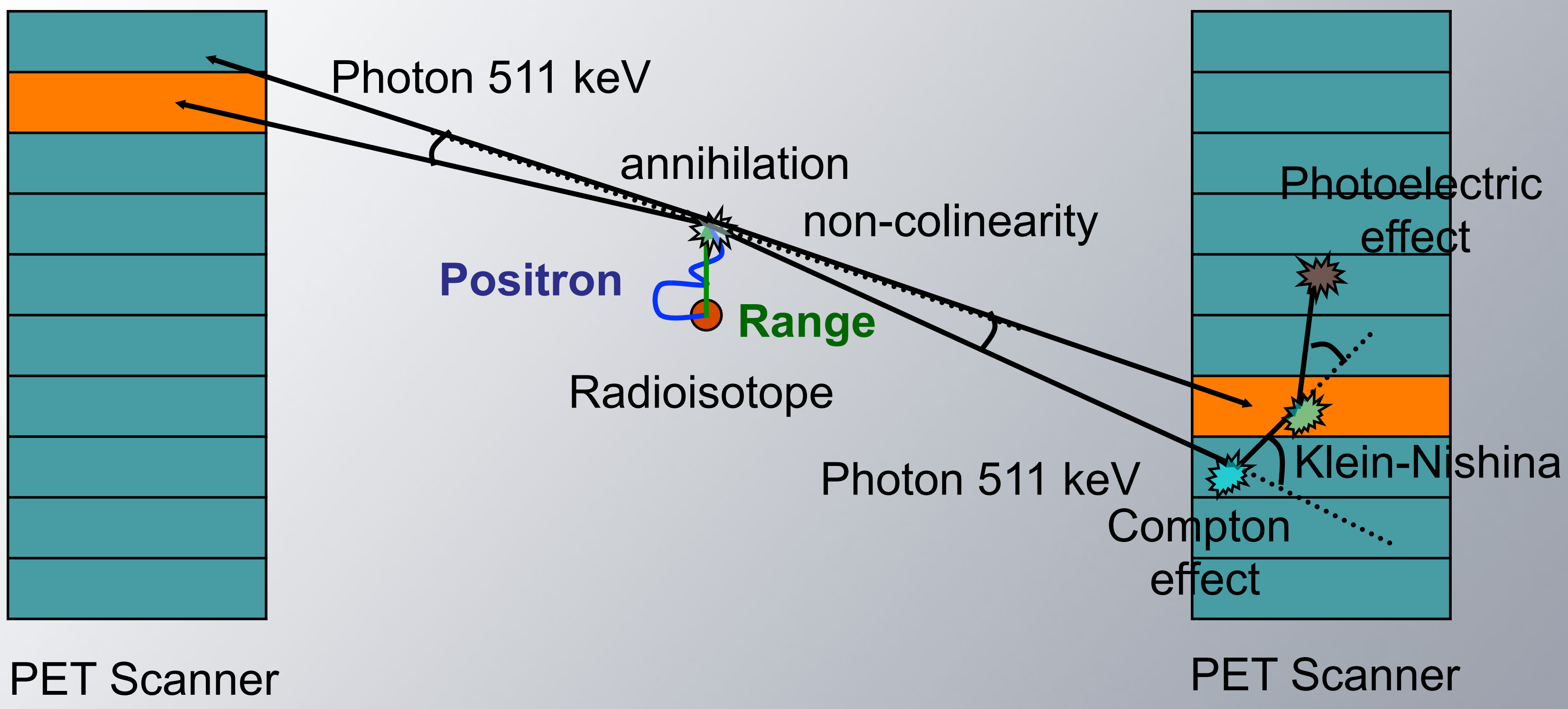
- ***Scanner*** - to perform the clinical exam
  - Includes a computer running algorithms for tomographic reconstruction & display
- ***Cyclotron*** - to produce the positron-emitter (radionuclide)
- ***Radiopharmacy***- to produce the labeled molecule



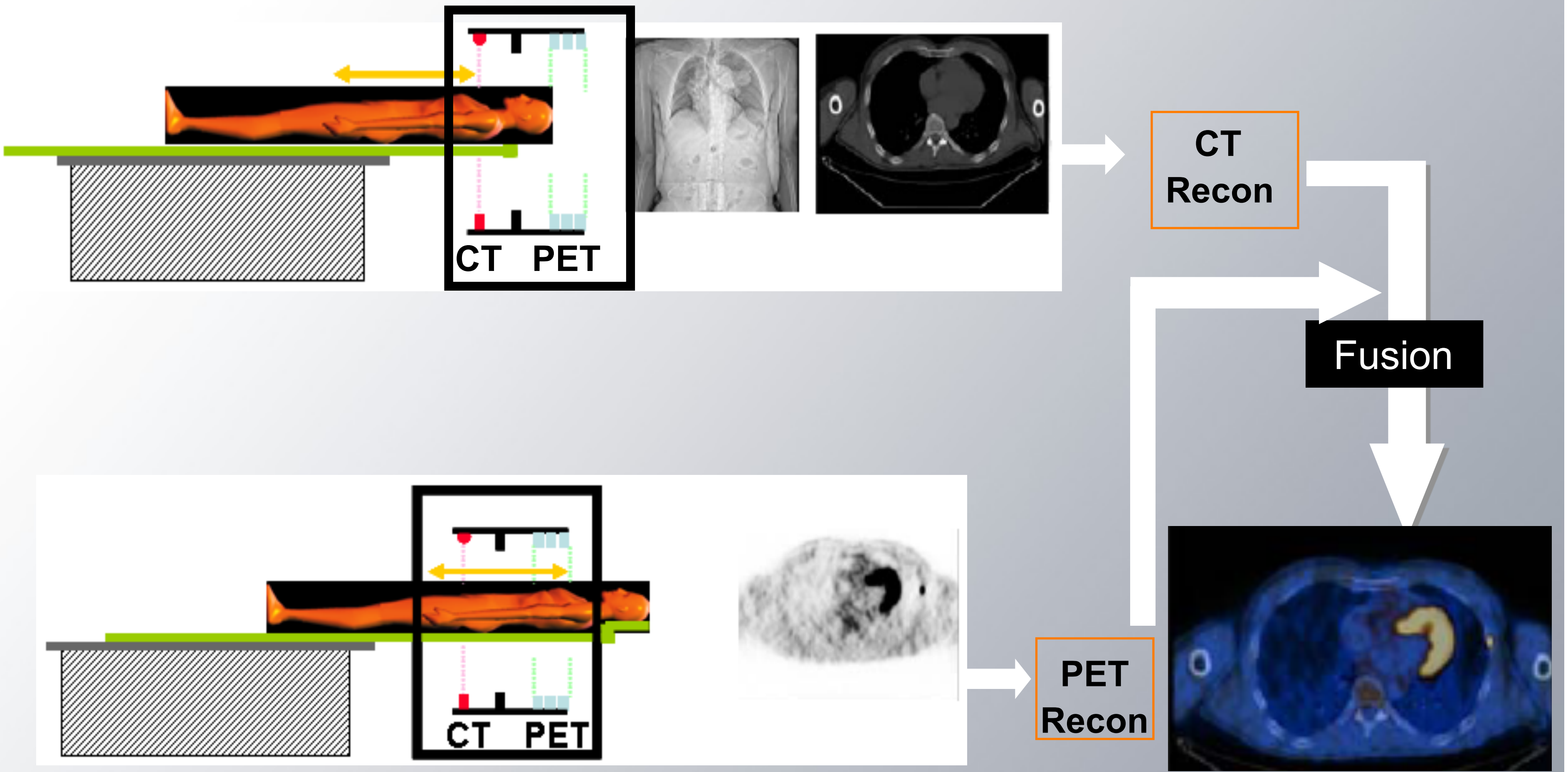
PET Procedure



Physics of PET



PET/CT scan protocol



Fusion (PET/CT)

Challenges for next generation PET scanners

Developments in PET technology aim to provide:

- ►**Better images** (more accurate information of the distribution of the radiotracer in the body)
- ► In **shorter** scanning and reconstruction **time**
- ► leaving **lower radiation dose** in the patient
- ► Using more **affordable** scanners

Improving one aspect may worsen some other

In order to improve current PET scanners, it is neccesary to be able to evaluate precisely the impact of new technology in all these different aspects.

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Simulation of clinical PET scanners

Image reconstruction

Monte Carlo simulation in PET

- *Methods in which all processes related to the experimental system under study are modelled in a computer.*
- *The name Monte Carlo (MC) is used because often random numbers processes are employed to generate simulated events.*
  - Because nuclear medicine imaging deals with the emission of radiation energy, MC simulations of radiation emission and detection are an important tool for research and development of PET scanners.
  - MC simulations are widely used for PET aiming to take into account all the processes involved in PET imaging.
  - MC simulations have been proven to be a useful tool to study performance characteristics and parameters that cannot be measured experimentally.

Monte Carlo simulation in PET

- *Applications:*
  - Scanners design
  - Data Processing
  - Data Correction
  - Image Reconstruction
- *Some existing codes:*
  - SimSET [Harrison et al., 1993]
  - GATE [Jan et al., 2004] (GEANT4)
  - Eidolon [Zaidi and Scheurer, 1999] (MCNP)
  - PETSIM [Thompson et al., 1992]
  - GAMOS [Arce et al., 2008] (GEANT4)
  - PeneloPET [España et al., 2009] (PENELOPE)

PeneloPET

- *PeneloPET* [1], is a Monte Carlo simulator for PET scanner based on PENELOPE [2].

  - *PENELOPE*

  ► Penelope is a code for the Monte Carlo simulation, it describes the transport and the interaction of *electrons, gammas* and *positrons*, in matter.

  ► Energies range from a few hundred *eV* to 1 *GeV* (suits well PET needs).

  ► Robust, fast and accurate (used in dosimetry and radiotherapy).

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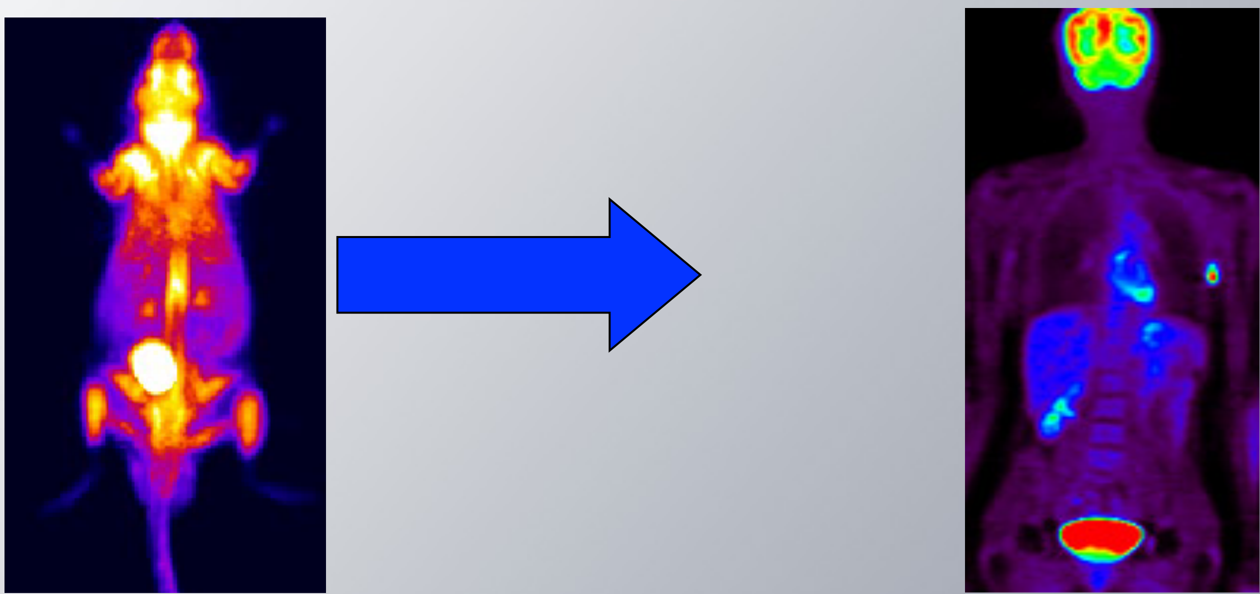
[1] S España et al (2009) P*hys Med Biol, 54*, ***1723-1742***
[2] Salvat et al (2008) PENELOPE-2008: A code system for Monte Carlo simulation of electron and photon transport.

