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Journées thématiques du Réseau Semi-conducteurs IN2P3-IRFU
Strasbourg 2-3 Juin 2022

A portable gamma camera for the optimization of the patient dosimetry in radioiodine therapy of thyroid diseases

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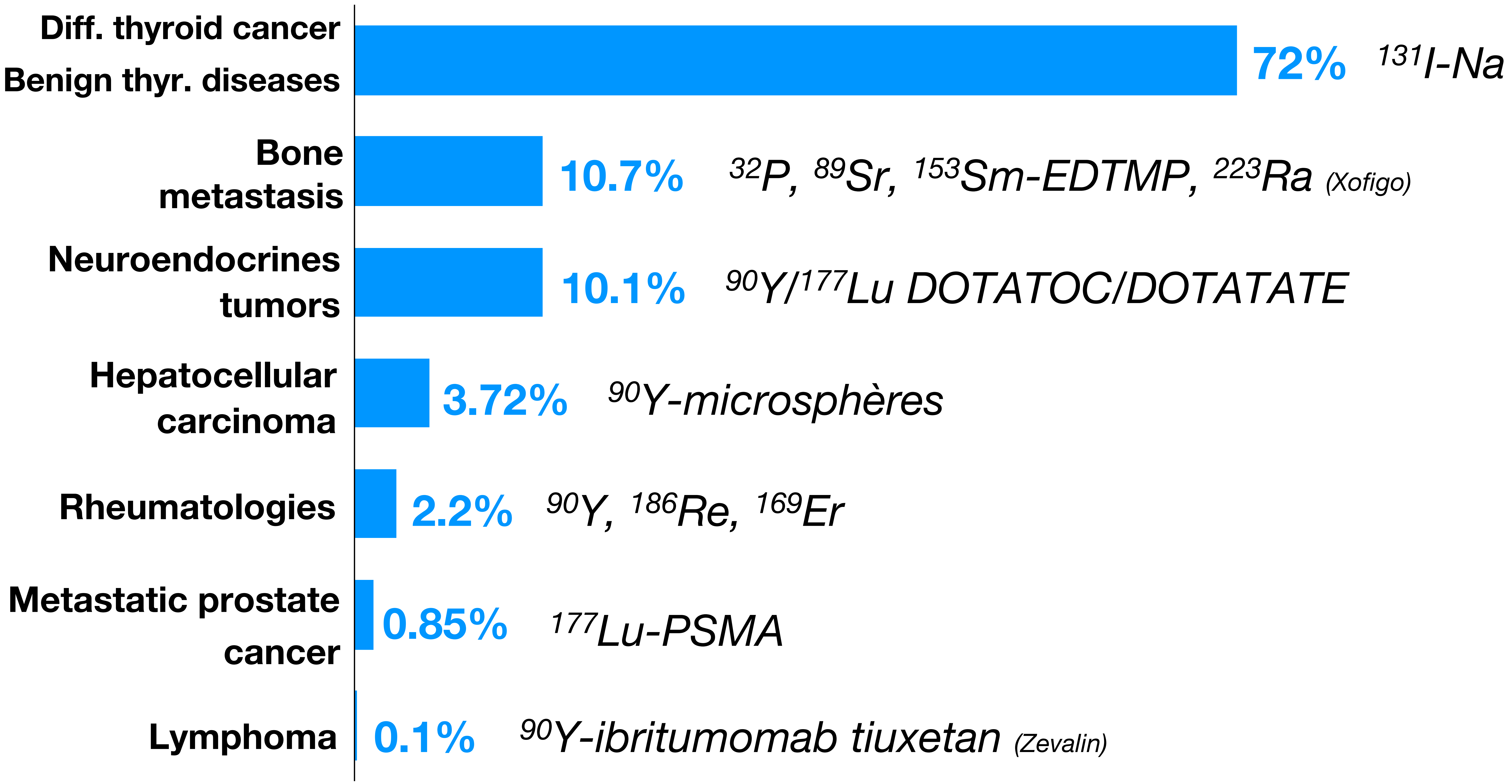
Molecular Radiotherapy

Radiopharmaceutical

Radionuclide + **Molecule**

Radionuclide	Molecule
Cells irradiation through β^- or α decays	Cell targeting

Most diffuse MRT procedures in Europe (42.500 treatments in 2015)



Towards more targeted therapies : new radiopharmaceuticals (peptides, antibodies) combined with novel radionuclides emitting alpha (^{211}At, ^{225}Ac, ^{149}Tb,…) or beta (^{47}Sc, ^{67}Cu, ^{177}Lu, ^{212}Pb,…) particles

Molecular Radiotherapy

Necessary to minimize the effect to healthy cells, while maximizing those of the target for which the radiological treatment is intended

- ✓ Big differences in the observed effects (response and toxicity) [1]
- ✓ Effects are dependent on the Absorbed dose (Gy = J/kg) delivered to the tissues [1]

↓

Need of a personalized dosimetry to reach the highest reasonably achievable treatment efficiency

[1] Strigari, Lidia, et al. "The evidence base for the use of internal dosimetry in the clinical practice of molecular radiotherapy." European journal of nuclear medicine and molecular imaging 41.10 (2014): 1976-1988.

Dose assessment in radionuclide therapy

$$D = \tilde{A} \times S$$

Cumulated activity

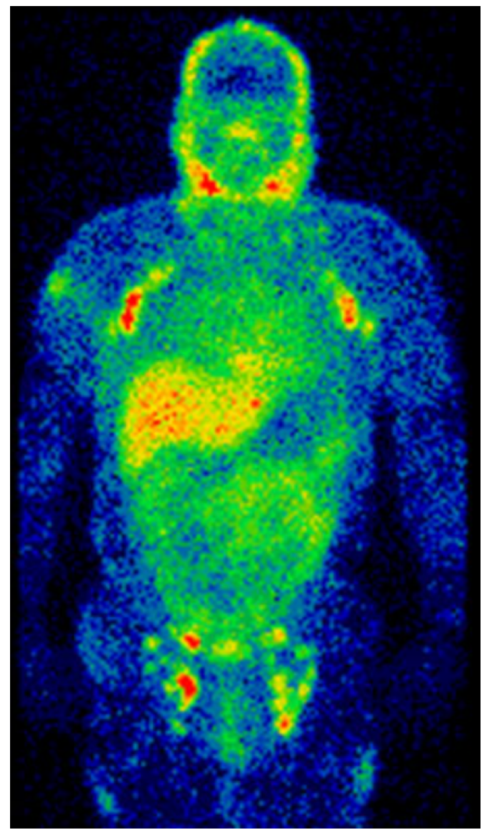
Mean dose for unit Ã

- Indirectly with compartmental models
- Directly measuring the A over time

Non-imaging

- Tissue biopsies
- Blood samples
- Excreta (urine and feces)
- Using external counting probes

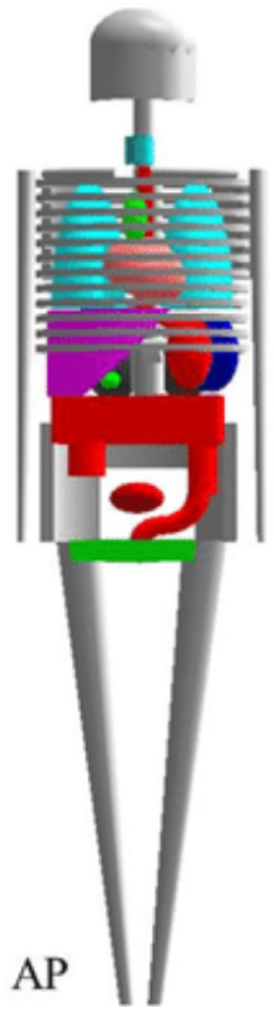
Imaging



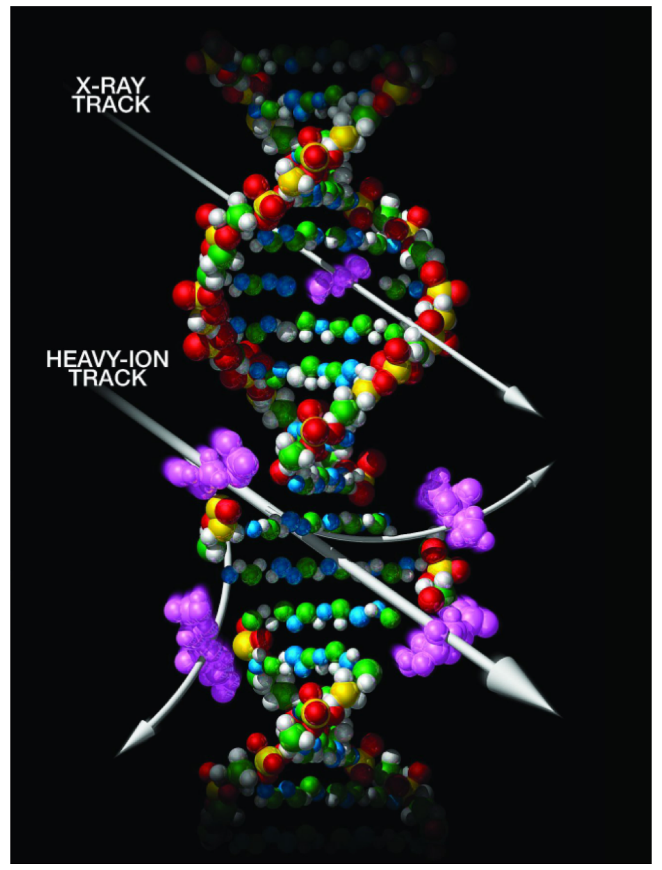
Need of quantification

Numerical Simulations

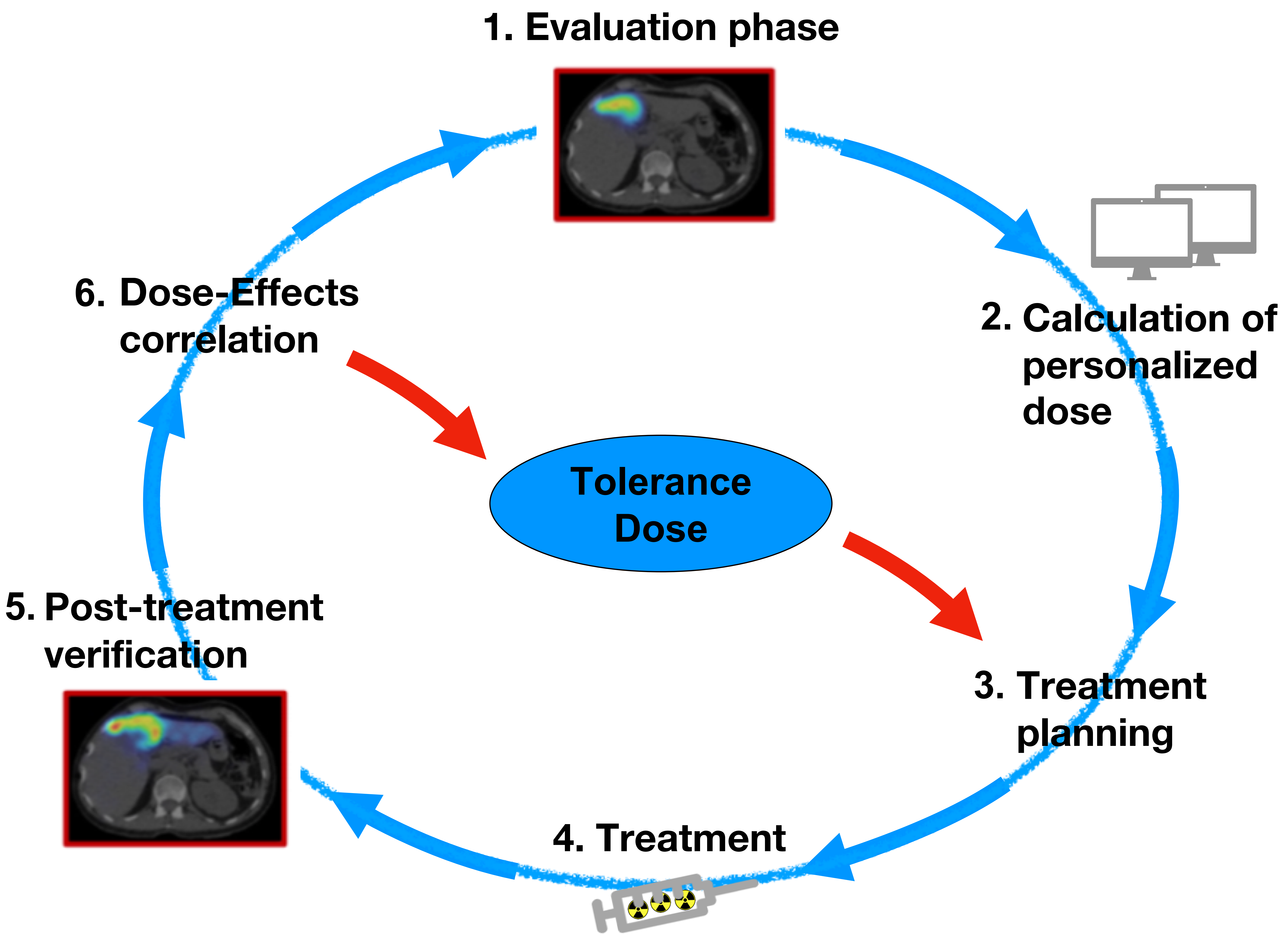
- Anatomical models



- Energy deposit calculation



Role of dosimetry in internal radiotherapy



Dose-based treatment planning : determine the activity to be injected according to the desired clinical outcomes and tolerance doses of organs at risk

