

Câmara gama compacta para imagem médica em tempo real



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LIBPhys - UC



16. Dez. 2020 Bem-vindos!



Café com Física...











😭 Início 🕨 Ouvir - 🎜 Que M	úsica Era 🚦 🏠 Top25 🛛 💻 Caf	é da Manhã 🛛 <table-cell> Rádio -</table-cell>	Podcasts ••• Mais -	
O Café com Física é um programa já com uns bons anos de emissão. Tem acompanhado várias gerações que passam e ficam ligadas ao Departamento de Física.	OCEANO PACIFICO Dom a QUI 22H - 02H		Uma persistência notável!	
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Ocenano Pacífico: agora com Marcos André (após 28 anos com João Chaves), convidado há uns tempos do Café da Manhã, na celebração dos 35 anos de emissão do programa

Musica calma, alguns clássicos. Hoje, no Café com Física, falaremos de um equipamento que já pode ser considerado um clássico da imagiologia médica. Foi inventado na década de 50 (séc. XX).

Hal Anger (1922-2005)

Hal Anger presented in **1958** an equipment able to provide the positions of **γ-ray** interactions in a largearea position-sensitive detector, the **Gamma Camera**.





H. Anger was an american electrical engineer and biophysicist at Donner Laboratory, University of California, Berkeley

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The Gamma camera is also called a **scintillation camera** or **Anger camera**



Research field – nuclear medical imaging

 \sum Gamma cameras are used to perform **scintigraphy**: a medical imaging modality used to obtain functional images. E.g. cardiology, pneumology, oncology (staging of tumors, evaluate therapeutic response)







Normal

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Bone scans





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> For scintigraphy, the patient is injected with a **radiotracer** (radioisotope + biochemical substance) which **emits gamma-rays**

 \sum Gamma camera obtains an image of the **projection** of the radiotracer through the collimator





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SPECT working principle

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SPECT stands for "Single-photon emission computed tomography"

SPECT working principle

 The 3D dataset of γ-emitter distribution is obtained in SPECT by piling up many slices usually reconstructed independently

Gamma camera rotates around the patient to obtain several projection of the radiotracer inside the body



3D tracer distribution



Brain example

Collaboration with Hospital (Coimbra)



Collaboration with Universitary Hospital of Coimbra – Nuclear Medicine Department

THYROID:



Thyroid scintigraphy with ^{99m}Tc showing a nodule of the left lower pole





GOAL: Real-time imaging system based on a **compact** gamma camera with **high-resolution**

Requirements of the gamma camera for SLN and thyroid imaging:

- Capable of real-time imaging
- Compact and Lightweight
- \sum High extrinsic spatial resolution 5 mm at 5 cm
- Sub-millimetric intrinsic resolution
- Sensitivity: 100 cps/MBq
- \bigcirc Gamma ray energy: 140 keV
- Equipped with an interchangeable collimator: a parallel-hole and a pinhole collimator

Small field of view gamma cameras



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Compact and lightweight devices appeared in the last 2 decades (commercial and research prototypes). They use different technologies.





Conventional (big) cameras



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Examples of state-of-the-art compact gamma cameras

Name	Scintillator	Photosensor	Semiconductor	Size (mm²)	Energy Res. (140 keV)	Spatial resolution (mm)	Collimator
Sentinella 102	Monolithic, CsI(Na)	PSPMTs	-	40x40	13%	9 @ 50 mm	Pinhole
Popovic	Monolithic, LaBr ₃	SiPMs	_	60 mm Ø	21%	10.3 @ 50 mm	Parallel- hole
HiReSPECT	Pixelated, CsI(Tl)	PSMPTs	-	48x89	19%	3.5 @ 50 mm	Parallel- hole
GE (Haifa)	_	_	CdZnTe	40x40	8%	5 @ 50 mm	Parallel- hole
CrystalCam	-	-	CdZnTe	40x40	7%	5.4 @ 35 mm	Parallel- hole
eZScope	_	-	CdZnTe	32x32	9%	8 @ 50 mm	Parallel- hole
Tsuchimochi	-	-	CdTe	40x40	7.8%	6.3 @50 mm	Parallel- hole