Objectives

The main objective of this thesis is to extend the capabilities of the tools developed in our group (GFN) for PET imaging, so far intended for the **preclinical** arena, to **clinical** settings, and to validate these tools against clinical measurements



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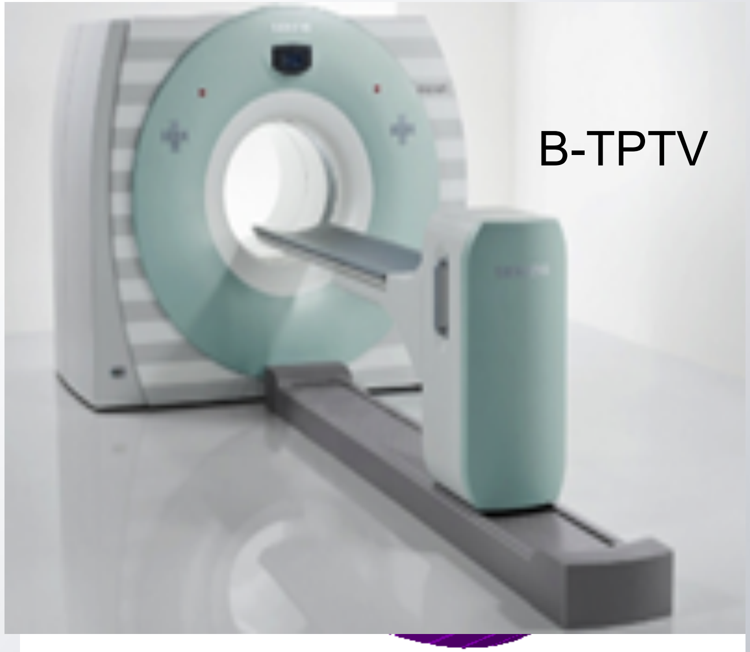
Simulation of clinical PET scanners

Image reconstruction

Characterizations of clinical scanners

Three Biograph PET Scanners

- Biograph TruePoint (*B-TP*)
- Biograph TruePoint with TrueV (*B-TPTV*)
- Biograph mCT PET/CT (*mCT*)



B-TPTV

Siemens Data sheet

Scanner	B-TPTV	mCT	B-TP
Number of block rings	**4**	4	3
Block detector per ring	**48**	48	48
Detector elements dimension	**4x4x20 mm**	4x4x20 mm	4x4x20 mm
Axial FOV	**218 mm**	218 mm	162 mm
Transaxial FOV	**680 mm**	700 mm	680 mm
Number of image planes	**109**	109	81
Coincidence time window	**4.5 ns**	4.1 ns	4.5 ns
Energy window	**425-650 KeV**	435-650 KeV	425-650 KeV
Energy resolution	**11.7%**	11.7%	11.7%
Pitch size	**4 mm**	4 mm	4 mm
Reflector thickness (estimated)	**0.4 mm**	0.4 mm	0.4 mm
Crystal length (thickness)	**20 mm**	20 mm	20 mm
Detector ring diameter	**856 mm**	856 mm	856 mm
CFOV -C. front of detector	**42.80 cm**	42.80 cm	42.80 cm
Maximum ring difference	**38**	49	27

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Unknown Information

- ►Some minor details of the geometry of the scanner.
- ►Materials (bed, shielding and covers).
- ►Detailed behavior of the acquisition electronics.

How to deal with the unknown

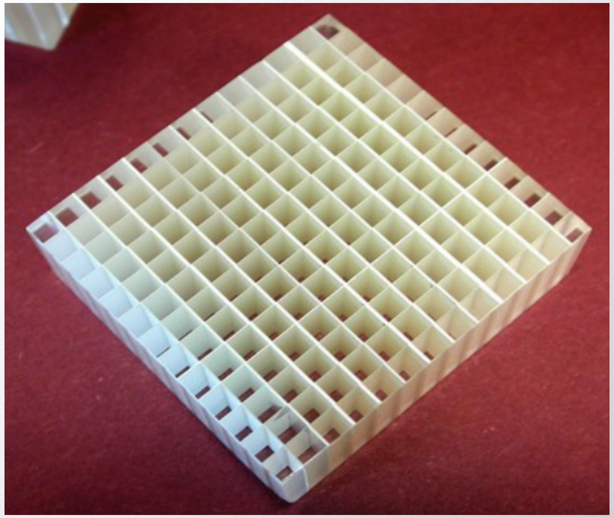
- ►***B-TPTV*** has been taken as a reference to tune some of the parameters of the simulations.
- ►Published experimental values of the B-TPTV have been used as reference (sensitivity, NEC, spatial resolution and TOF).

Simulation parameter	Measured properties
Reflector thickness	Sensitivity (B-TPTV)
Singles, coincidences dead time and integration time	NEC curve, randoms and trues (B-TPTV) rate curves
Time jitter	TOF, FWHM (B-TPTV)

Sensitivity

- The sensitivity of a PET scanner quantifies the ability of a scanner to detect the coincident photons emitted from inside the FOV.

Reflector thickness?



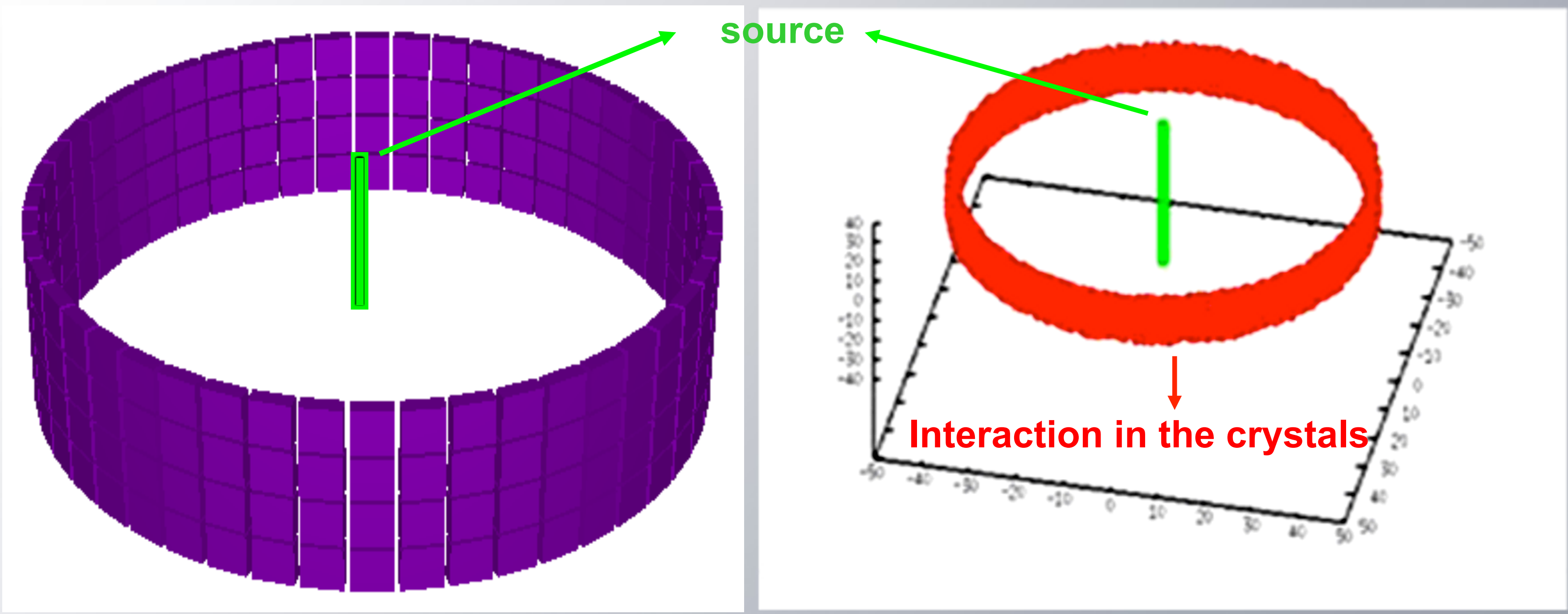
Detector elements/block
($4×4×20mm^3$)

Parameters employed

Scanner	B-TPTV	mCT	B-TP
Detector ring diameter (mm)	856	856	856
Axial FOV (mm)	218	218	162
Coincidence time window (ns(	4.5	4.1	4.5
Energy window (keV)	425-650	435-650	425-650

Sensitivity

- **NEMA [3] protocol**
  - A line source (70 cm), low activity (3.9 MBq).
  - Dead time loss <1% and random <5%.
  - Sensitivity at 2 transaxial position (0 and 10 cm) was obtained.



[3] National Electrical Manufacturers Association (2007) *NEMA standards publication* NU 2-2007

Sensitivity

Energy window >(425-650 KeV), Time window >(4.5 ns)

Sensitivity [kcps/MBq] @ 0 and 10 cm off center

Scanner	*Simulated (this work)*	*Simulated (GATE)* [4]	*Experimental* [5], [6]
B-TP	*4.6*	*4.8*	*4.5*
B-TPTV	*w/o reflector 9.2* *with reflector 8.2*	*8.7*	*8.2*
mCT	*9.8*	-	*9.7*

- The use of a reflector thickness of the order of 0.4 *mm* yields good agreement with the measured sensitivity.
- This reflector thickness was employed in all simulations in this work.

[4] Eriksson et al., (2007) *Nuc Inst and Meth in Phy Res Sec A* 580, **836–842**
[5] Jacoby et al., (2009) *Trans Nucl Sci* 56, **633–639**.
[6] Jacoby et al., (2011) *Phy Med Biol* 56, **2375–2389**

Scatter fraction (SF)

- The proportion of accepted coincidences which have undergone Compton scattering prior to detection is called *scatter fraction (SF)*.
- The SF is a critical component of the NEC rate computation, and in our work it is a genuine prediction of the simulations, no parameters have been fitted to reproduce it.
- The SF was measured from low activity simulations, where random counts are negligible .
- Its used as a golden measure to optimize timing and energy windows.

$$\mathrm{SF} = \frac{S}{T+S}$$

Scatter fraction (SF)

Number of block rings	Scatter fraction (%)		
	Simulated (this work)	Simulated (GATE)	Experimental
B-TP	34.3	33	32.0
B-TPTV	31.3	35	32.5
mCT	34.8	-	33.5

- ►Simulated and experimental values of SF are within 4%.
- ►It remains fairly constant for all the scanners simulated.