Post-treatment verification : control that the absorbed dose corresponds to the one estimated from the evaluation phase

Correlation between the dose released to the tumors/organs at risk and the clinical effects

Current procedures : a lack of individualized dosimetry

European Council

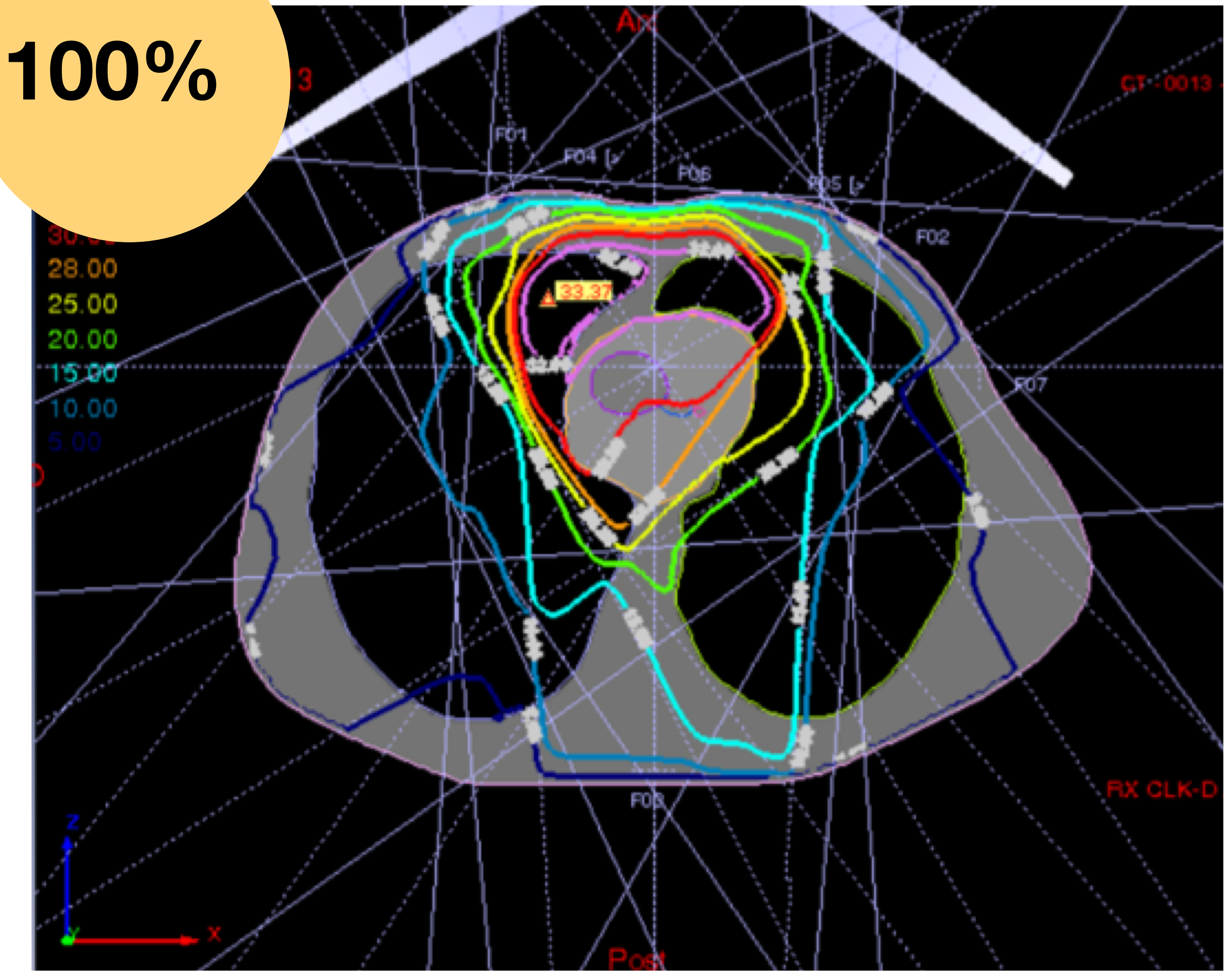
Directive 2013/59,

Article 59

For all medical exposure of patients for radiotherapeutic purposes, exposures of target volumes shall be individually planned and their delivery appropriately verified, taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure.

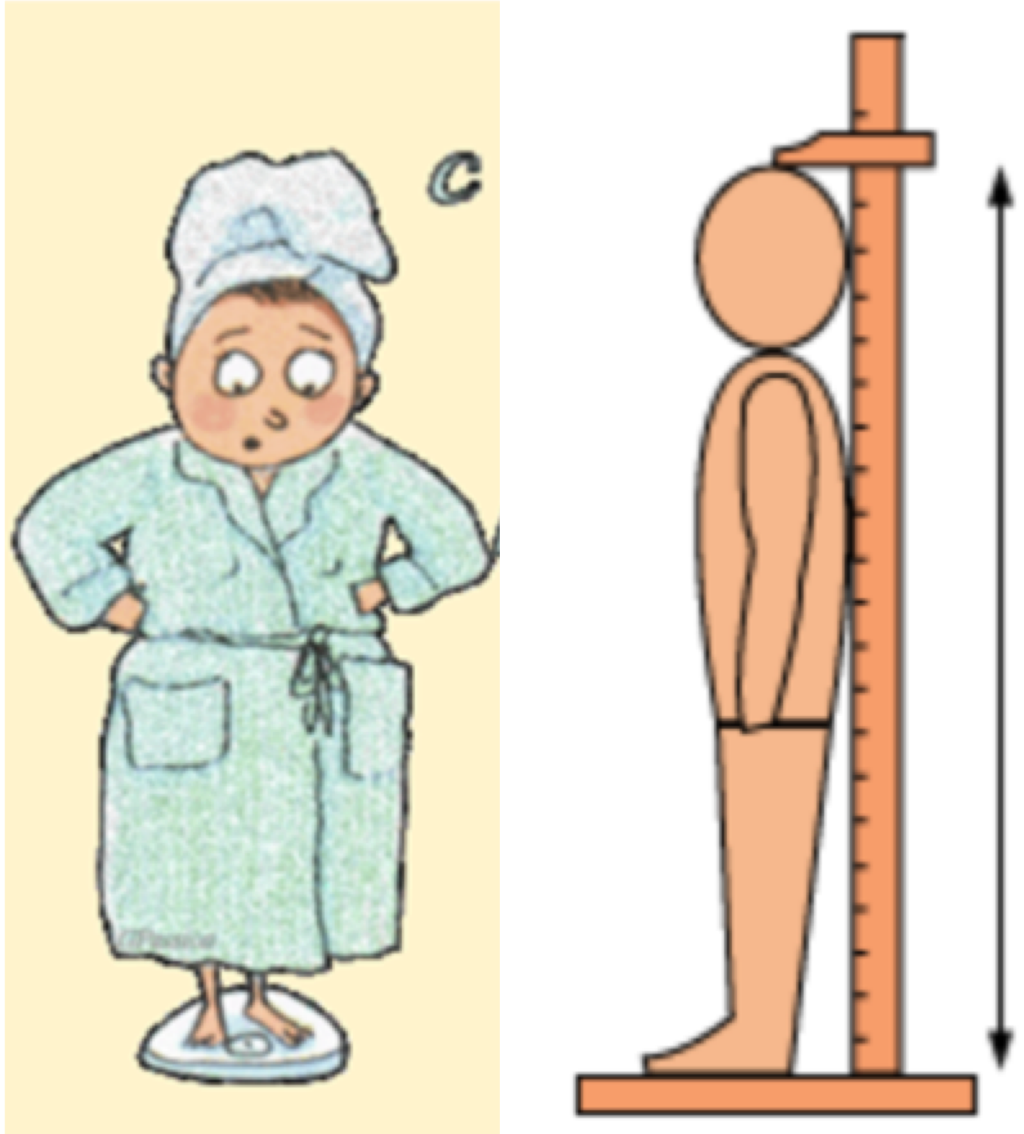
Dosimetry in external radiotherapy or brachytherapy

100%



Dosimetry Molecular Radiotherapy

Fixed activity protocols



36%

Dose-based planification

26%

Post-therapy control

Challenges and constraints of dosimetry for MRT

Why lack of dosimetry-based treatment planning and post-treatment verification nowadays?

Existing protocols considered to be well working

Dosimetric protocols are heavier and time consuming

Patient accessibility (radiation safety)

No availability of the existing cameras for treatment imaging

Lack of specified gamma cameras for quantitative imaging

Challenges and constraints of dosimetry for MRT

Improve the individual quantitative assessment of the heterogeneous distribution and biokinetics of ^{131}I before and after treatment administration for thyroid diseases

Development of a high-resolution mobile camera, 10x10cm² Field of View, for imaging with high energy gamma rays (>300 keV) **and high photon fluence rates** (200 kcps @ 364 keV)