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 \sum The spatial resolution is mainly given by the collimator

Camera main components and features

- Based on the **experience of the group** it was decided to use a scintillator based camera, namely with:
 - Monolithic scintillator crystal
 - Allows to apply powerful methods for the reconstruction of scintillation events
 - To collect high amount of light (depending on the crystal light yield)
 - An array of **silicon photomultipliers** (SiPM)
 - Gain up to 10⁶
 - Quantum efficiency up to 40%
 - Not sensitive to magnetic fields
- Using an algorithm of the group might be possible to adapte automatically the camera response model in time (self-calibration). If so, it should be possible to reduce the mantainance procedures, reducing the camera downtimes. I have exploited this possility.

Objective:

To offer a state-of-the-art performance camera at a significantly lower price and which requires reduced mantainance procedures!











If the gamma ray deposit energy in the scintillator, optical photons are emitted isotropically



To obtain the (x, y) position of the scintillation events, the **mainstream method** of the available cameras is the centroid method:

$$x = \frac{\sum_{i} A_{i} x_{i}}{\sum_{i} A_{i}}$$
 and $y = \frac{\sum_{i} A_{i} y_{i}}{\sum_{i} A_{i}}$

Centroid is robust, simple, but has three **significant drawbacks**:

- Periodic calibrations are required
- **Systematic spatial distortions**: look-up tables are used to correct the distortions
- Limited capability to discriminate multiple events: only by energy, which might fall within the total absorption peak

Statistical reconstruction

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- I wanted to use **more advanced techniques** that permits to avoid the problems associated with CoG method and that can reduce maintenance
- The know-how of LIP on **statistical reconstruction methods** (e.g. dark matter search projects LUX/Zepplin) were previously applied to medical gamma cameras by some colleagues



Try different (X, Y, E) candidates

Statistical reconstruction methods require a **model** of the camera response to light



How to build the model?

Options

- 1. Register the photosensors signals for positions of scintillation events with energies within the photopeak the position is assumed to be that of a pencil beam source moved along the entire camera field of view (experimental calibration)
- 2. Use data from simulation (signals vs source position)

3. Run a procedure that can **reconstruct automatically** the sensor responses to light from **food field** irradiation of the detector – I have exploited this approach

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Self-calibration: adaptive algorithm



Adaptive algorithm for LRFs evaluation

Two sets of data are required as input for the LRF iterative reconstruction method:

- Vectors of measured photosensor signals fixed during the iterative process.
- Estimated positions and energy (x, y, e) updated at at each iteration.



I have developed a **script for automatic execution of the interative procedure** to estimate the camera response model (LRFs)

Self-calibration of conventional camera

The **iterative method** works very well with a conventional (**big**) camera, both in simulations and using a Retrofitted **clinical gamma camera** (Vladimir Solovov and Andrey Morozov work)





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Phantom made of lead bars

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Retrofitted clinical gamma camera





List mode readout



Self-calibration iterations

 \sum The reconstruction results have many distortions using the initial guess on LRFs. The image quality improves using LRFs obtained in advanced iterations of the iterative method

Initial guess on LRFs: simulated LRF



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Iteration

Phantom made of lead bars

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13th Iteration





A. Morozov et al. 2015 Physics in Medicine and Biology, vol. 60, 4169

Design and optimization



 \sum **1**st **objective**: design and optimization of a compact gamma camera:

- 1) that respects the specified requirements
- 2) that is suitable for applying the adaptive method for LRFs reconstruction.

Method: Several rounds of Monte Carlo simulation vs experimental measurements (prototype)

Steps:

- 1) Create a camera model to be used in Monte Carlo simulation
- 2) Validate the simulation models by comparing with experimental data obtained from prototypes
- 3) Perform optimization of camera components

Camera parameters to optimize:

- Crystal thickness: efficiency vs spatial resolution
- Lightguide thickness: resolution vs distortions
- Coupling compound (low index vs high index compounds): the best resolution and the lowest degree of distortions

Camera optimization: ANTS2 and Geant4

- I made a model of the compact camera in ANTS2 simulation package (LIP) for the tracing of the optical photons
- \sum During the **validation** against experimental results, I found some discrepancies and I have concluded that ANTS2 is not good enough for tracking gamma-rays
- In the group, Andrey Morozov have created a tool to **delegate the energy deposition** (tracking of gamma-rays) **to Geant4** (and send back the deposition positions to ANTS2)

Geant4 simulates three processes not present yet in ANTS2:



Geant4 results (spatial resolution) are closer to the experimental results than in ANTS2.