Noise equivalent count (NEC) rate

- NEC is a global measure, taking into account scatter and random coincidences, of the scanner ability to acquire useful counts.
- It describes the effective number of counts measured by PET scanner as a function of activity in the FOV.

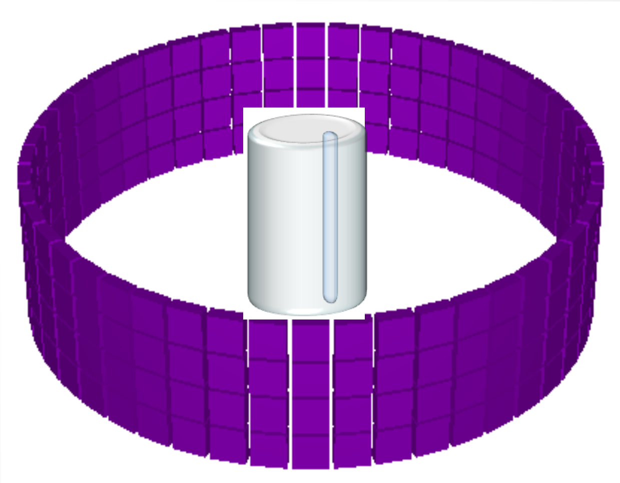
$$NEC = \frac{T^2}{T + S + R}$$

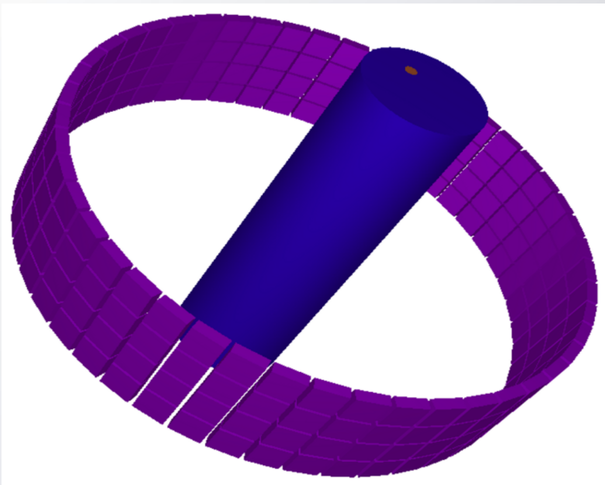
T > True coincidence count rate

S > Scatter coincidence

R > Random coincidence

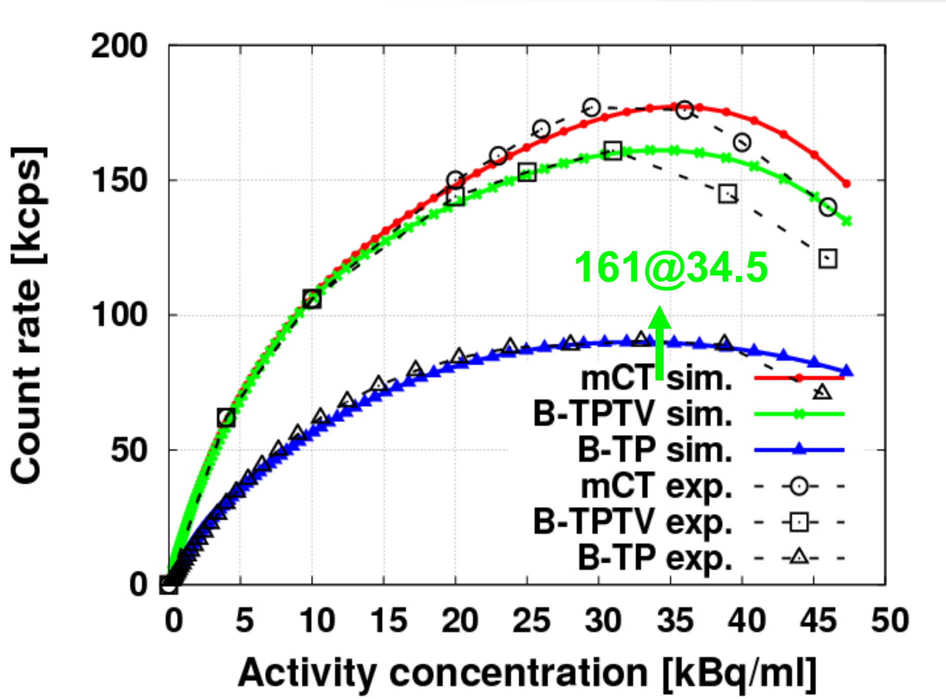
Noise equivalent count (NEC) rate

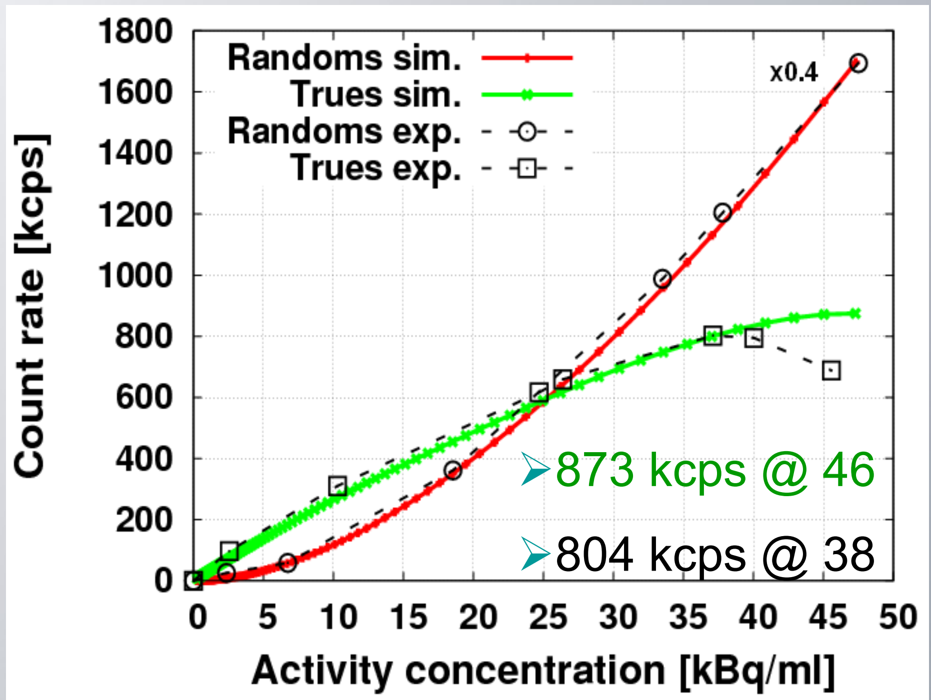




- **NEMA protocol**
  - Initial activity (1.04 GBq ^{18}F).
  - Data simulated for 35 frames.
  - NEC plotted as a function of activity.
- **PeneloPET includes simulation of acquisition electronics**
  - *Singles dead time* > applied to every photon that reaches the scanner.
  - *Coincidences dead time* > further dead time involved in the processing of events identified as coincidences.
  - *Integration time* > pile-up (and pile-up rejection) effects.

Noise equivalent count (NEC) rate

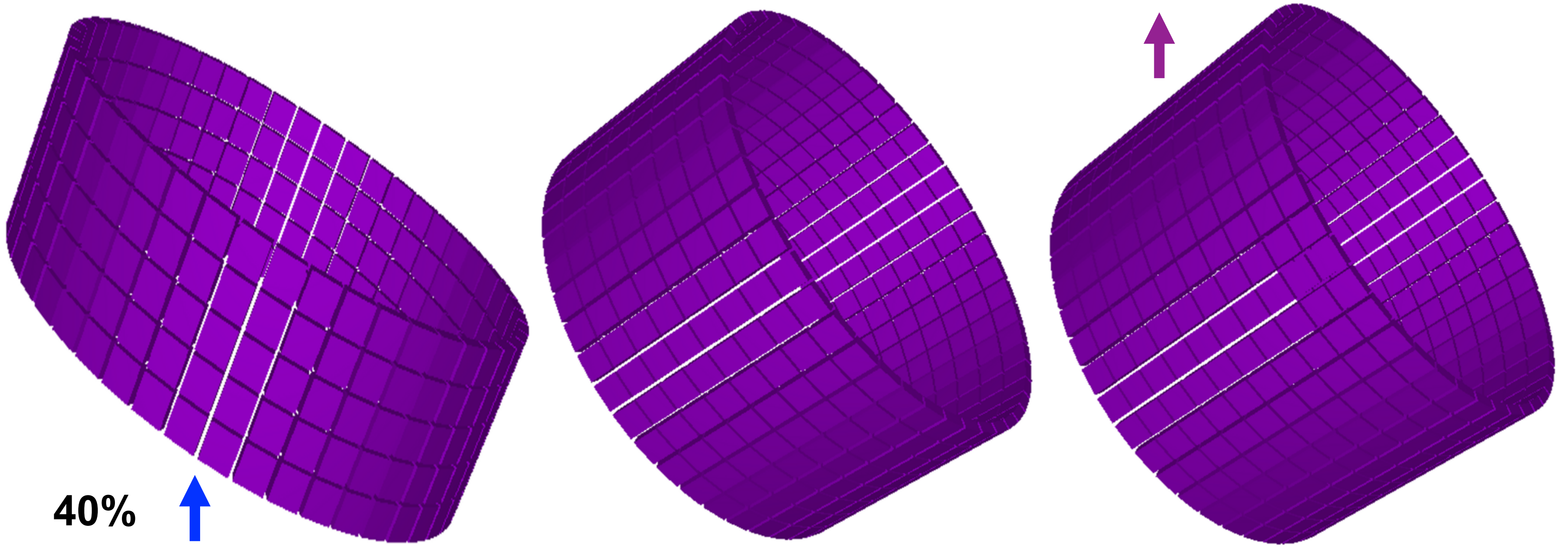




Scanner	*NEC Peak (Kcps) @(kBq/ml)*		
	Simulated (this work)	*Simulated (GATE)*	*Experimental*
B-TP	*90 @ 34*	*100@34*	*93@34*
B-TPTV	*161@34.5*	*177@34*	*161@31.5*
mCT	*177@35.5*	*-*	*180.3@29*