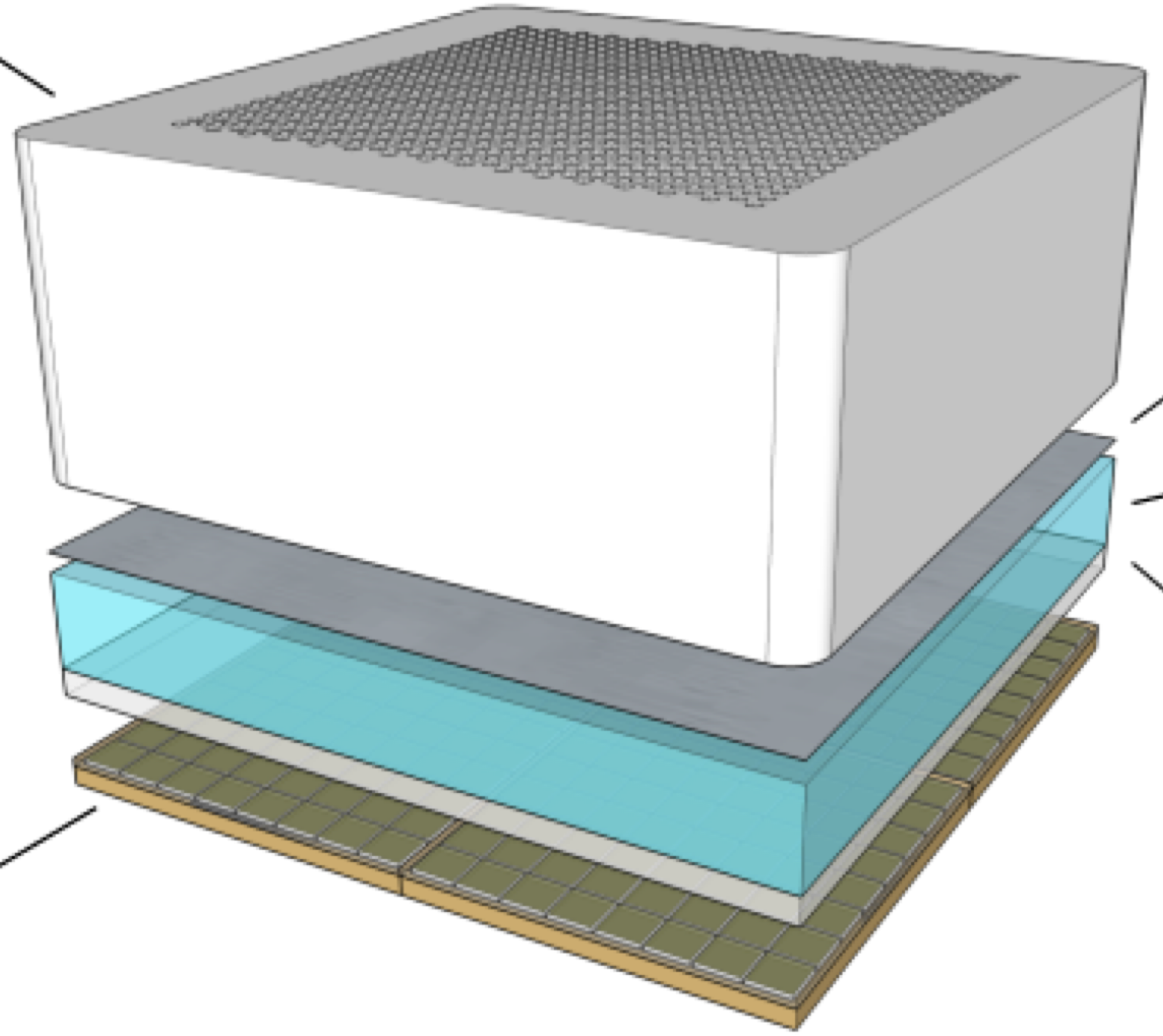
Mobility to perform exams at the patient's bedside or in an isolated room for an accurate temporal sampling of the ^{131}I biokinetics

Compactness to improve image contrast (reduced camera/source distance and optimized angular view)

High spatial resolution (3 to 6 mm FWHM) to improve detectability and quantification of small activity heterogeneities (reduction of the partial volume effect)

High energy resolution (<8% FWHM @ 364 keV) to reduce scatter from high energy gamma rays

Design of the miniaturized gamma camera



Proof of concept prototype

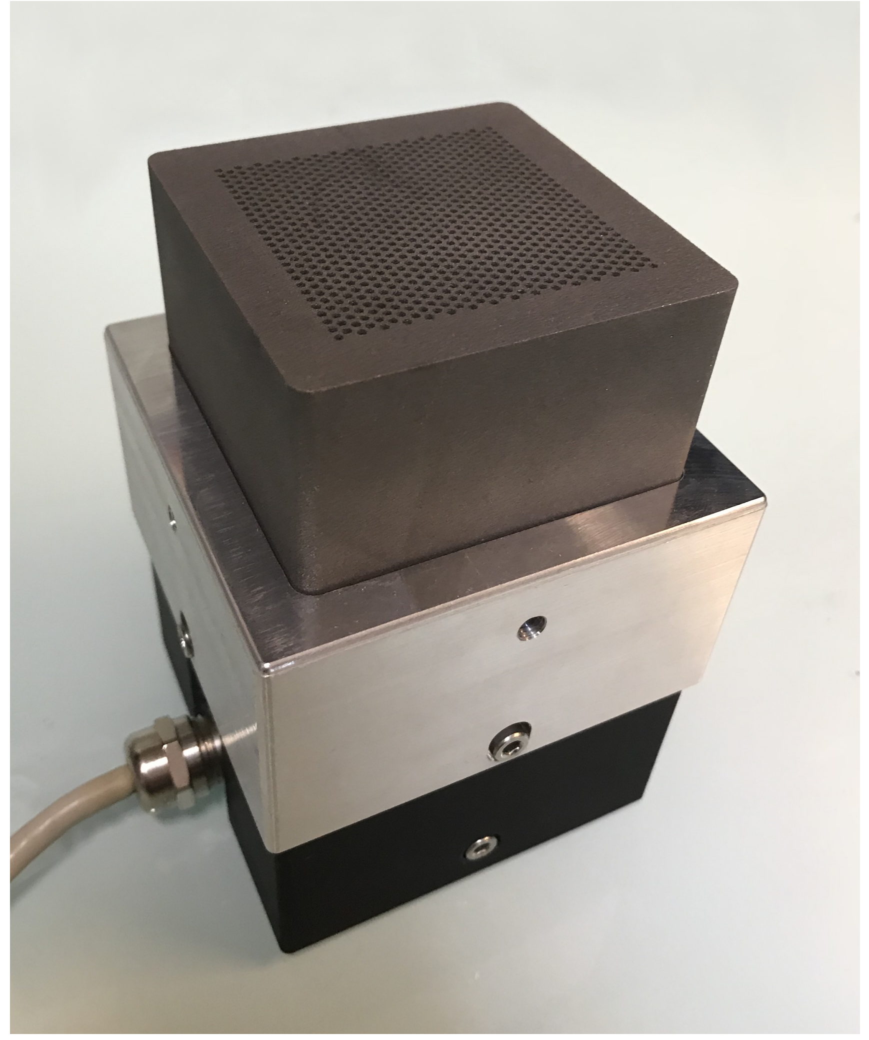
$5x5cm^2$ FoV proof of concept prototype

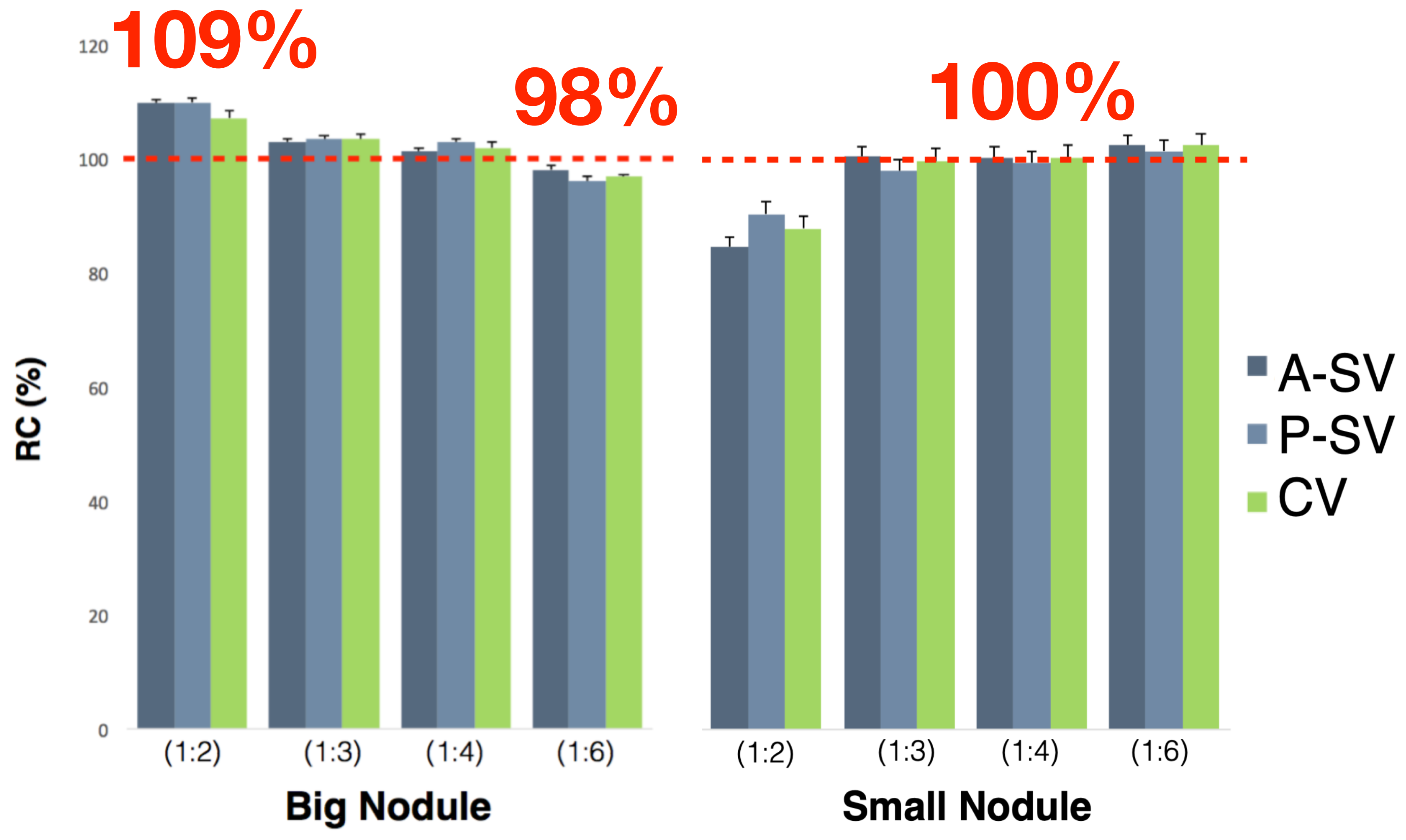
Design

- 256 Hamamatsu S13361-6050NE-04 monolithic arrays ($3x3\ mm^2/50\mu m$) mounted on a single PCB (Four 8x8 arrays)
- Custom acquisition electronics made at LAL Laboratory
- 6mm thick $CeBr_3$ continuous scintillator with reflective coated edges

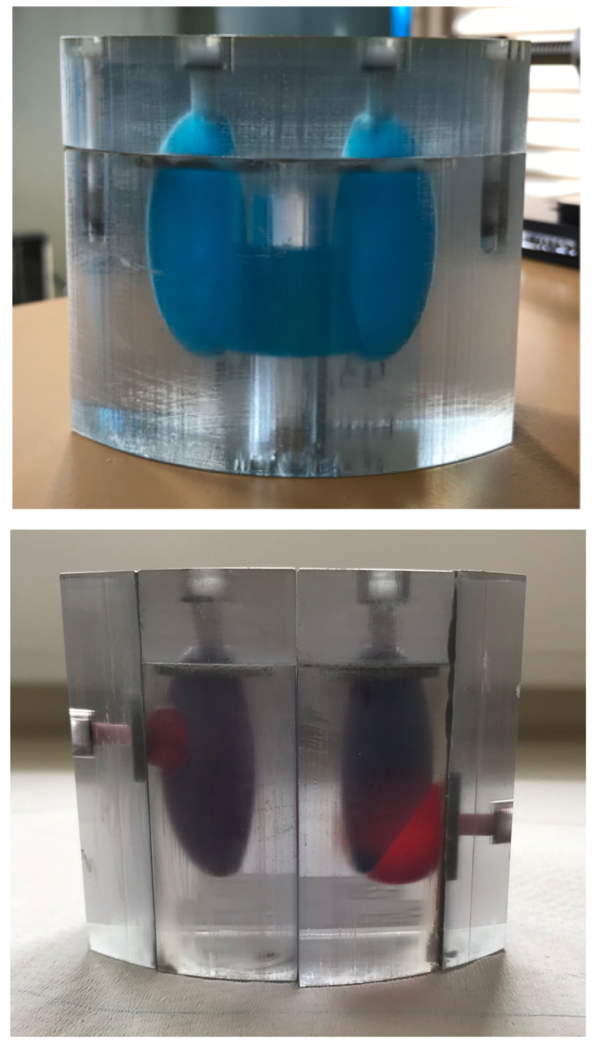
Intrinsic performances

- Energy resolution @ 364 keV : 7.86% FWHM
- Spatial resolution : 0.61 mm FWHM
- Acquisition rate : ~13 kcps