Optimization of camera prototypes

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- \sum I have started with LYSO prototype as the crystal is already available: sufficient for thyroid
- Σ Due to **the intrinsic radioactivity of LYSO** (due to ¹⁷⁶Lu), for weak sources as in SLN imaging, the images obtained have low contrast
- \rangle I needed to find an **alternative material**: I proposed **GAGG** (when compared with LYSO, has: higher light yield and no self-radiation)



GAGG (3 mm thick) prototype

Ce:GAGG, Gd₃Al₂Ga₃O₁₂:Ce

 \sum

 \rangle



LYSO (2 mm thick) prototype



Reflector wrapped by an

Ce:LYSO, $Lu_{1,8}Y_{0,2}SiO_{5}:Ce$

Perspective view - reflector removed

LYSO has better efficiency and intrinsic resolution, however it is radioactive

GAGG, with no self-radiation, is more suitable for SLN localization imaging



Array of photosensors selection

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Analysis of the SiPMs PDE spectrum and scintillators emission spectrum



SensL Array-C, model 30035 was selected because it was offered for free to the Gamma Camera group by SensL company. Besides this, the SensL SiPMs have the lower dark count rate, a very important parameter.

Sir Isaac Newton: "Annus mirabilis"

Em Junho de **1665**, devido à grande peste de 1655 (só em Londes fez mais de 70.000 vítimas), a **Universidade de Cambrigde fechou portas.**

Newton acabado de se diplomar (com 23 anos) irá passar o ano na sua província natal (Lincolnshire, entre Londres e a Escócia), um ano rico em descobertas: o **"ano maravilhoso"**.

A partir de 1964 Newton anota as suas leituras. Sabemos que reflectiu sobre os Diálogos de Galileu, sobre a Geometria de Descartes e sobre os trabalhos de Kepler, em particular os que se referem à **luz e ao problema das cores**

Descobre que a luz "branca" é uma mistura de luz de todas as cores (e o prisma desvia-as em diferentes sentidos):

"... arranjei um prisma de vidro para realizar a célebre experiência das cores. Tendo para tal efeito obscurecido o meu quarto, e uma vez feito um buraquinho nas portadas para deixar entrar uma quantidade conveniente de raios de sol, coloquei o meu prisma encostado a esse burado, para refractar os raios na parede oposta. (...) foi muito agradável contemplar as cores vivas e intensas assim produzidas." Dispersão da luz

Mais à frente, com a ajuda de um furo numa prancheta, isola a parte azul (mais desviada pelo prisma) e **envia essa luz azul para um segundo prisma. Essa luz não se desdobra nem se tinge de outra cor!**

Prisma

Fenda



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Collimator design

2nd objective: design and optimization of the collimators

Previously: validation of the adequacy of the analytical equations available in literature for cameras of reduced sizes (simulations vs analytical results).

Target Minimal requirements for **SLN imaging** also suitable for **thyroid**: parameters:

- Spatial resolution: < 5 mm at 5 cm
- Efficiency: > 0.0001 (100 cps/Mbg)

Ex: Parallel-hole collimator trade-off curves:



Parallel-hole collimator

Parallel-hole collimator optimized parameters:/

d = 0.05 cmsepta t = 0.03 cm height = 0.8 cm

Spatial resolution: 4.1 mm (at 5 cm) Sensitivity: 120 cps/MBa



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Pinhole collimator



Collimator prototypes

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Collimators are commonly made of **lead** (toxic). **Tungsten** can be used instead (shorter attenuation lenght than lead, which allows to use less material)

I have designed and ordered two collimators.