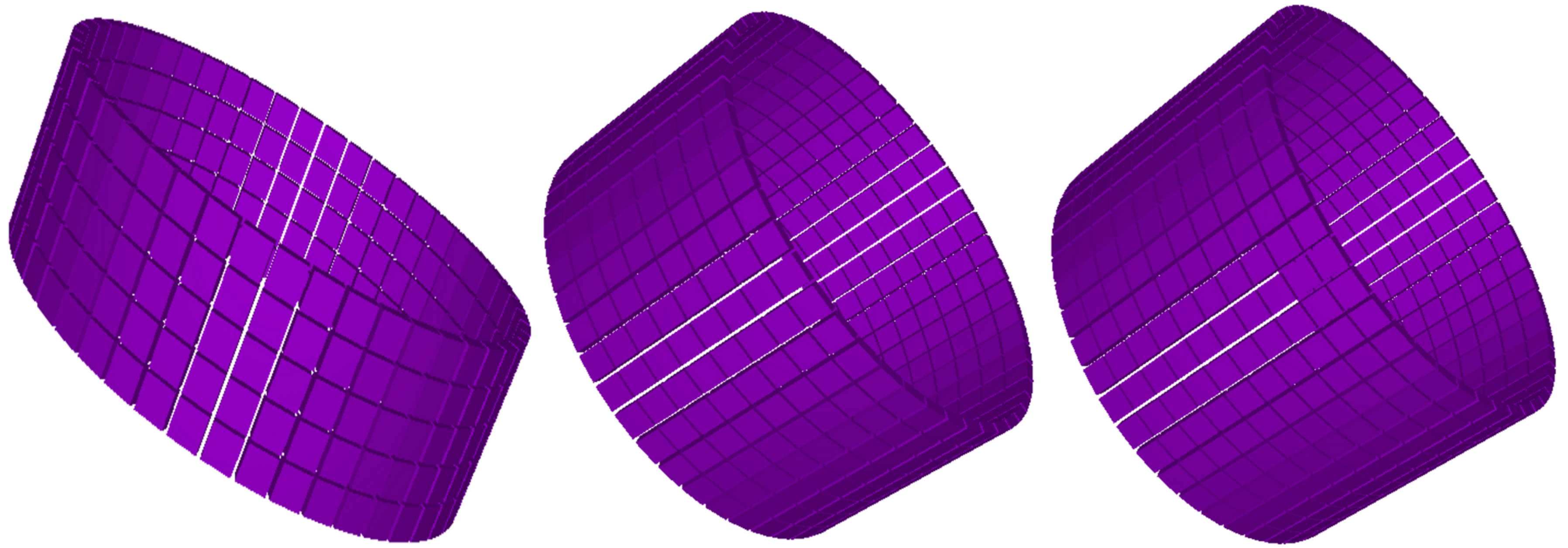
Sensitivity (extended rings)

► sensitivity increased 6 times > BTPTV



Number of block rings	Sensitivity [kcps/MBq] @ 0 and 10 cm off center			
	Axial FOV (cm)	Simulated (this work)	Simulated (GATE)	Maximum ring difference
5-rings	27.2	12.5	-	38
8-rings	43.6	31.7		38
10-rings	54.5	48.7	47.8	38

NEC (extended rings)

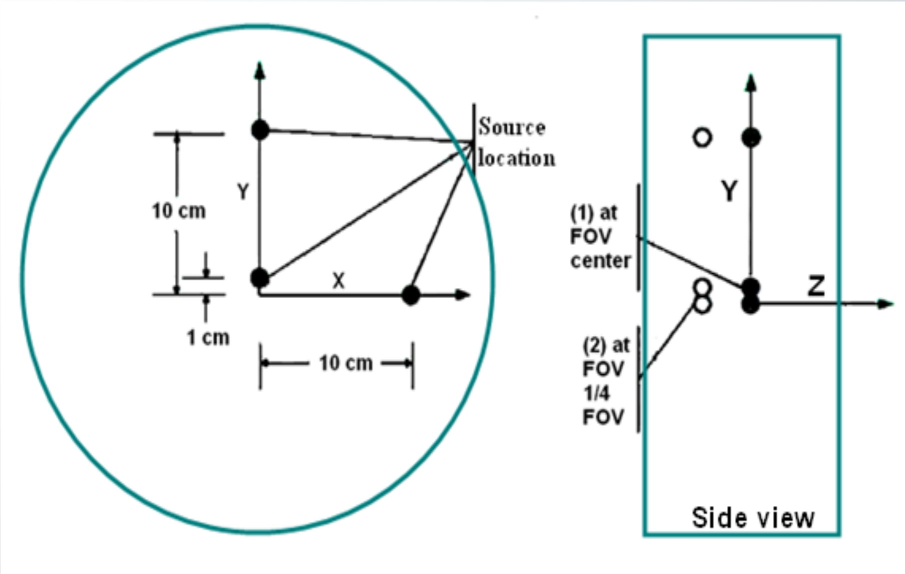


Number of block rings	NEC Peak (Kcps) @(kBq/ml)		Scatter fraction (%)	
	Simulated (this work)	Simulated (GATE)	Simulated (this work)	Simulated (GATE)
5-rings	259@36	-	30.8	-
8-rings	489@35	-	32.0	-
10-rings	787@30	800@31	33.1	35

Spatial resolution

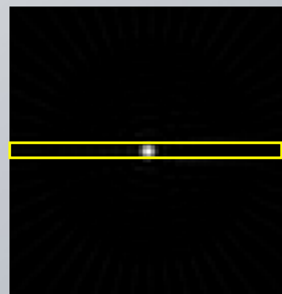
- The spatial resolution of a PET scanner represents its ability to disentangle two close point sources.

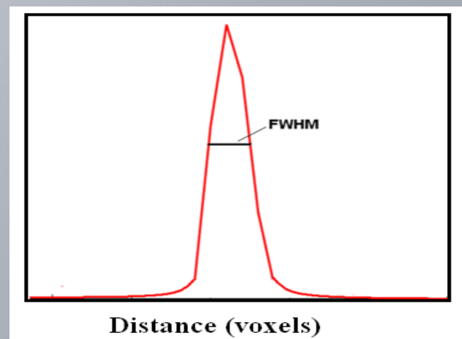
- ***NEMA protocol***



- ***Acquisition methods***

  - Filtered back projection reconstruction of sinogram data into images with 336 × 336 × 109 voxels (voxel size of 2 mm)





Spatial resolution

	FWHM (mm)		FWTM (mm)	
	Simulated	Experiment	Simulated	Experiment
	1 cm off center			
Transverse	4.6	4.2	8.5	8.1
Axial	4.2	4.5	8.4	9.2
Average resolution	4.4	4.4		
	10 cm off center			
transverse radial	5.5	4.6	9.0	9.4
Transverse tangential	5.6	5.0	10.2	9.4
Axial	4.4	5.5	7.5	10.5
Average resolution	5.3	5.0		

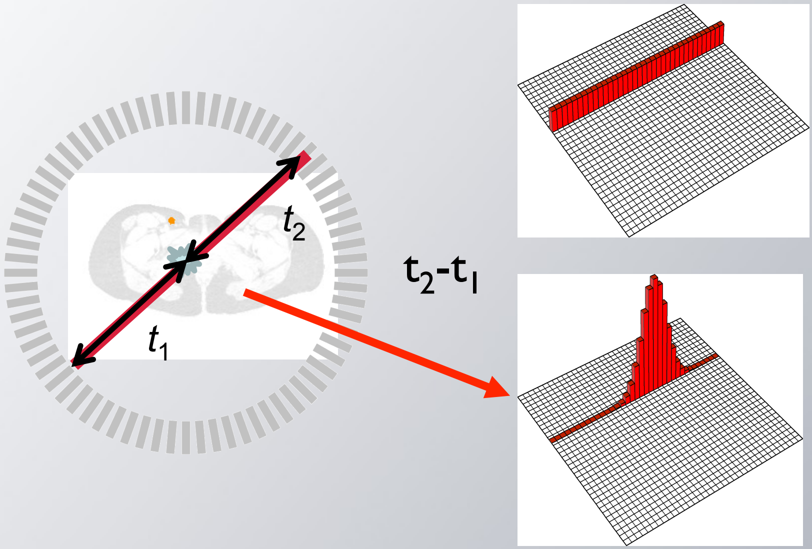
► The experimental reconstructed image size was 336 x 336 x 109 with a voxel size of 2 mm

Time of flight (TOF) PET scanners

principle of operation

- TOF-PET systems exploit the time difference between the two emitted photons to improve the location of the annihilation position along LOR.

- The measured time difference is used by the reconstruction algorithm to locate the annihilation point **Δx** inside the LOR (**Δx** =c Δt/2).



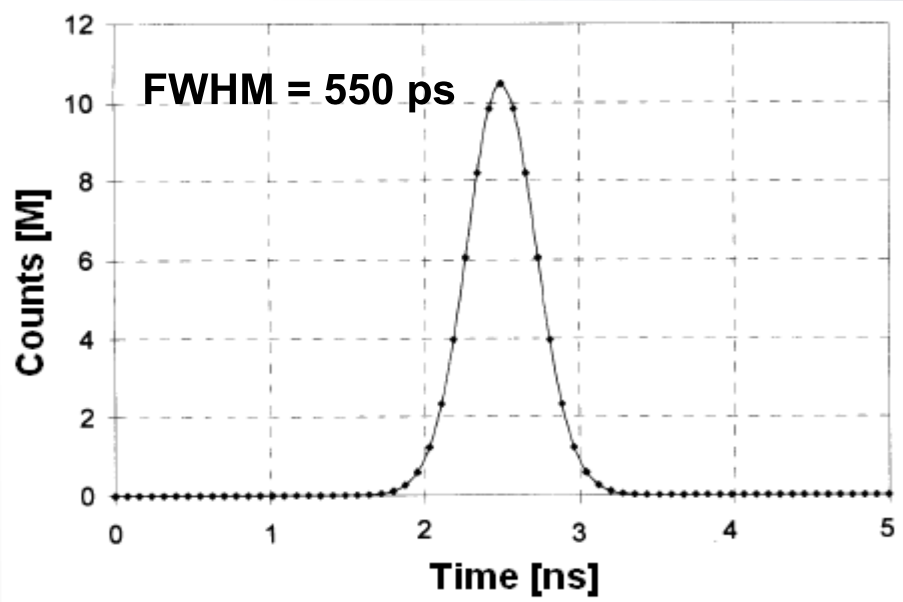
PET traditional

The probability for the event to be located along the LOR is uniform

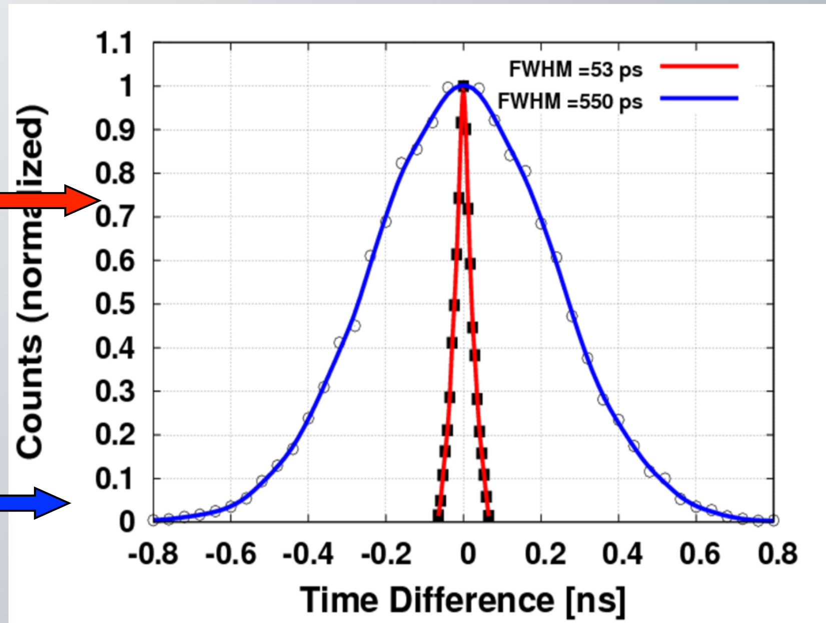
PET Time-of-Flight

The most likely position has to be compatible with the measured TOF value

TOF has been incorporated in PeneloPET



Measured time distribution [7]



- An additional time jitter of 170 ps is introduced in the simulations to produce a TOF resolution of 550 ps (FWHM) for the B-TPTV scanner.
- Simulated TOF distribution from a centered source.