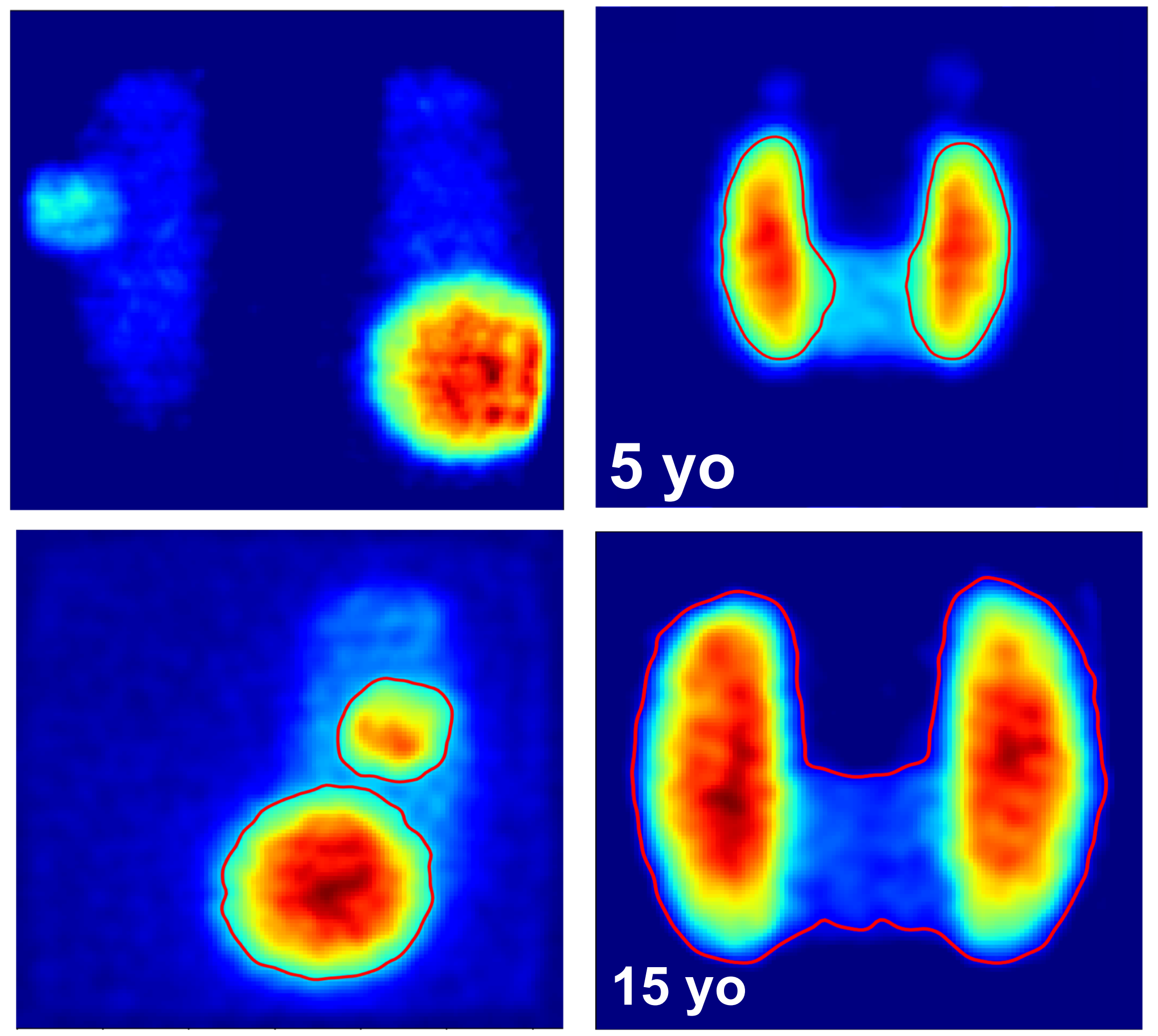




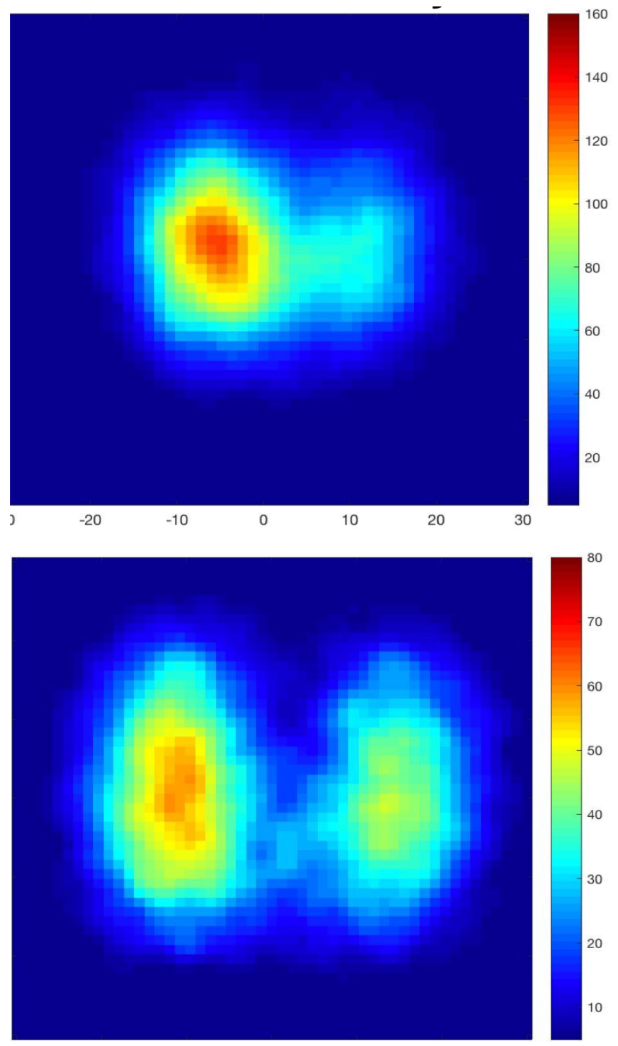
Thyroid phantoms (IRSN)



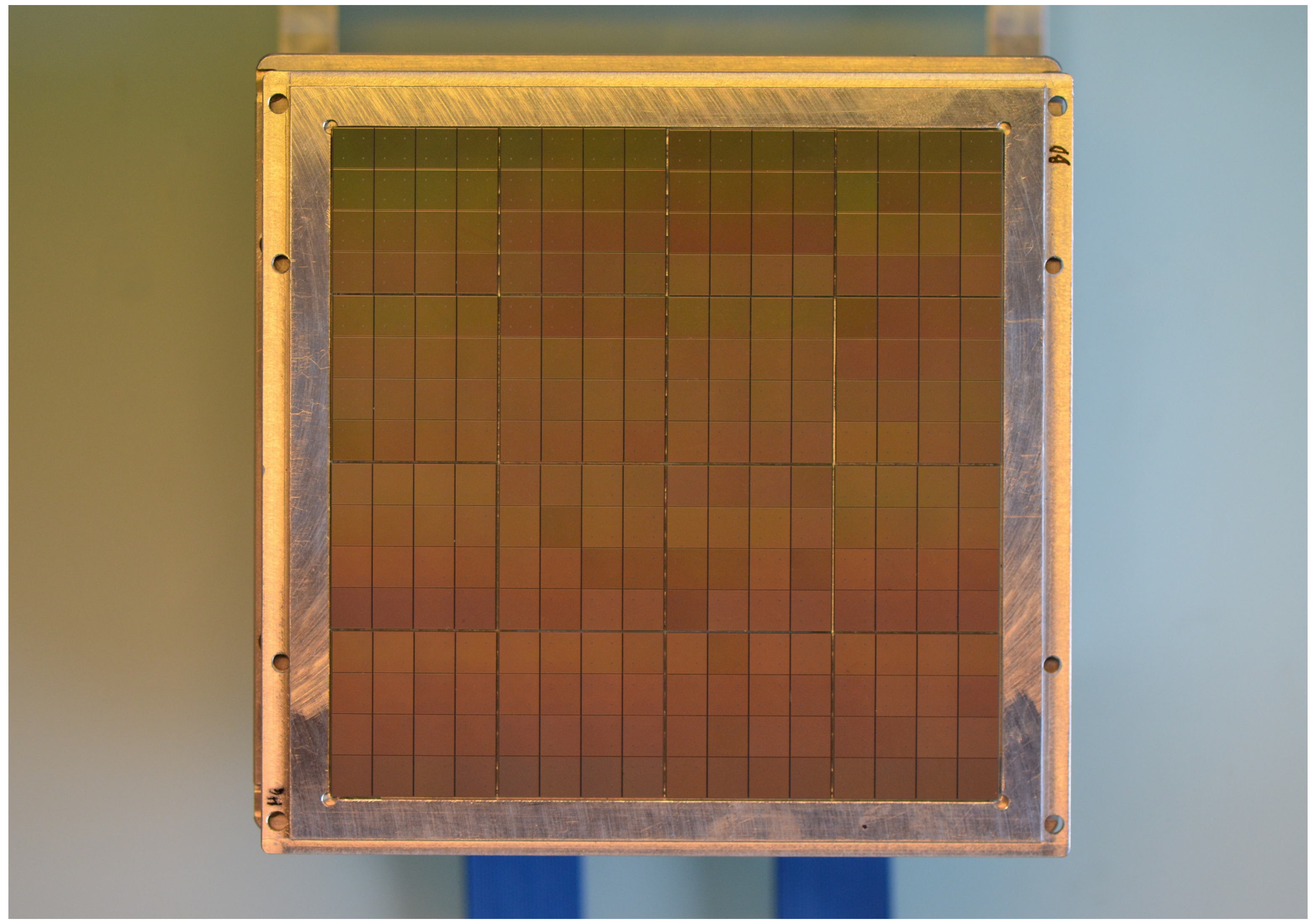
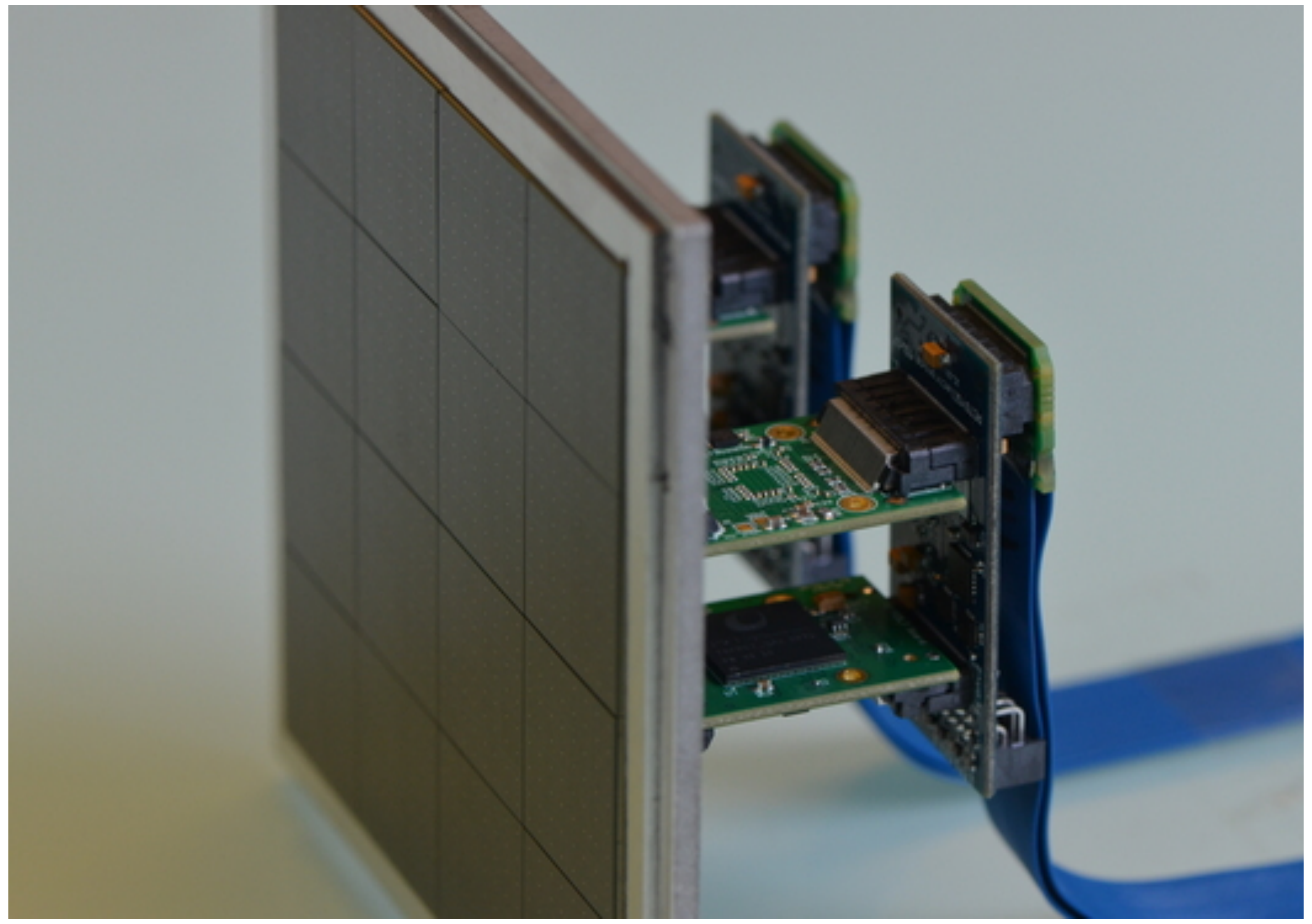
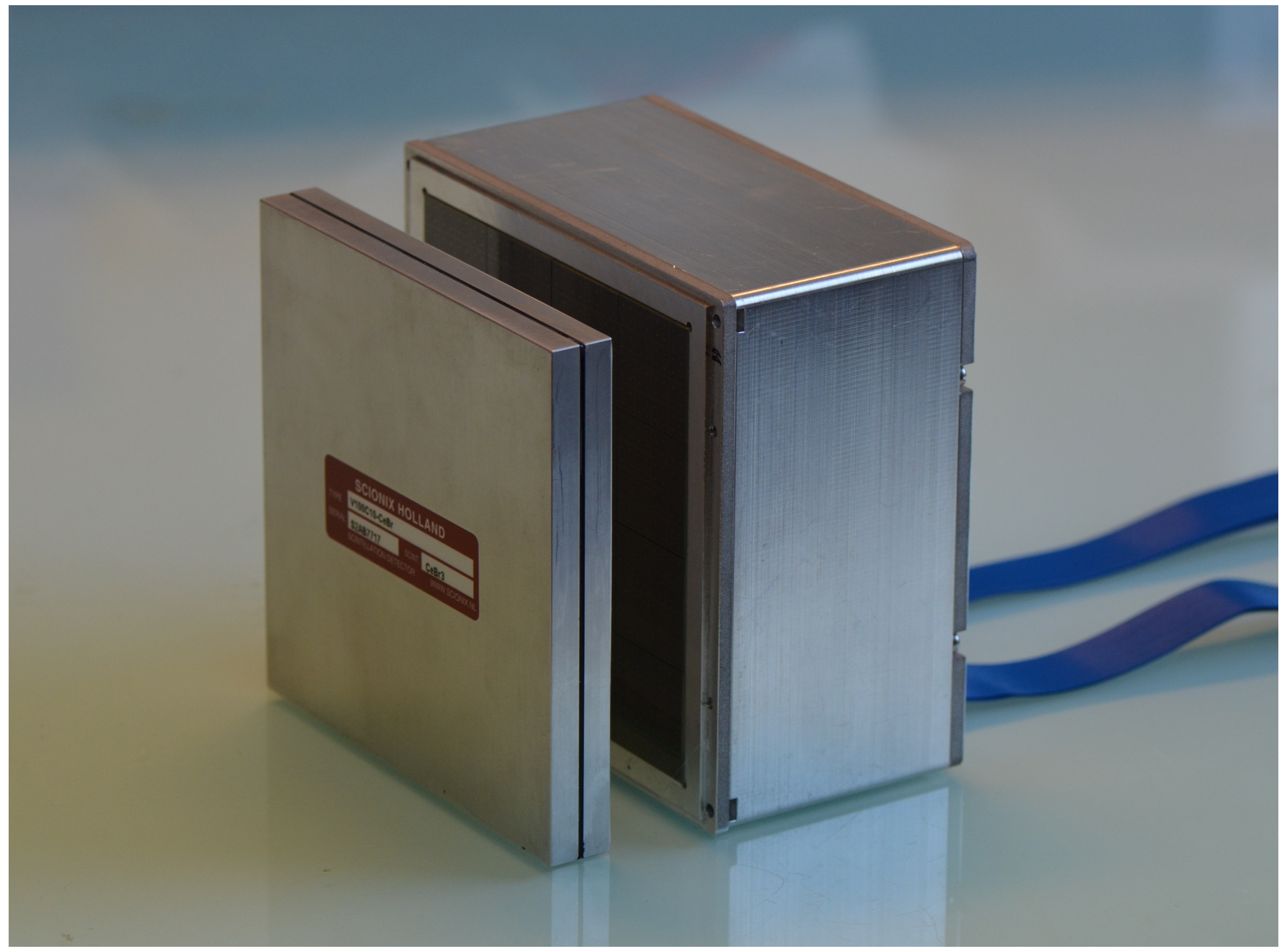
Mobile camera Anterior (A) view
SR 3.1 mm @ 5cm