Parallel-hole collimator (hexagones with 0.5 mm "diameter" d, septa t of 0.3 mm):

CAD design: Eng^o Rui Alves (LIP workshop) **Manufacturer**: M&I Materials (UK)





Pinhole collimator (1 mm diameter hole and 0.5 mm channel height):

CAD design and manufacturing: DURIT (Albergaria-a-Velha)



Made of **tungsten alloy** (95.5% W, 4.5% Co) using Electric discharge machining (EDM)



Readout and acquisition system



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Selected readout: TRB3 (GSI) based readout for 64 channels



Acquisition rate up to 10 kHz

Example of a scintillation event:

64 SiPM Signal waveform

0	1	2	3	4	5	6	7
8	9	10	11	12	13	14	15
16	17	18	19	20	21	22	23
24	25	26	27	28	29	30	31
32	33	34	35	36	37	38	39
40	41	42	43	44	45	46	47
48	49	50	51	52	53	54	55
56	57	58	59	60	61	62	63

Number of detected photons



Signal waveform



ADC channels per photoelectron



Real-time workflow

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Real-time imaging has some challenges: acquisition rate, processing speed (waveforms, reconstruction algorithm)

The **scripts** required to extract waveform samples sent from the DAQ and the consecutive processing chain until the visualization of the event positions were prepared

For real-time processing, a loop waits for waveform files and triggers their processing:



Processing chain workflow

For each event in the file: \rangle

Calculation of signal integrals 1050, Integration 1000, window 950,E 900,E 850, 800, 750, 700,Ē 650,E 600. 20 25, **Conversion** into number of photons

algorithms): XY positions and energy Measured signals: {A;} Detector + front-end + DAO Expected 11 23 22 signals: {a;} Select position Detector model giving the best match $a_i = C_i E \eta_i(X,Y)$ Т between (A,) and (a,) Try different (X, Y, E) candidates **Real-time** buffer (FIFO)

Save event signals (in number of photons) and / reconstructed XY positions

Apply event reconstruction (statistical

Visualization of the reconstructed XY event positions in a density plot







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Prototypes characterization

 \sum The prototypes assessment was performed in the Universitary hospital of Coimbra (CHUC), with access to high activity source (^{99m}Tc, 140 keV)



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Masks and phantoms

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Source position



Masks:

Parallel bars 2 mm wide



Four parallel 0.2 mm slits



Capillary tube Phantom (Filled with a ^{99m}Tc source solution):



Intrinsic assessment

 \sum Results without any scanning calibration, only flood field data used to run the adaptive algorithm (for LRFs)

Spatial resolution:

GAGG prototype: 0.90 mm FWHM | LYSO prototype: 0.72 mm FWHM

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Extrinsic spatial resolution



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Extrinsic spatial resolution

Distance between source and pinhole (mm)



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Phantom imaging UNIVERSITY HOSPITAL OF COIMBRA (CHUC)



Brain slice phantom Event density vs XY Y, mm 50 15 10 40 30 20 -10 10 -15 -15 -10 5 10 15 X, mm -5 0

PINHOLE COLLIMATOR





Crossed capillary tubes phantom (parallel-hole collimator)







Main results



- \sum The predictive power of the simulation **model** of the camera was successfully validated
- A **prototype** of the compact camera was assembled and was characterized in the hospital (^{99m}Tc source). It was shown that the **requirements are met**
- **Intrinsic spatial resolution** better than 1 mm
- **Extrinsic spatial resolution** (with collimator):

1.0 mm FWHM (pinhole and 2x magnification)3.9 mm FWHM @ 50 mm source - parallel-hole collimator

- **Self-calibration** was confirmed for the new design GAGG camera
- Script **for automatic execution of the interactive procedure** was developed to estimate the camera response model (light response functions)
- **Real-time imaging** was demonstrated
- **Real-time monitoring** of the camera response model, which can trigger an alarm for self-calibration

Nuclear imaging experts from the hospital have confirmed that the developed system can be beneficial for **thyroid nodules functional studies** and for **sentinel lymph node biopsy**