[7] Jacoby et al., (2008) *Conference record, NSS'08. IEEE* ***3738-3743***

Conclusion

- ►PeneloPET is flexible enough to easily accommodate different parameters in the simulations.
- ►Good agreement between simulations and experiment can be obtained.
- ►PeneloPET is suitable for simulating and investigating clinical systems.

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Simulation of clinical PET scanners

Image reconstruction

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Analytical and iterative methods

- ***The basic role of image reconstruction is to convert the measured counts at projections with many different angles around the object, into an image that reflects in a quantitative way the distribution of positron-emitting atoms.***

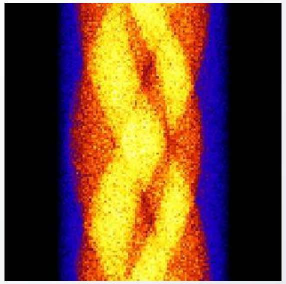
- ***There are two main approaches to image reconstruction.***

Analytical and iterative methods

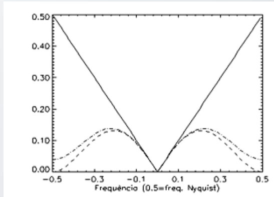
Analytical method (FBP)	Based on the formalism of computed tomography that relates line integral measurements to the activity distribution in the object. It does not model the physics in detail.
Iterative method **Based on statistical methods** **Require a system model**	The data collection process in a PET scanner is modeled in some detail. In a series of successive iterations, the image that is most consistent with the measured data is obtained.

Analytical and iterative methods

Analytical method (FBP)



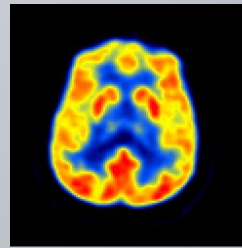
PET DATA



FILTER

SIMPLE SYSTEM MODEL

BACK-PROJECTION



IMAGE

Iterative method

Based on statistical methods

Requires a system model

ESTIMATED OBJECT

INITIAL OBJECT (uniform)

PROJECTION

ESTIMATED DATA

SYSTEM MODEL

PET DATA

BACK-PROJECTION

GFIRST-GPU

- GFIRST is an implementation of FIRST (*Fast Iterative Reconstruction Software for (PET) tomography*) code [8] developed by our group.
- It is implemented in CUDA (Computer Unified Device Architecture).

- GFIRST was designed to work with sinograms.

- ***This part of the thesis aims to demonstrate that GFIRST can incorporate TOF information, and to investigate with the help of realistic simulations the gain in image quality that can be achieved using TOF in different situations.***

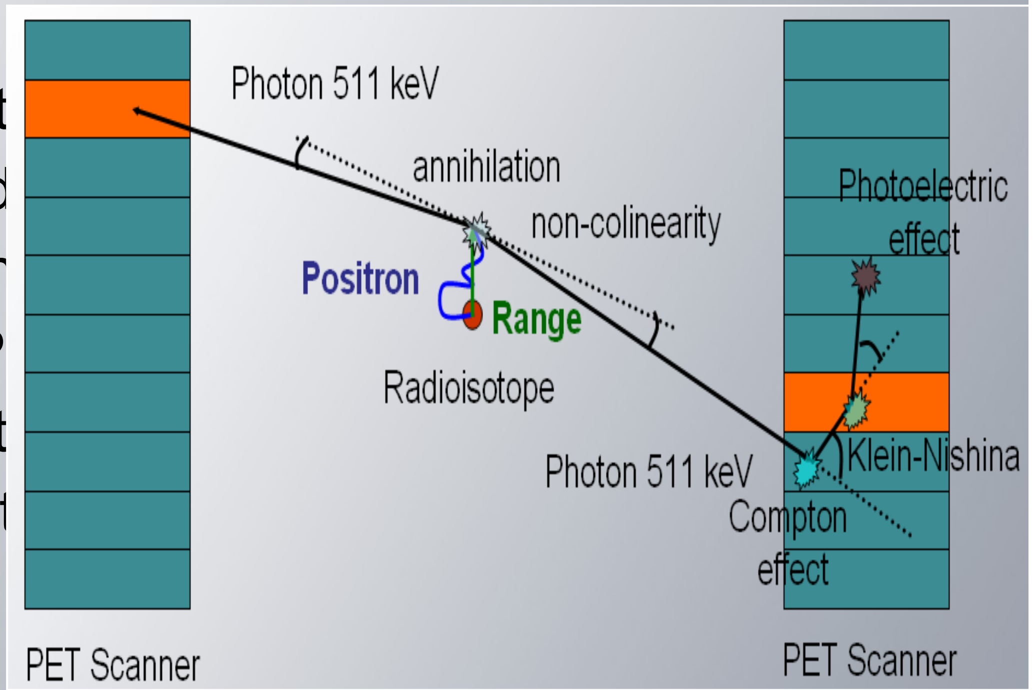
[8] Herraiz et al., 2006 *Phys Med Biol, 51, 4547–4565*

GFIRST Improvements

Point Spread Function (PSF)

- Blurring effects in PET such as positron-range, non-collinearity of the gamma rays, limit the maximum resolution achievable in reconstructed PET images.

- In order to improve t
reconstruction method and
increase the converger
rate of the algorithm, a P
was used to model t
physics blurring effects in t
reconstruction.



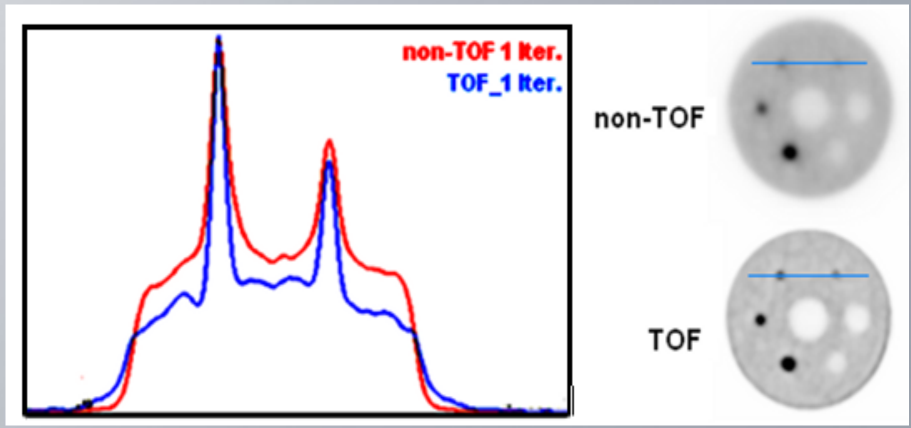
PSF

GFIRST Improvements

Median filter and TOF

- We extended GFIRST to include median filter regularization.
- In this case, after every iteration, the image is smoothed by applying a penalty to those voxels which deviate significantly from their neighbours.

- GFIRST was extended to incorporate TOF information. GFIRST was initially developed for non-TOF sinogram reconstructions.



Effect of TOF in image quality

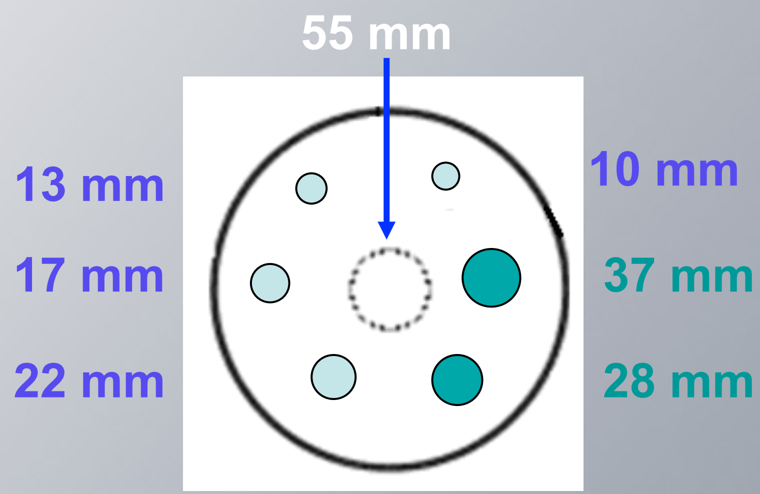
Methods and materials

✓ *PET scanner*

- The scanner employed for the simulation was the B-TPTV PET/CT. The TOF resolution of this system is 550 ps.

✓ *Image quality phantom*

- The NEMA image quality phantom was used.



✓ *Sinograms*

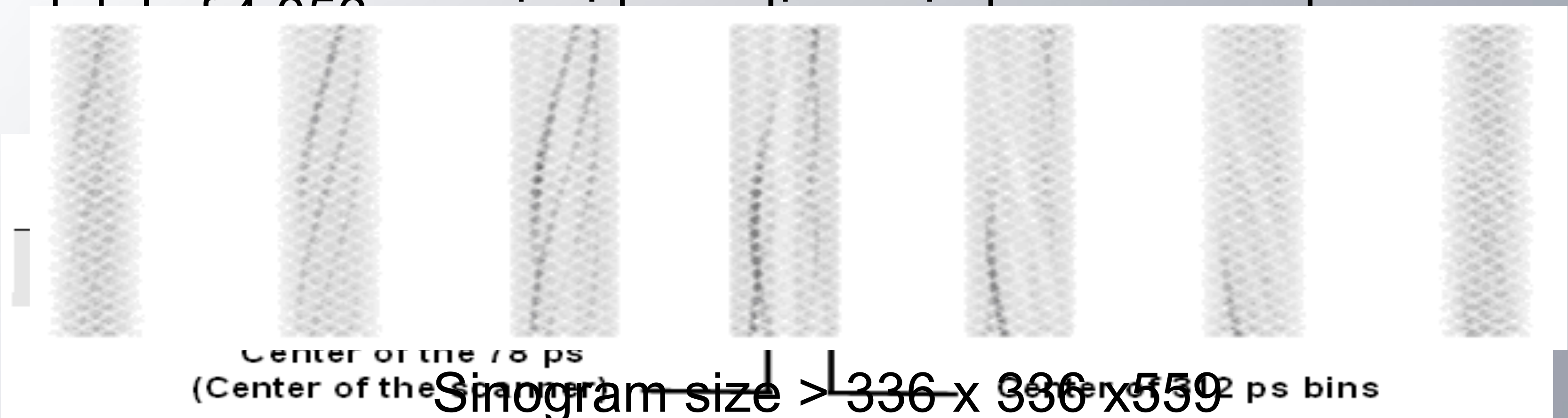
- In PeneloPET, sinograms corresponding to different combinations of rings in which each of the gamma ray has been detected are grouped together using *Michelograms*.

Effect of TOF in image quality

Methods and materials

✓TOF Sinograms

- TOF information is encoded in the list-mode data with time bins of 78 *ps*. The data is later reorganized into sinograms with 312 *ps* time bins, four bins of 78 *ps* are added to form the 312 *ps* bins.
- A TOF sinogram with 13 TOF bins (each 312 *ps* wide) covering a



Sinogram size > 336 x 336 x559

Effect of TOF in image quality

Methods and materials

✓ *Signal to noise ratio (SNR)*

► Defined as the difference between the lesion and background relative to the noise level in the background:

$$SNR = \frac{Signal - Background}{\sigma_B}$$

✓ *Contrast*

► The contrast can be used to measure the convergence of an iterative algorithm.

$$Contrast = \frac{Signal}{Background}$$

✓ *Noise*

► It is defined as the ratio between the standard deviation of the background and the background level.