Siemens Symbia T2
SR 13.4 mm @ 10 cm



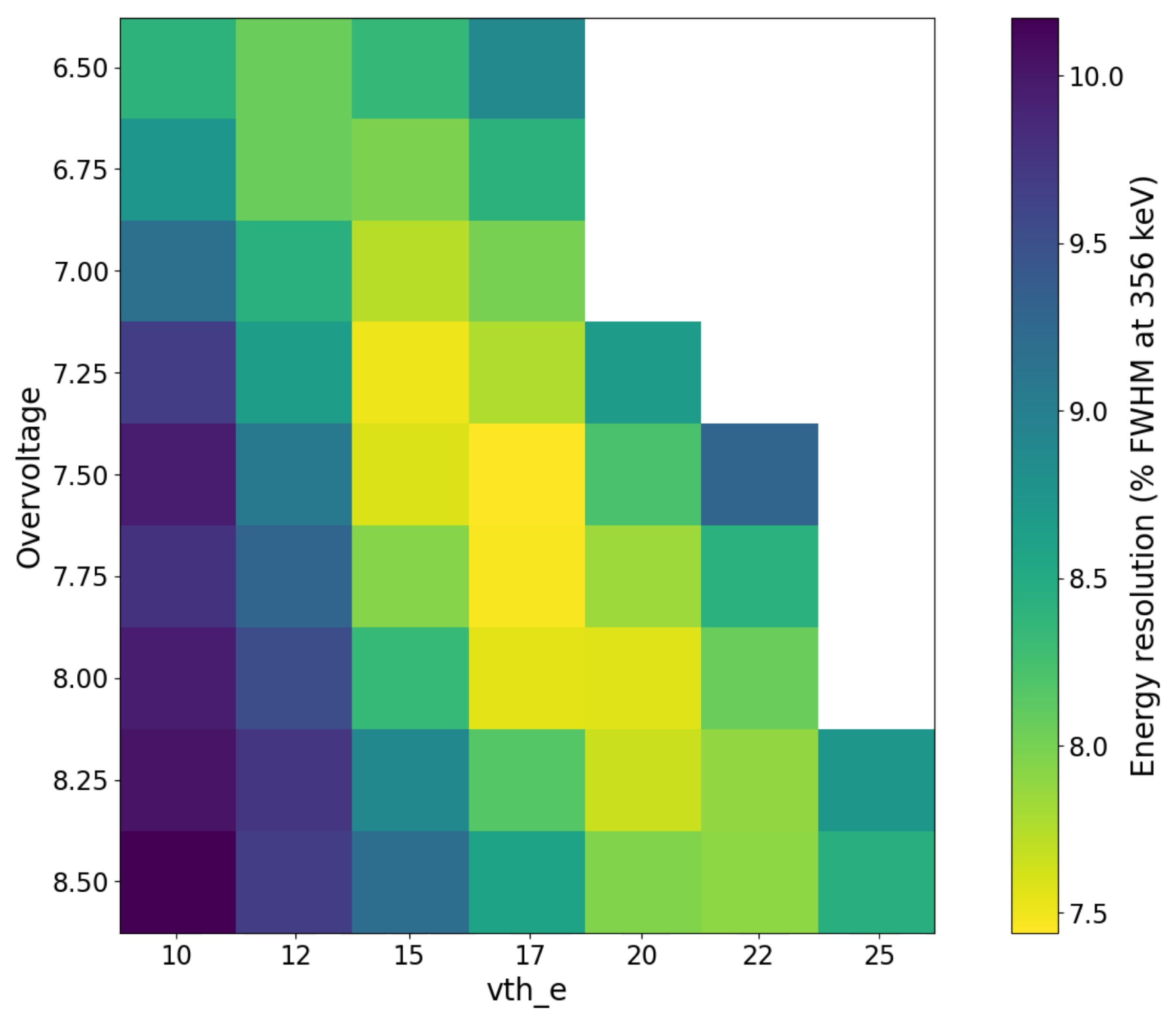
10x10cm² Field of View clinical prototype

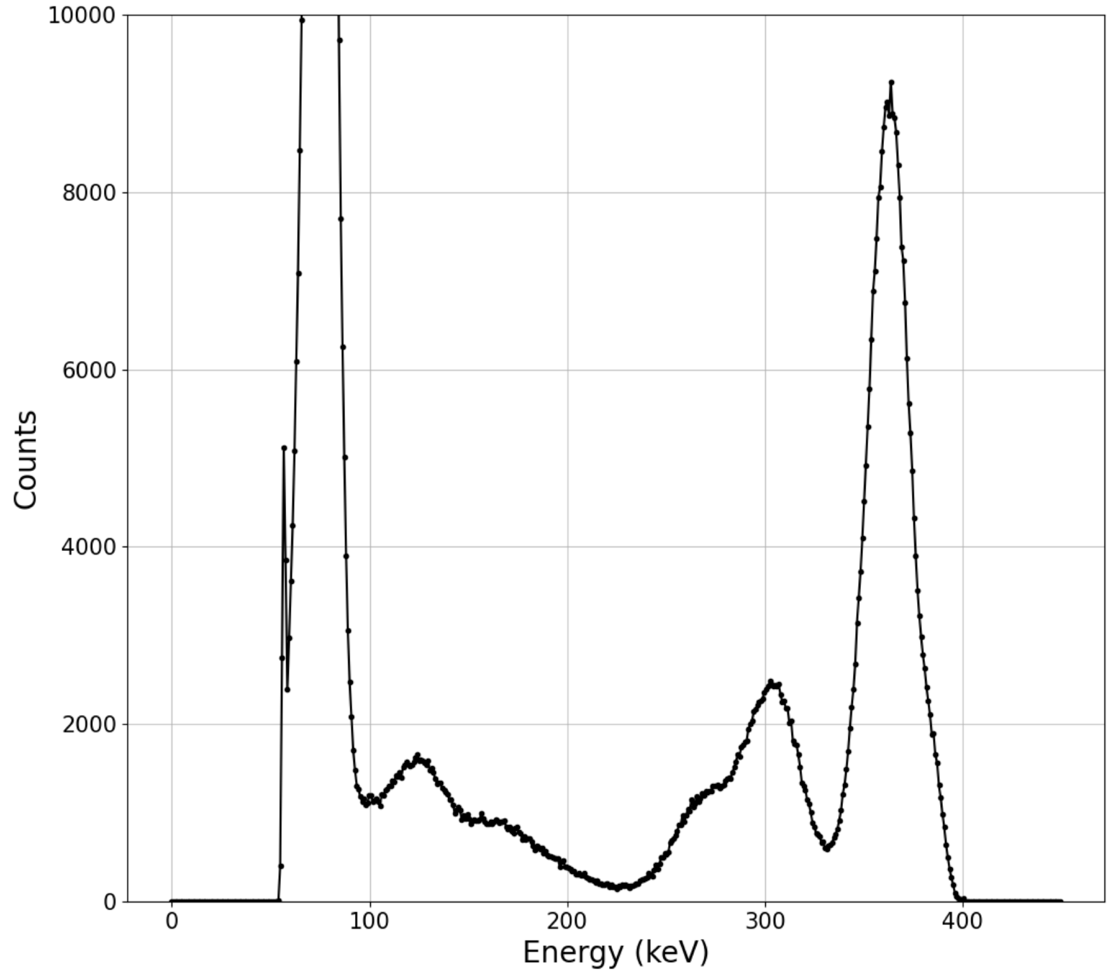
The photodetection system

- 256 Hamamatsu S13361-6050NE-04 monolithic arrays (6x6 mm²/50µm) mounted on an interface PCB (Sixteen 4x4 arrays)
- 10x10cm² and 1 cm thick $CeBr_3$ continuous scintillator with reflective coated edges
- Commercial acquisition electronics (TOFPET 2B ASICs - PETSys Electronics)
- Spatial coincidence trigger to reject dark counts
- Acquisition dead time < 1% at 150 kevents/s