- Perform *in vivo* imaging of small organs: clinical test of full-scaled camera (50x50 mm²) for thyroid imaging at nuclear medicine department of University Hospital of Coimbra
- Evaluate the possibility of apply **self-calibration using the radiation from** the radiotracer already injected into the **patient (method does high degree if uniformity)**
- To build and to test a prototype of a **gamma camera with a larger FOV**, as for large organs (e.g. heart, kidney, lung) the FOV of the developed camera is insufficient
- Integration of the developed camera in a **SPECT device to image the 3D distribution** of the radiotracer inside the body





Thank you very much for your attention CAFÉ COM FÍSICA AUDIENCE

Special thanks to Doctor Vladimir Solovov and Doctor Andrey Morozov (colleagues in the Gamma Cameras Group) and Doctor Vitaly Tchepel











15 X. mm



End of presentation DISCUSSION OPENED TO COMMENTS AND QUESTIONS



EXTRA slides below IF FURTHER CLARIFICATIONS ARE REQUIRED



Camera design: optimization of lightguide thickness DEPTH OF INTERACTION ANALYSIS





Optimization of lightguide thickness

SIMULATION STUDY (3 mm thick GAGG crystal and lightguide thickness from 0.3 mm to 1.5 mm)

SIMULATION: emission of **one million 140 keV γ-rays** uniformly distributed over that area

The XY density plot of the reconstructed positions using the LRFs estimated with all events but filtering out the scintillation positions out of **(a)** the central, **(b)** bottom, **(c)** top regions, respectively. **(d)** All events included

The analysis on the reconstruction performance was only performed for a quarter of the camera area (16.6×16.6 mm 2 in the upper-right corner).

XY density plot of the average differences between the X coordinate of the reconstructed and true positions (**0.3 mm thick lighguide**)



Figure 3.33: XY density plot of the average differences between the X coordinate of the reconstructed and true positions (3 mm thick GAGG and 0.3 mm thick lighguide). a Using only events from the bottom region of the scintillator; b Using only events from the central region of the scintillator; c Using only events from the top region of the scintillator; d Using all event.

Density plot of reconstructed positions (**1.0 mm thick lightguide**)





Density plot of reconstructed positions (0.3 mm thick lightguide)



Figure 3.34: Density plot of reconstructed positions (3 mm thick GAGG and 0.3 mm thick lightguide). a Using only events from the central region of the scintillator; b Using only events from the bottom region of the scintillator; c Using only events from the top region of the scintillator; d Using all events.



Optimization of lightguide thickness SIMULATION STUDY

XY Density plot of reconstructed positions of a 99m-Tc source projection through a diagonal slit



Figure 3.35: XY Density plot of reconstructed positions of a ^{99m}Tc source projection through a diagonal slit (3 mm thick GAGG). a b and c 0.8 mm thick lightguide; d e and f 0.3 mm thick lightguide; a and d Using only events from the bottom region of the scintillator; b and c Using only events from the top region of the scintillator; c and f Using all events.

Optimal lightguide thickness: 0.8 mm - 1.0 mm





Optimization of coupling between camera elements Using commercially available optical adhesives

Single optical grease (low refractive index, n = 1.465)

Teflon n=1.37Optical grease n = 1.465GAGG:Ce n = 1.93Optical grease n = 1.465Lightguide n = 1.51Optical grease n = 1.465SiPM epoxy n = 1.47 **Three** optical adhesives (high refractive index)

Teflon n= 1.37	
Optical adhesive $n = 1.66$	
GAGG:Ce n = 1.93	
Optical adhesive $n = 1.73$	
Lightguide n = 1.73	
Optical adhesive $n = 1.57$	
SiPM epoxy n = 1.47	

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\sum Diagonal line of pencil beam sources



Figure 5.7: Example of the automatic algorithm capacity to accurately estimate LRFs. a: XY density plot of the reconstructed pencil beam sources using LRF₁ (initial camera configuration). The read circles are the true source positions. b: Map with the relative gains randomly set to each SiPM (active areas are delimited by a thin green lines). c: XY density plot of the reconstructed pencil beam sources using LRF₁ (changed camera configuration). Strong distortions are apparent. d: XY density plot of the reconstructed pencil beam sources using LRF_{new} (changed camera configuration).