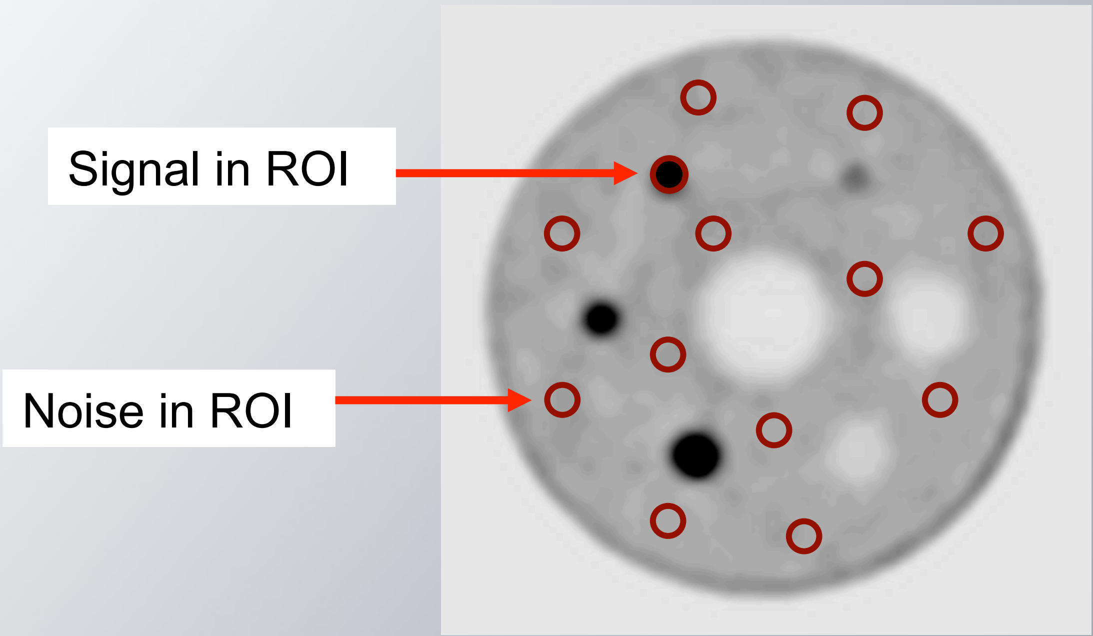
$$Noise = \frac{\sigma_B}{Background} X100$$

Effect of TOF in image quality

Acquisition method

- Several list mode acquisitions were simulated with different number of counts covering typical high and low count cases counts rates (970×10^6, 112×10^6, and 12×10^6 counts).

- Drawing circular regions of interest (ROIs) on the spheres as well as on the background regions (manually defined).



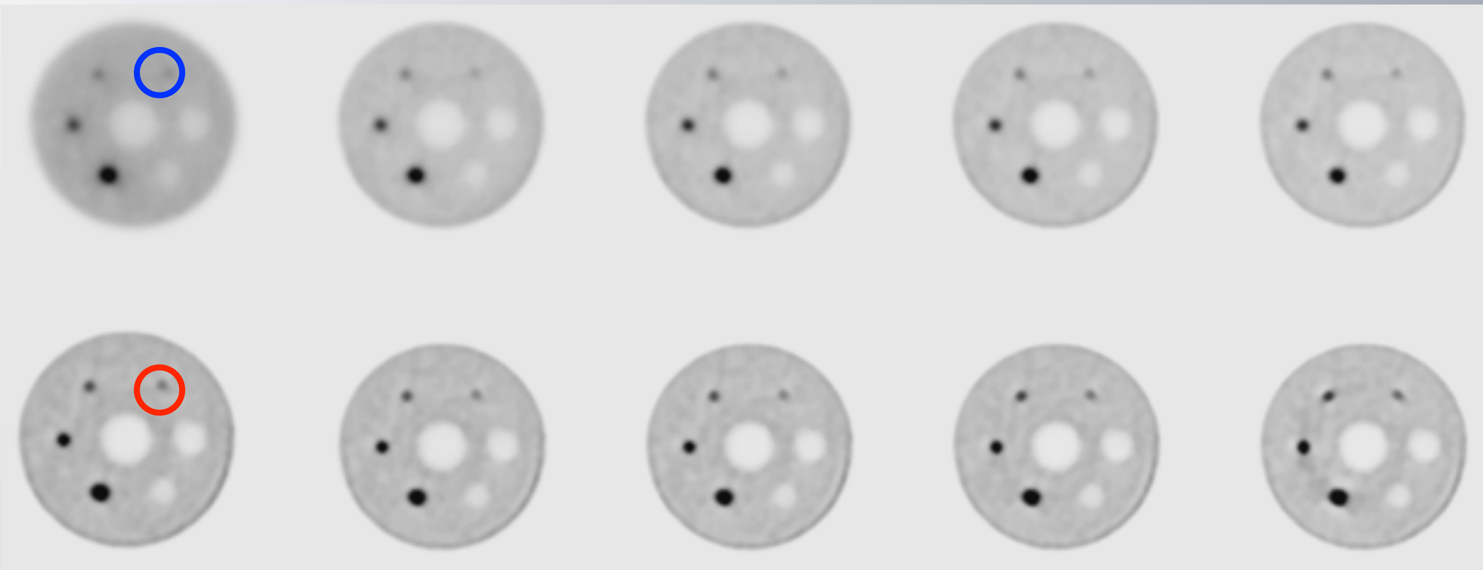
Effect of TOF in image quality

Reconstructed images

- A central slice of the reconstructed volume of the IQ phantom containing the hot spheres.
- Improvement in image quality can be observed for the smallest lesion (10 mm sphere) when images are reconstructed with TOF information.