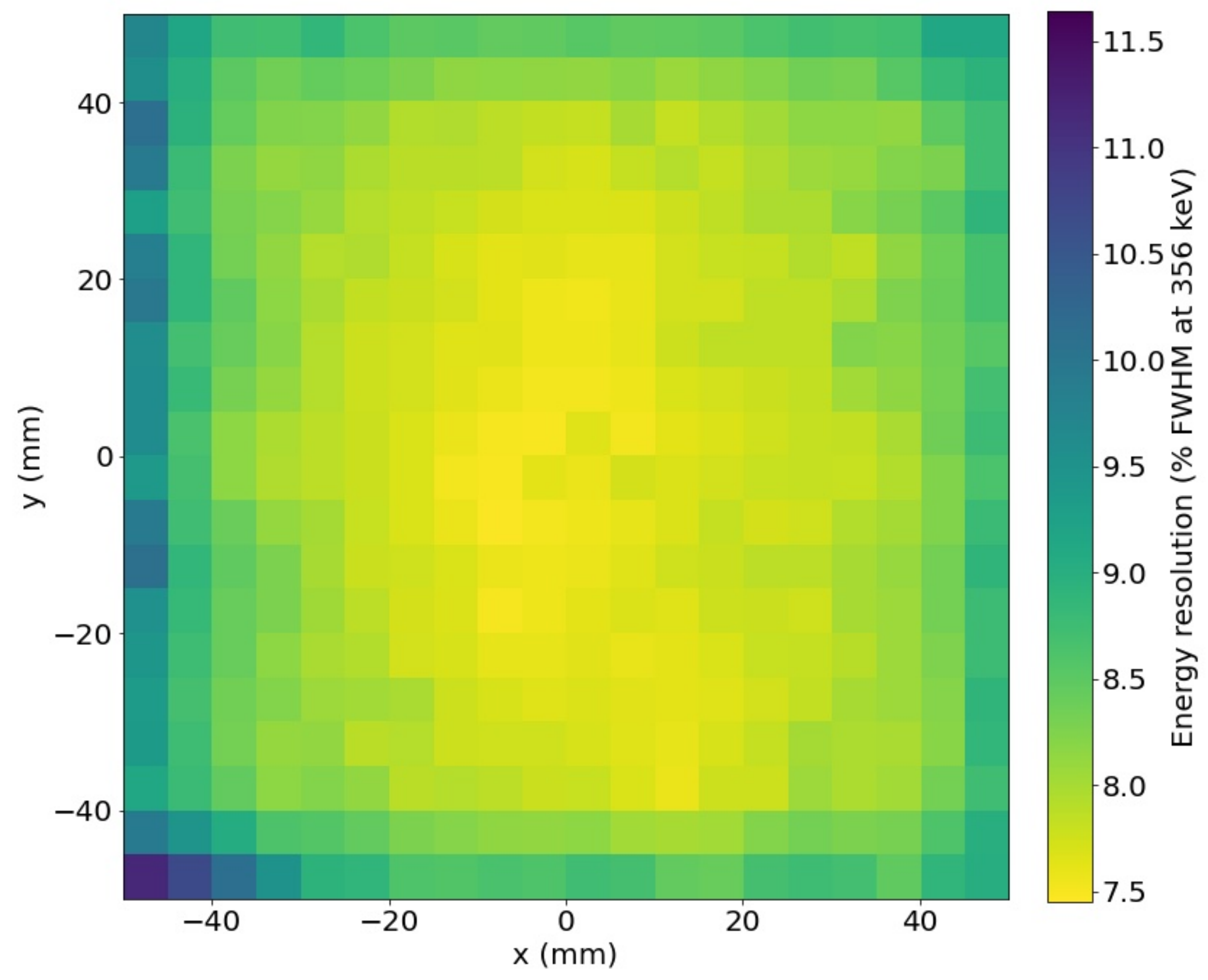
Intrinsic performances : energy response



Energy resolution vs electronics and detector settings



133-Ba spectrum (central FoV)



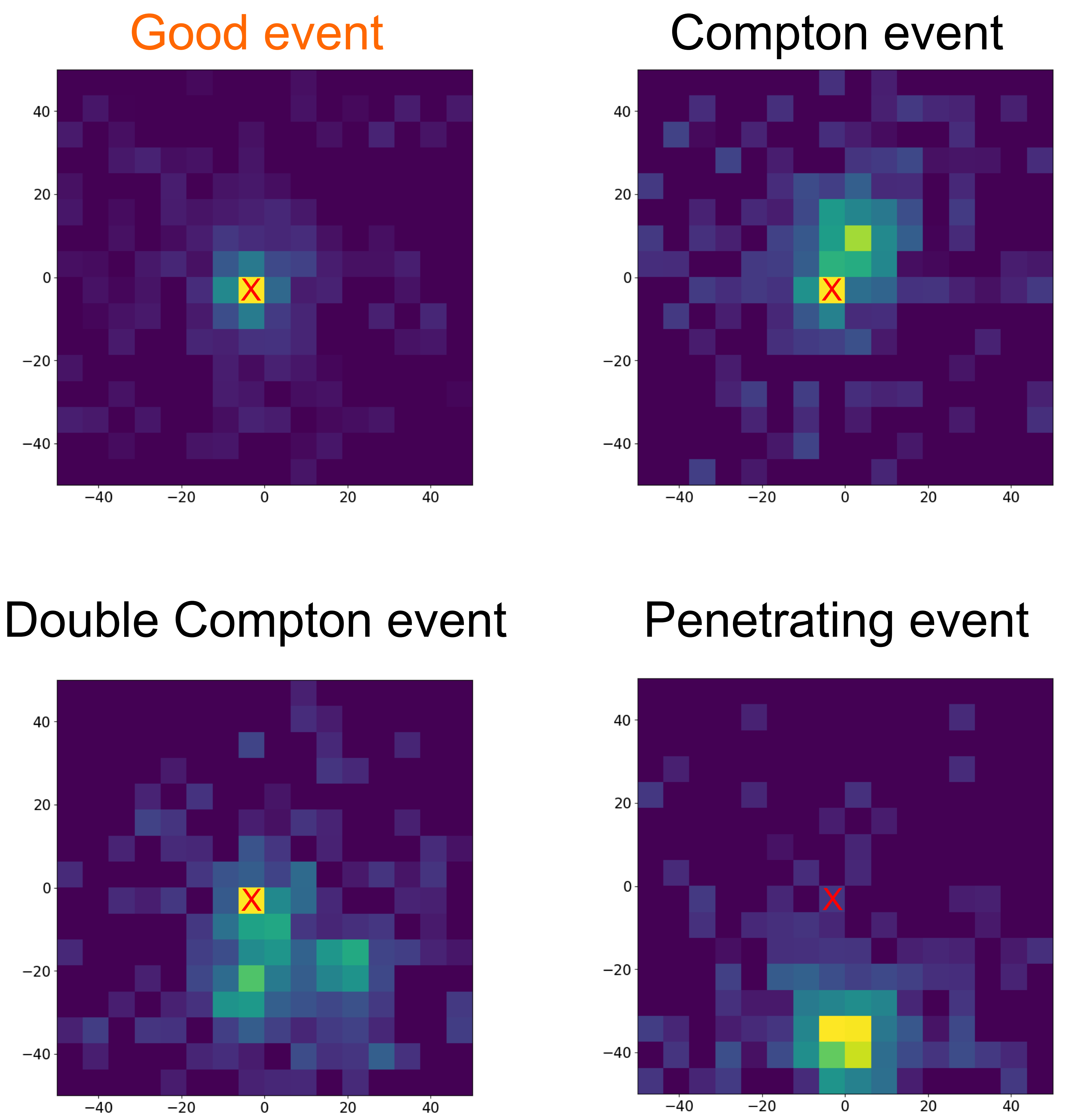
Energy resolution map

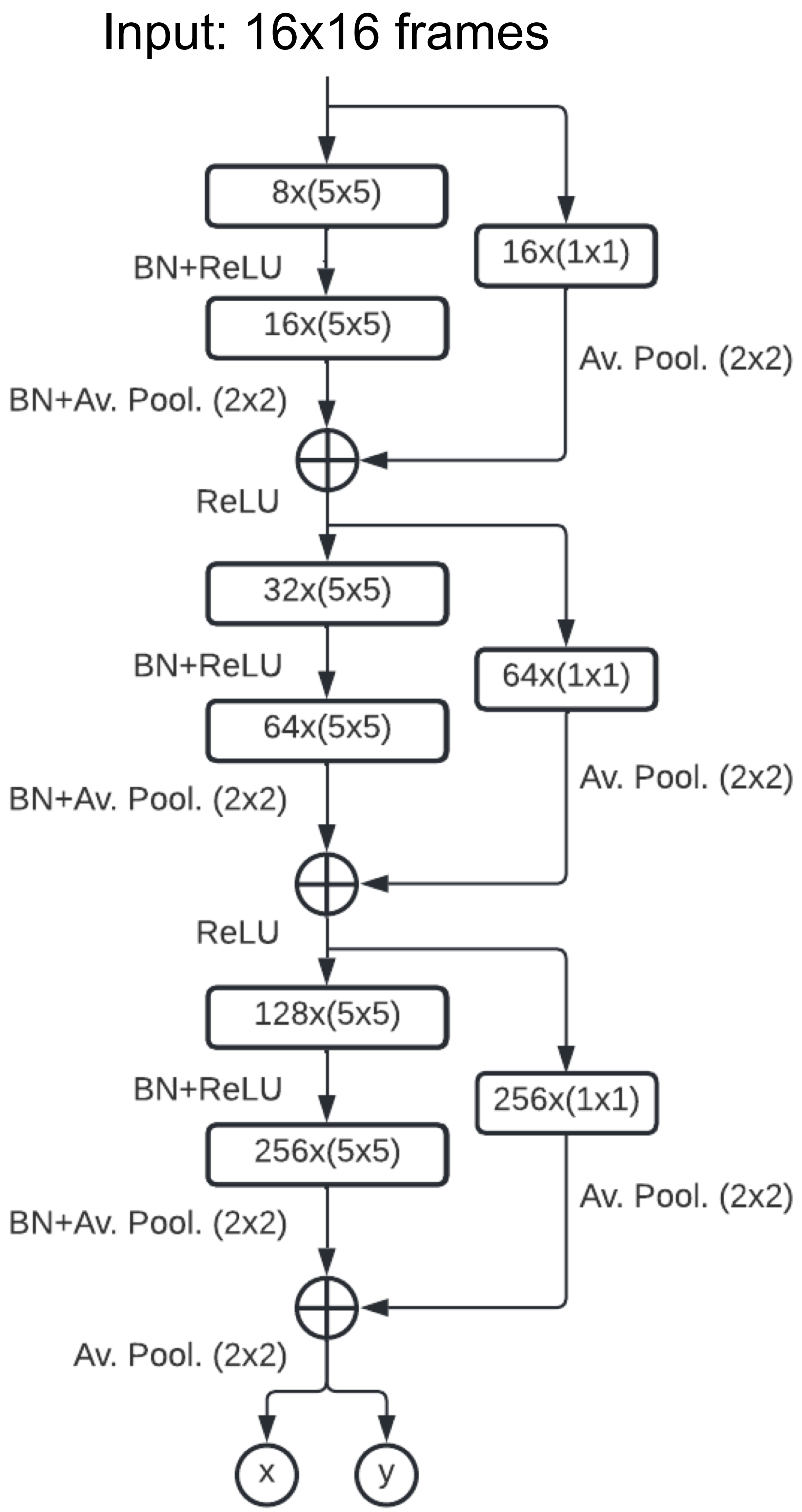
Intrinsic performances evaluation

- Climatic chamber at 21°C
- Collimated ^{133}Ba source (356 keV) mounted on a 3D motorized platform
- Optimal set of electronics parameters:
- ER = 8.06±0.21% in CFOV (75% of full FoV)