Characterisation of the difference

BETWEEN THE EXPECTED AND OBSERVED VALUES

Maximum Likelihood

$$W(x, y, e) = \prod_{i}^{PMTs} P_i(A_i, a_i(x, y, e))$$
Least squares

$$\chi^{2}(x, y, e) = \sum_{i}^{\# PMTs} (A_{i} - a_{i}(x, y, e))^{2}$$

D I I !!!!

Optimization

Process of finding the position which gives the best match between the vector of measured signals and that with the predicted signals.

Simplest approach (and slowest): Brute force Alternatives: **Contracting grids**, migrad and simplex

 \rightarrow The "contracting grids" technique, which is faster than brute force because it does not perform high resolution search over the entire parameter space. A grid is defined around a certain region and the search is performed. Depending on the required precision, a new, finer grid is defined around the optimal position and the search starts again. The new optimal position is calculated and this process can iterate, decreasing the step between the grid nodes until the finest grid, which is usually smaller than the spatial resolution.

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The vacancy created by the electron ejected from the atom will be filled with other electron from an upper shell, reestablishing the atom lowest energy state. This **relaxation** can occur either through **fluorescence**, with the emission of an X-ray, or through a nonradioactive transition, with the emission of an Auger electron.

These two secondary effects of photoelectric absorption have complementary probabilities



Figure 2.2: Photoelectric absorption and secondary effect representation. One γ -ray (red arrow on the left) interacts with an atom and a photoelectron is ejected (blue arrow on the left) leaving a vacancy. Fluorescence or a emission of an Auger electron can occur with complementary probabilities. The image was copied from 14.





Using **CrystalCam** hand-held camera:



Anterior (**a**) and posterior (**b**) static images from the thoracal region were taken by dual-headed gamma camera. Axillar (*black arrow*) and epitrochlear (*red arrow*) lymphatic drainage was seen on the right upper extremity

The Utility of Intraoperative Handheld Gamma Camera for Detection of Sentinel Lymph Nodes in Melanoma Elgin Ozkan and Aydan Eroglu

Nucl Med Mol Imaging. 2015 Dec; 49(4): 318-320. doi: 10.1007/s13139-015-0341-5

Geant4 vs ANTS2 energy deposition







Geant4 vs ANTS2 simulation of energy deposition SPATIAL RESOLUTION RESULTS COMPARISON (LYSO crystal)

Geant4

ANTS2



This difference of 23% is attributed mostly to K-shell fluorescence of Lu (53-63 keV), which is only simulated in Geant4.



Geant4 vs ANTS2 simulation of energy deposition ENERGY RESOLUTION RESULTS COMPARISON (LYSO crystal)





Readout and acquisition system

TRB3 (GSI) BASED READOUT FOR 64 CHANNELS





Data acquisition system performance TRANSFER RATE AND ACQUISITION RATE



Masks and phantoms

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Source position



Masks:

Parallel bars 2 mm wide



Four parallel 0.2 mm slits



Phantoms (Filled with a ^{99m}Tc source solution):

Capillary tubes



"Brain slice" phantom



Real-time imaging



ANTS2 reconstruction and visualization in real-time





Prototype details photographs









Light response functions One LRF for each photosensor

 The model is a set of light response functions (LRFs)

LRF for one photosensor in a 30 x 30 mm square camera





LRF for a clinical gamma camera Ø500 mm







Scintillator materials

EXAMPLES OF INORGANIC CRYSTALS

Material	Density (g/ cm ³)	λ _{max} (nm)	Refractive index	τ (ns)	Light yield (Ph/MeV)
NaI(TI)	3.67	415	1.85	230	38000
CsI(Tl)	4.51	540	1.80	800	60000
Bi4Ge3O12	7.13	480	2.15	300	8200
BaF ₂	4.89	220, 310	1.56	0.6, 630	1500, 9500
CeF ₃	6.16	340	1.68	27	4400
Lu ₂ SiO ₅ (Ce)	7.4	420	1.82	47	25000
LaBr ₃ (Ce)	3.79	350	1.9	27	49000