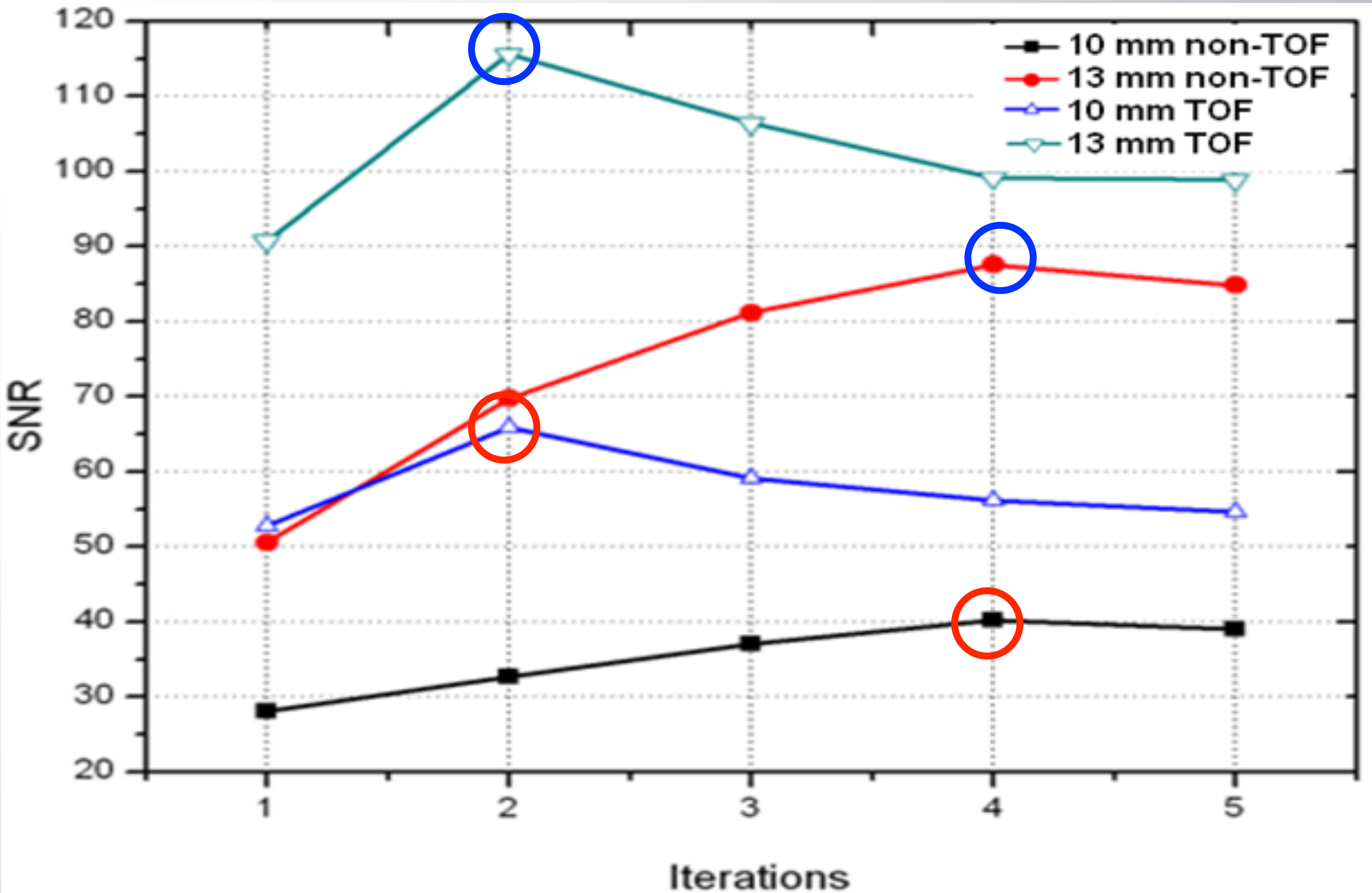
Non-TOF

TOF



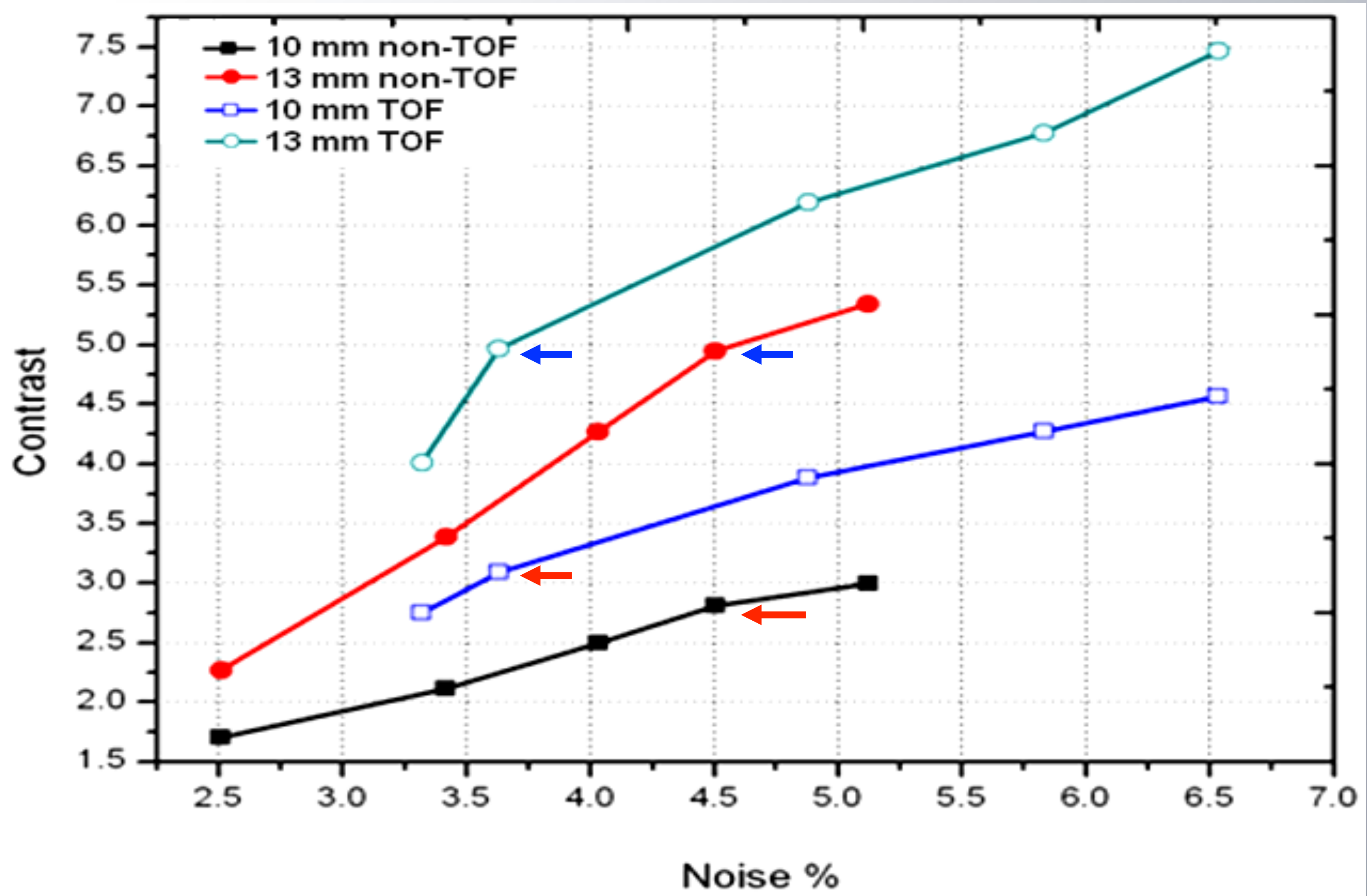
Effect of TOF in image quality

- ***High statistics (970 Mcts)***



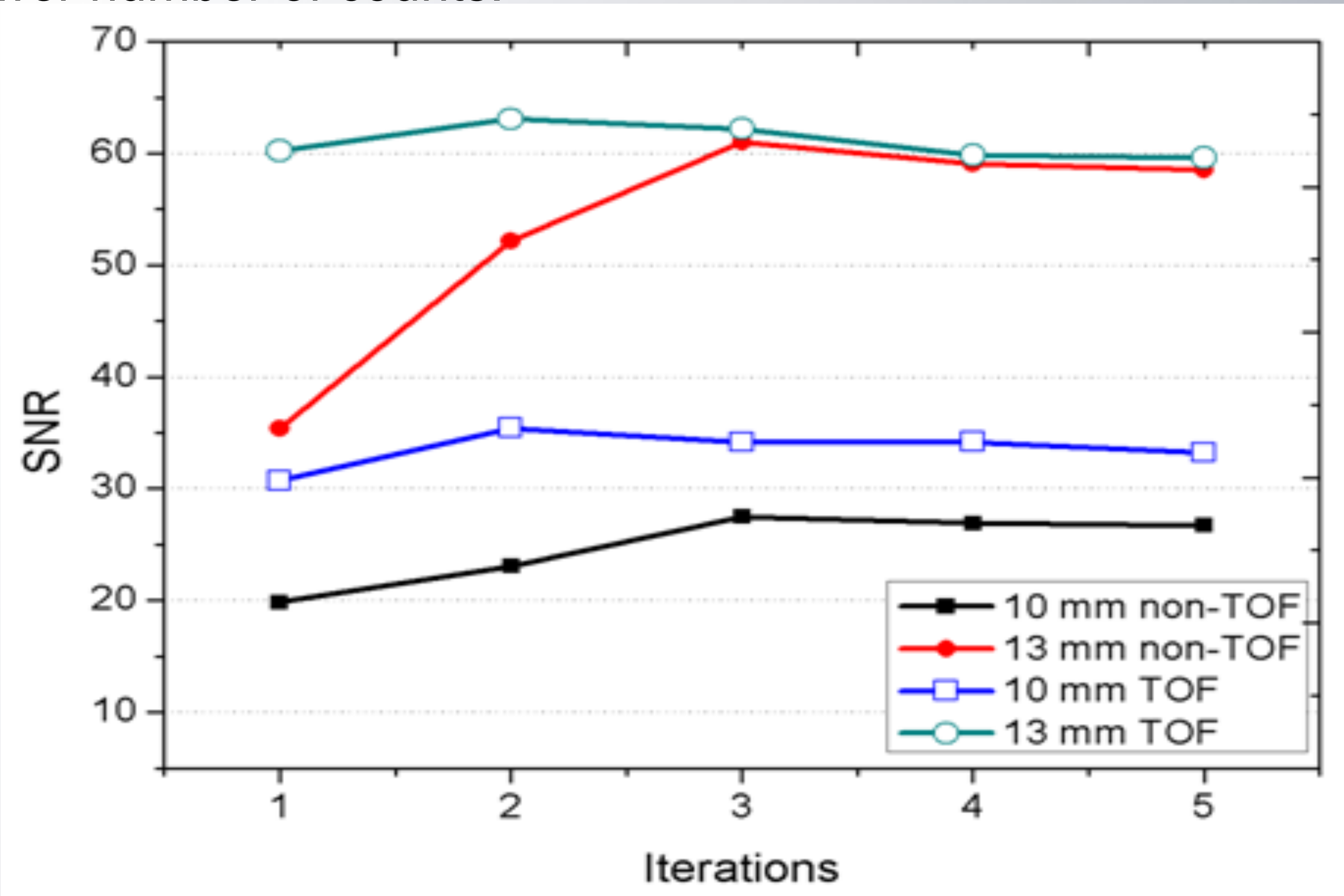
Effect of TOF in image quality

- *High statistics (970 Mcts)*



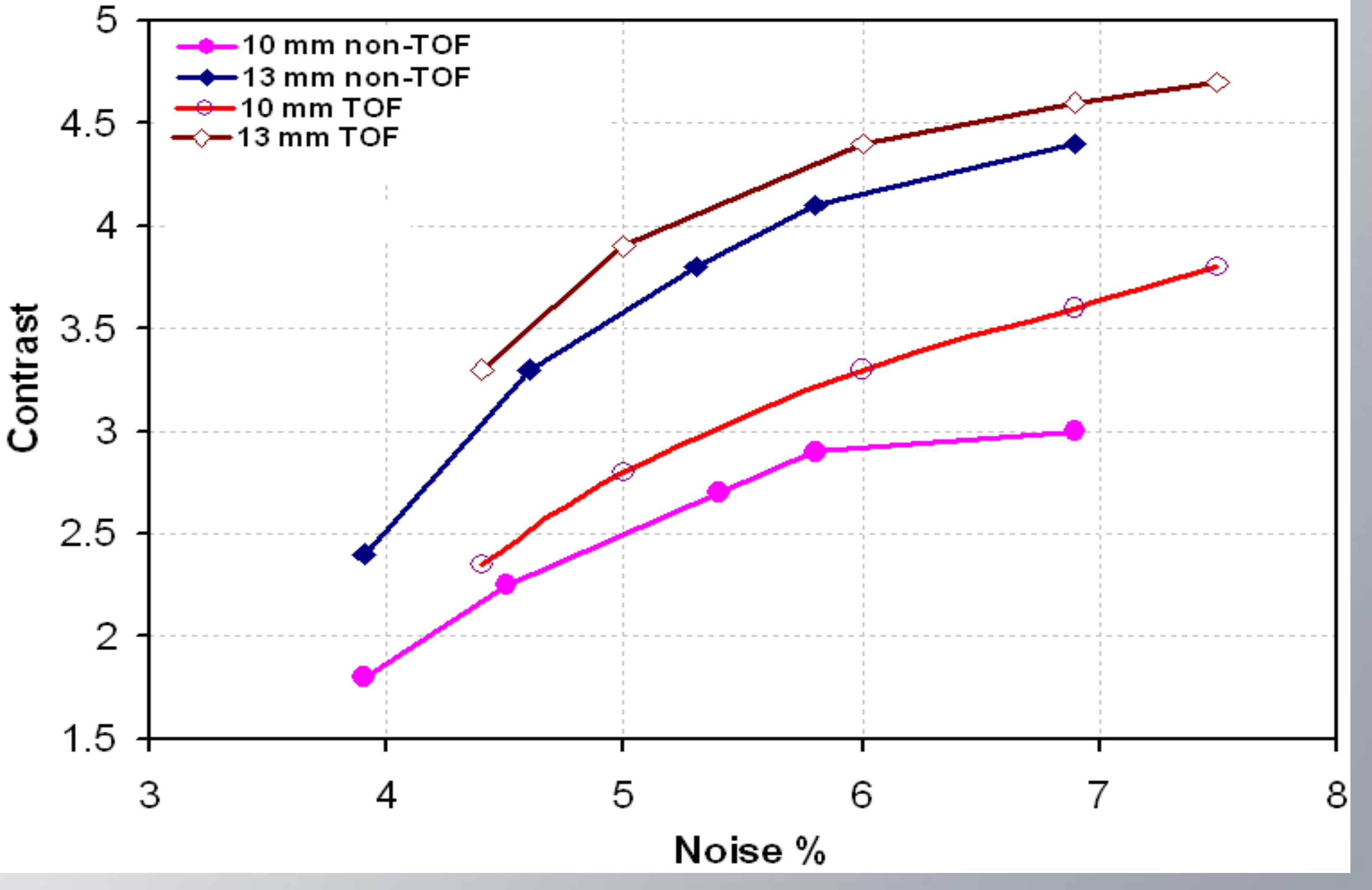
Effect of TOF in image quality

- ***Intermediate statistics (112 Mcts)***
  - ►The SNR reached is lower than in the previous case, due to the lower number of counts.