Deep Residual Convolutional Neural Network

- Complete scan of the FoV with a 0.5mm collimated ^{133}Ba source (356 keV) and a 1mm step (around 2 kevts/pos)
- Training dataset (800 evts/spot) with selected events
- Supervised training of a Deep Residual Convolutional neural network on the shuffled dataset
- Validation of the ability of the network to generalize on a flood field uniformity acquisition





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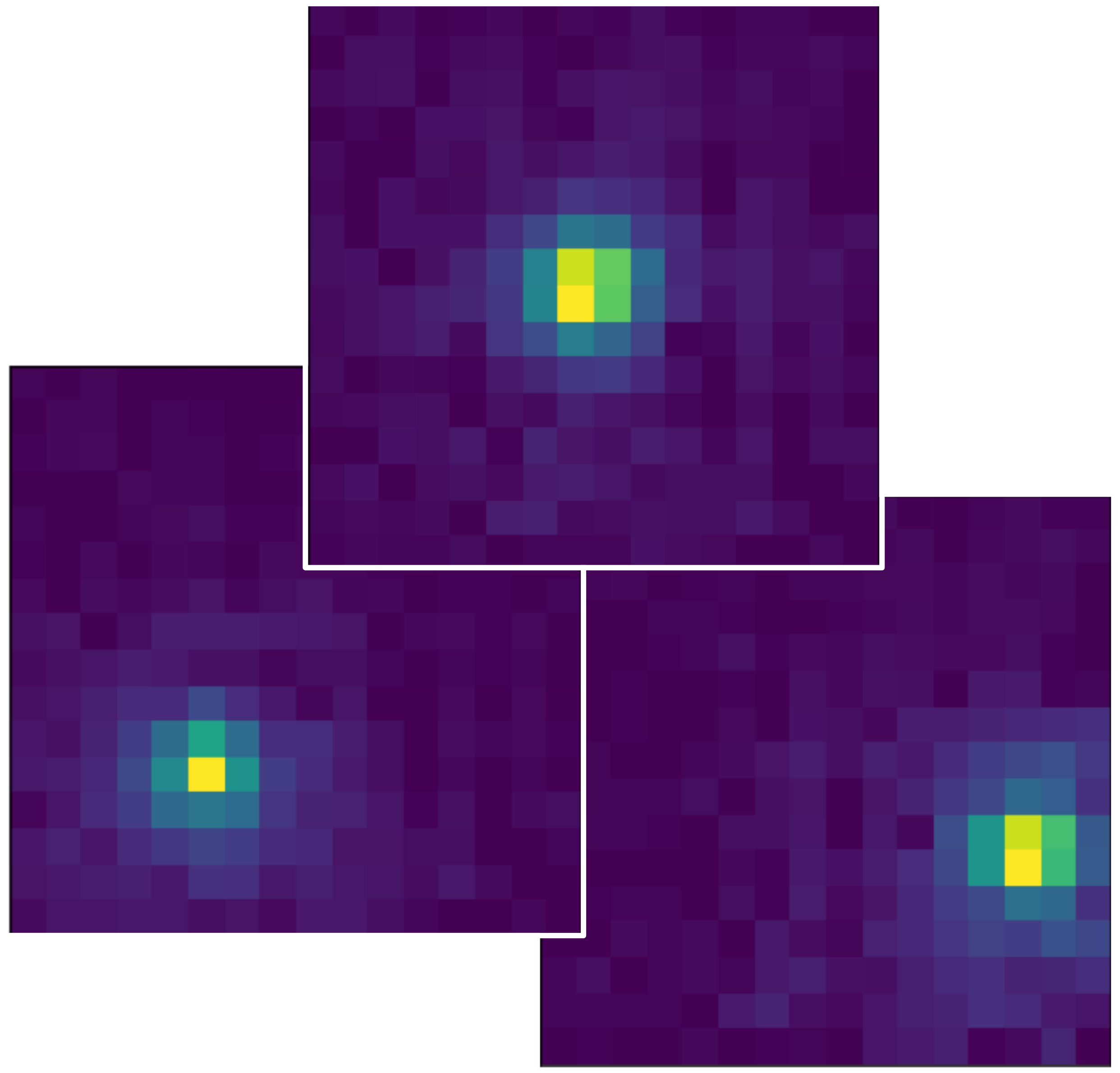
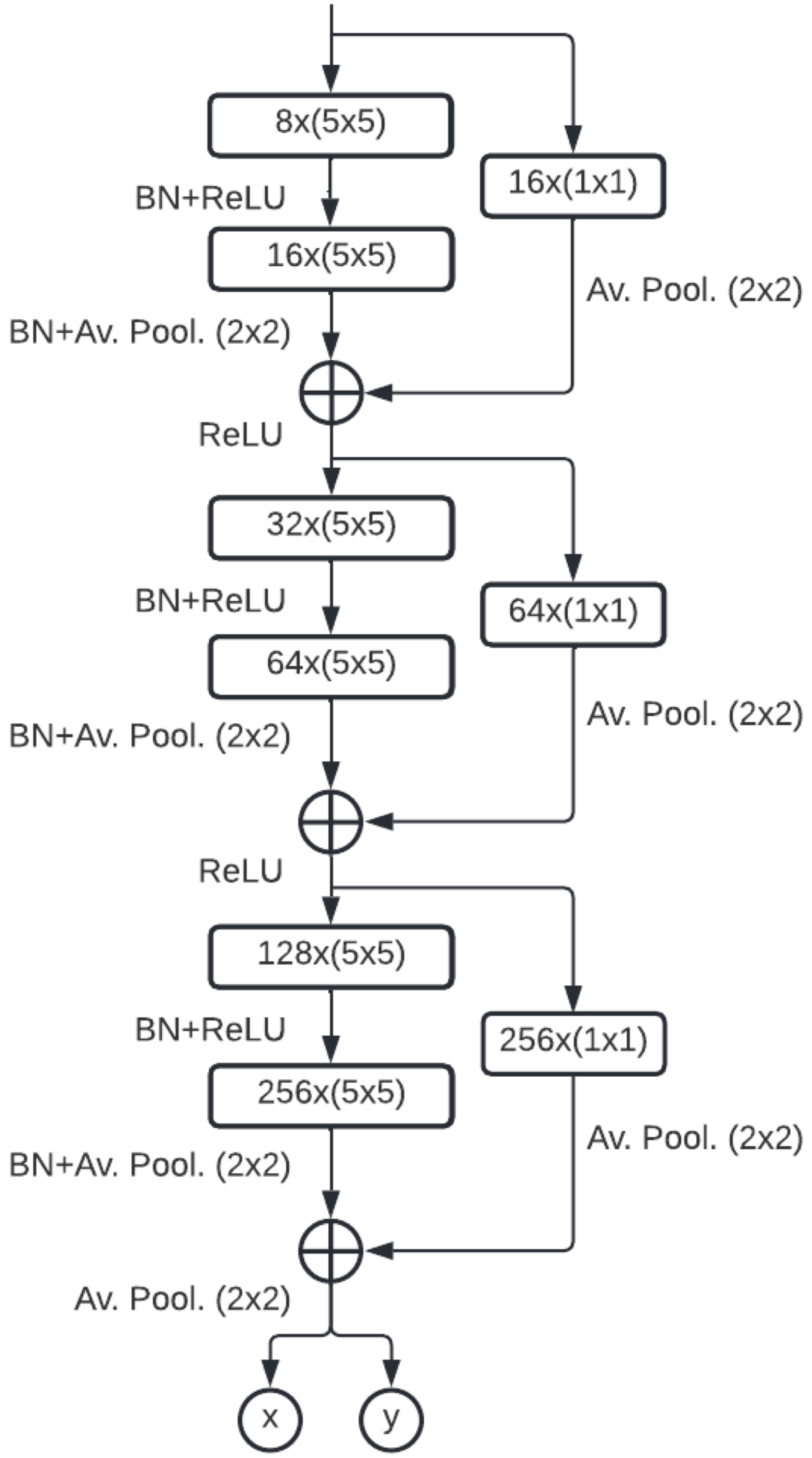