Effect of TOF in image quality

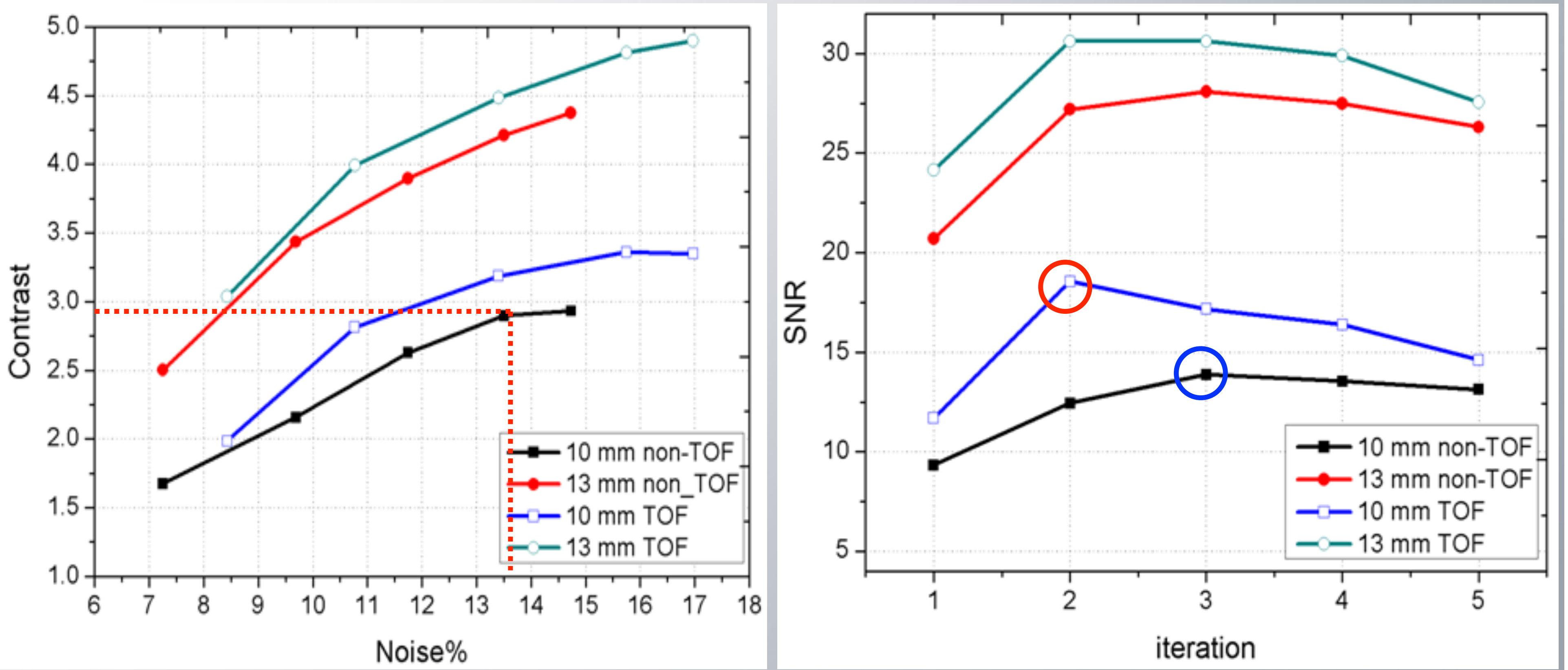
- *Intermediate statistics (112 Mcts)*
  - The contrast-noise trade-off is better for TOF compared with non-TOF images.



Effect of TOF in image quality

- **low statistics (12 Mcts)**

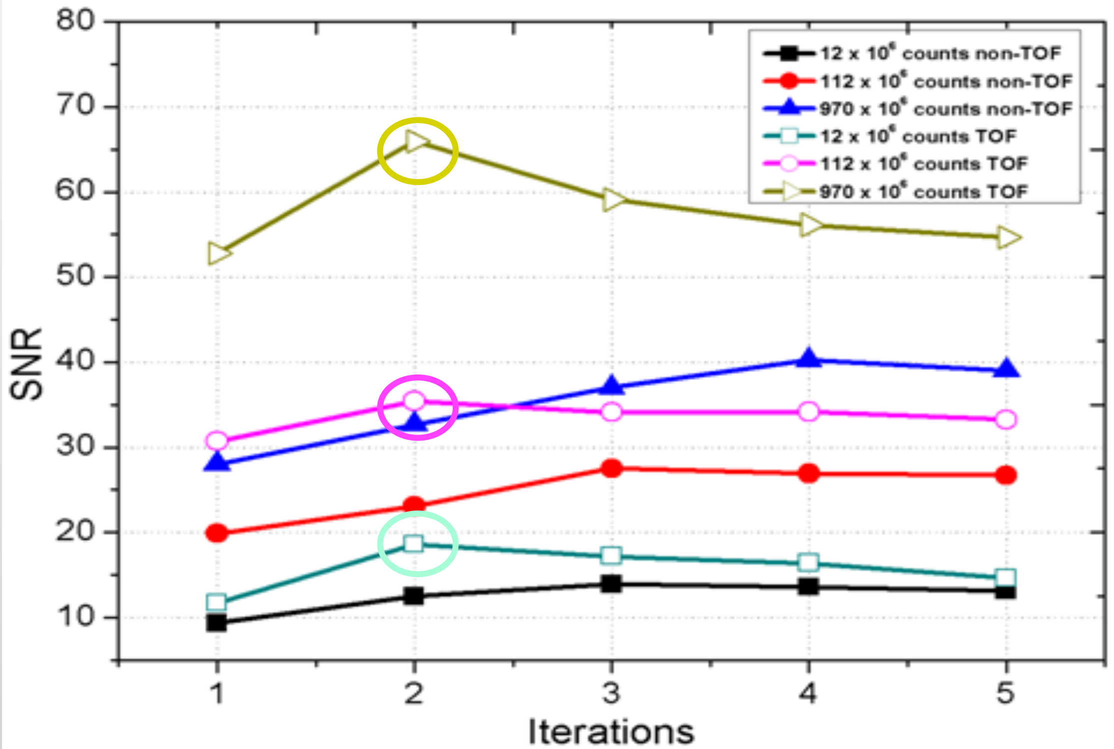
▸ The SNR reached is lower than in the previous case, due to the smaller number of counts.



Effect of TOF in image quality

Comparison of TOF and non TOF results (10 mm)

- The high-counts study has significantly higher SNR compared with the low-statistics one, for both TOF and non-TOF.
- **SNR** gain when using TOF is larger for the high-count study compared with the lower statistics one.

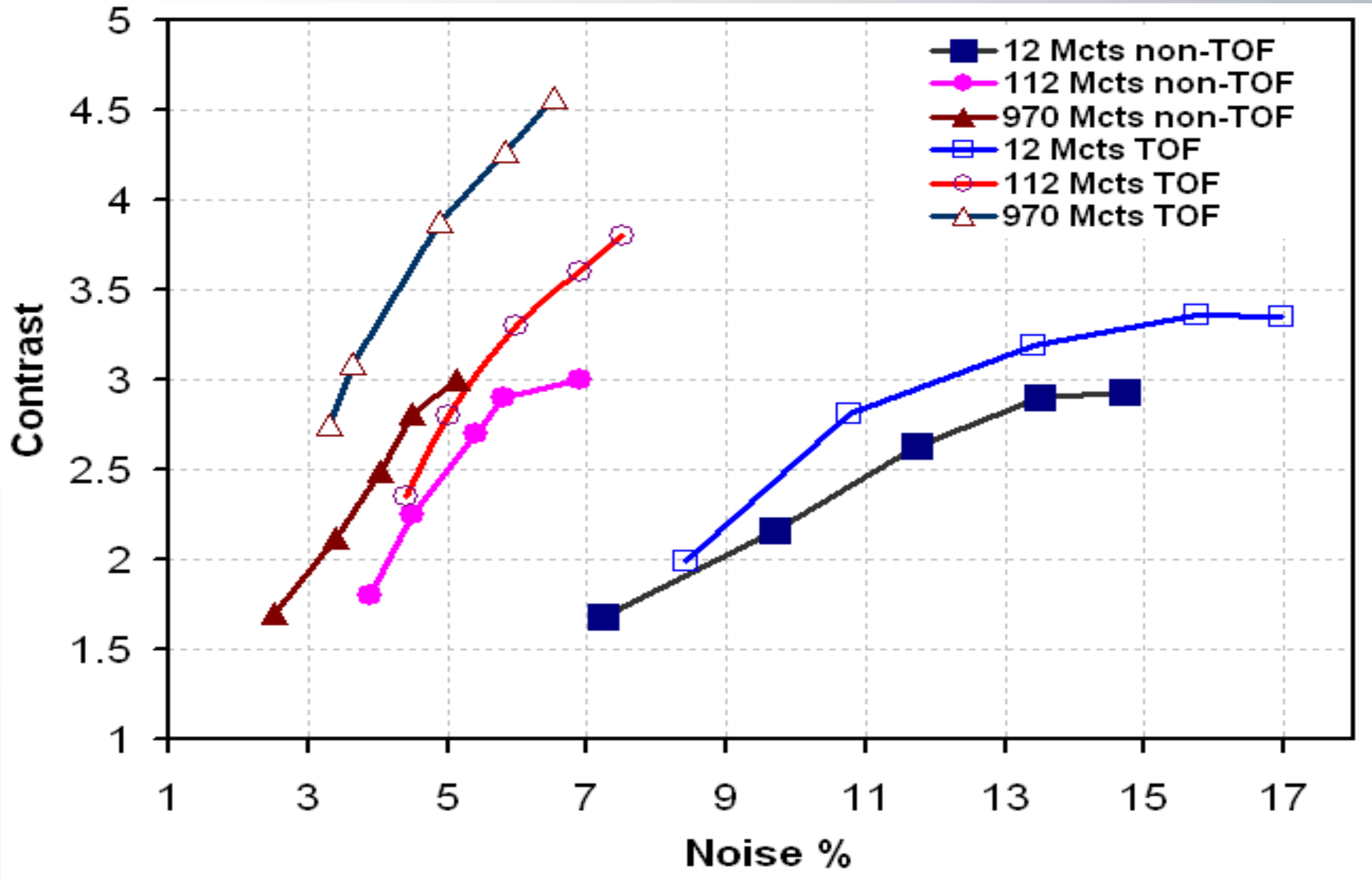


Counts (Mcts)	970	112	12	Real data [9]
SNR_{gain}	2.0	1.6	1.5	1.2 to 2

[9] *Lois* et al., 2010 *Journal of Nuclear Medicine* 51, **237–245**

Effect of TOF in image quality

- *Comparison of TOF and non TOF results (10 mm)*



Effect of TOF in image quality

Conclusion

- GFIRST is flexible to include PSF, median filter and TOF information, with low reconstruction time (1 minute per iteration in a 500 EUR GPU card), so that it could be used for real clinical TOF PET scanners.
- This was expected, due to the better localization of the annihilation events when TOF is included .

Table of contents

Main contributions of this thesis

- A PET Monte Carlo simulation tool (PeneloPET) has been extended and validated for clinical scanners.
- We have shown that PeneloPET is capable of incorporating TOF properties of the scanners in the simulation. This is of paramount importance to describe modern clinical PET systems.
- The reconstruction software GFIRST was modified to incorporate TOF information.
- The incorporation of TOF information results in better contrast/noise trade-off.

Main contributions of this thesis

- It has been shown quantitatively that the SNR gain due to TOF has larger effect in higher count acquisitions, provided the activity level is low.

Simulation speed (B-TPTV)

Processor	*Simulation speed (NEC NEMA)*	*GFIRST speed*
Intel(R) Xeon(R) CPU E5-2650@2.00GHz (16 threads)	*3000 detected coincidences per wall clock second*	*1 Minute per iteration (NVIDIA, GPU – TESLA C1060–4 GB – 27SM)*

- The simulation speed with a total of 16 PeneloPET threads working in the same processor (eight cores) achieves nearly 3000 detected coincidences per wall clock second at the peak of the NEC NEMA simulation.
- It is possible to obtain several million counts in a couple of hours.

Goals achieved

Preclinical area

Attention

Clinical

area !

Universidad Complutense de Madrid
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Grupo de Física Nuclear

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2012