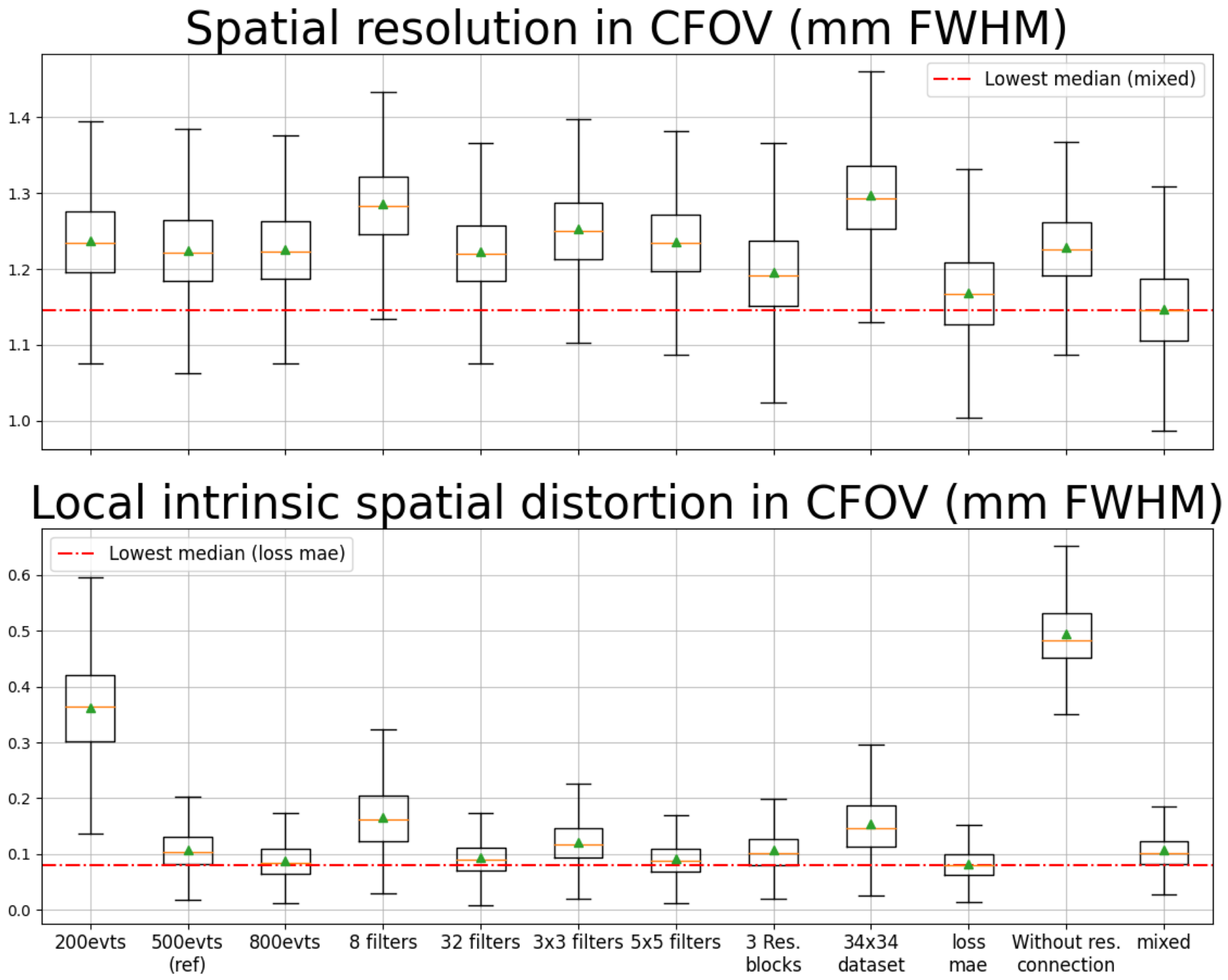
Input: 16x16 frames

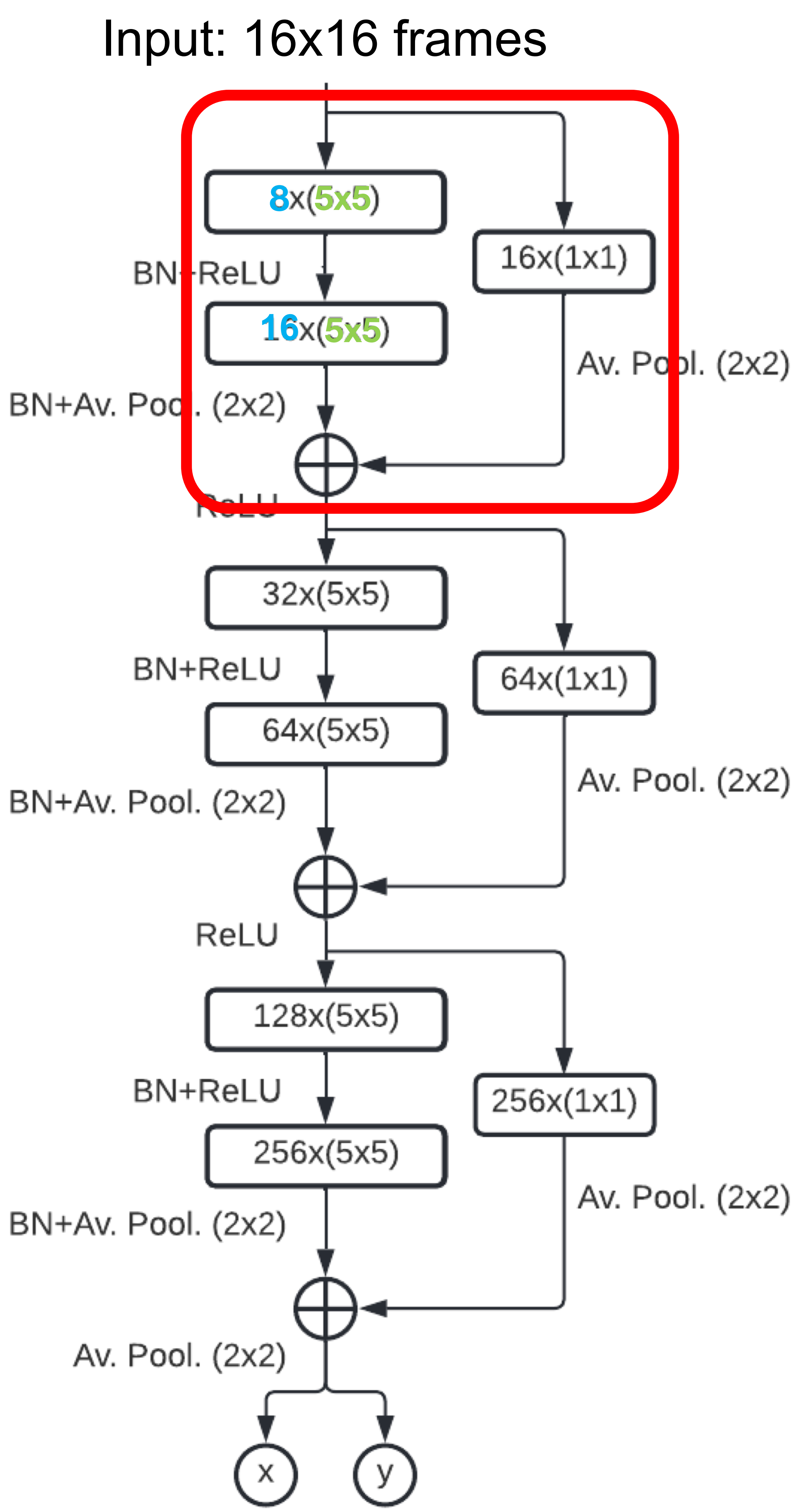


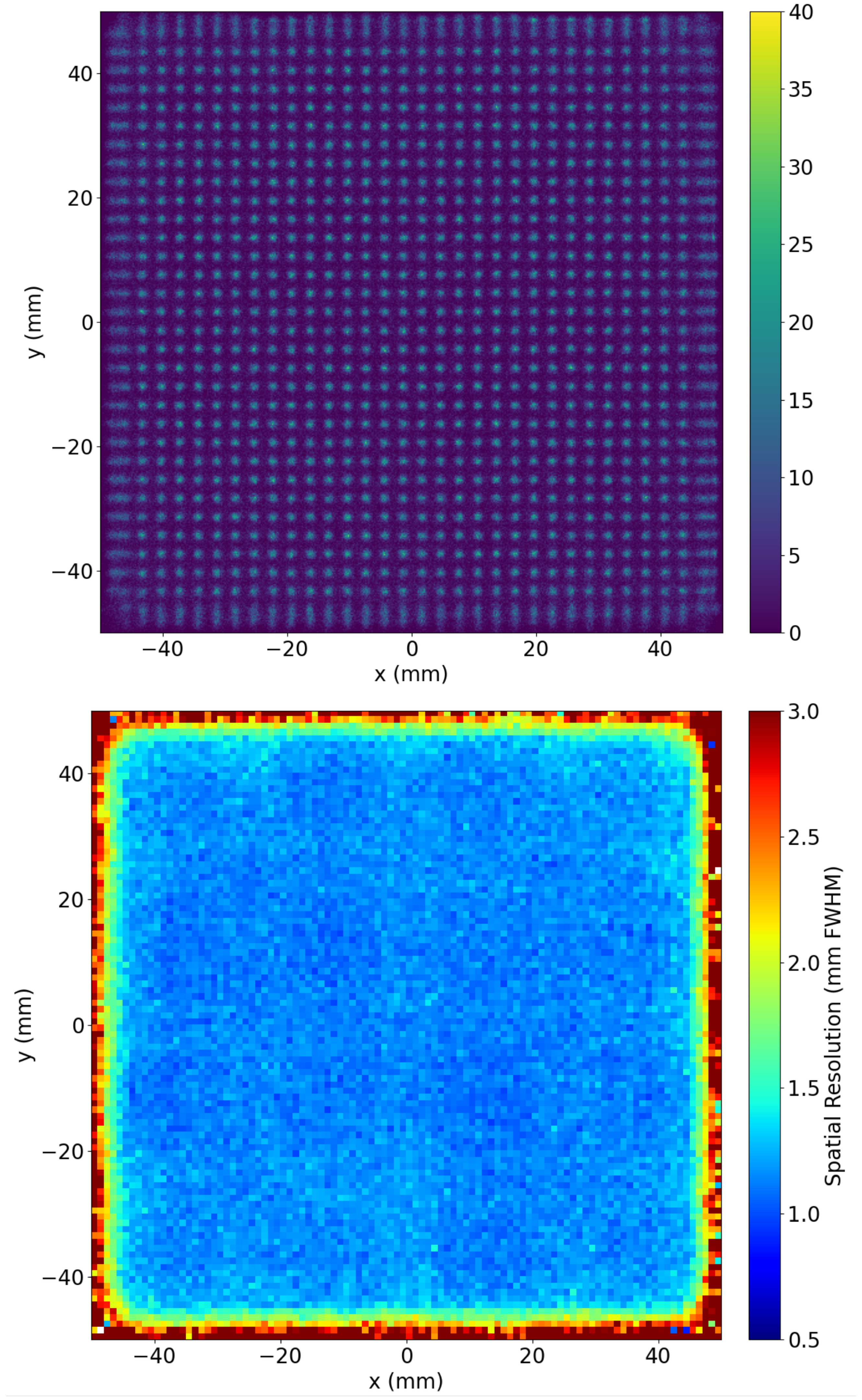
Deep Residual Convolutional Neural Network

Optimization of the Network parameters

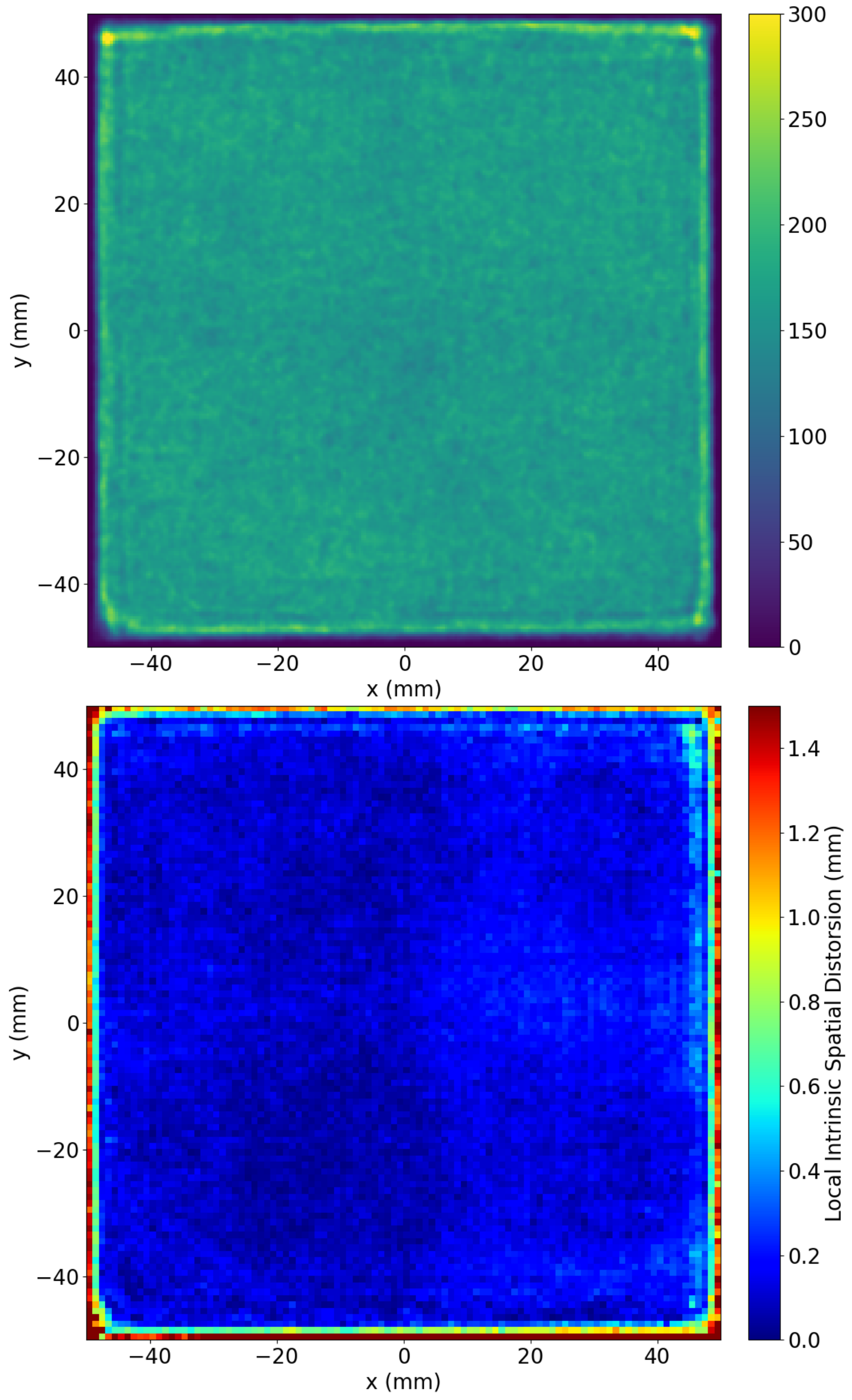
- Number of residual convolution bocks (two convolution layers + “skip” connexion)
- Number of filters for each layer
- Size of the filter (3x3 and 5x5)
- Loss function (MSE and MAE)
- Size of the training data set (200-800 evts for each position)
- Step of the training data set (1 and 2 mm)







Resolution map



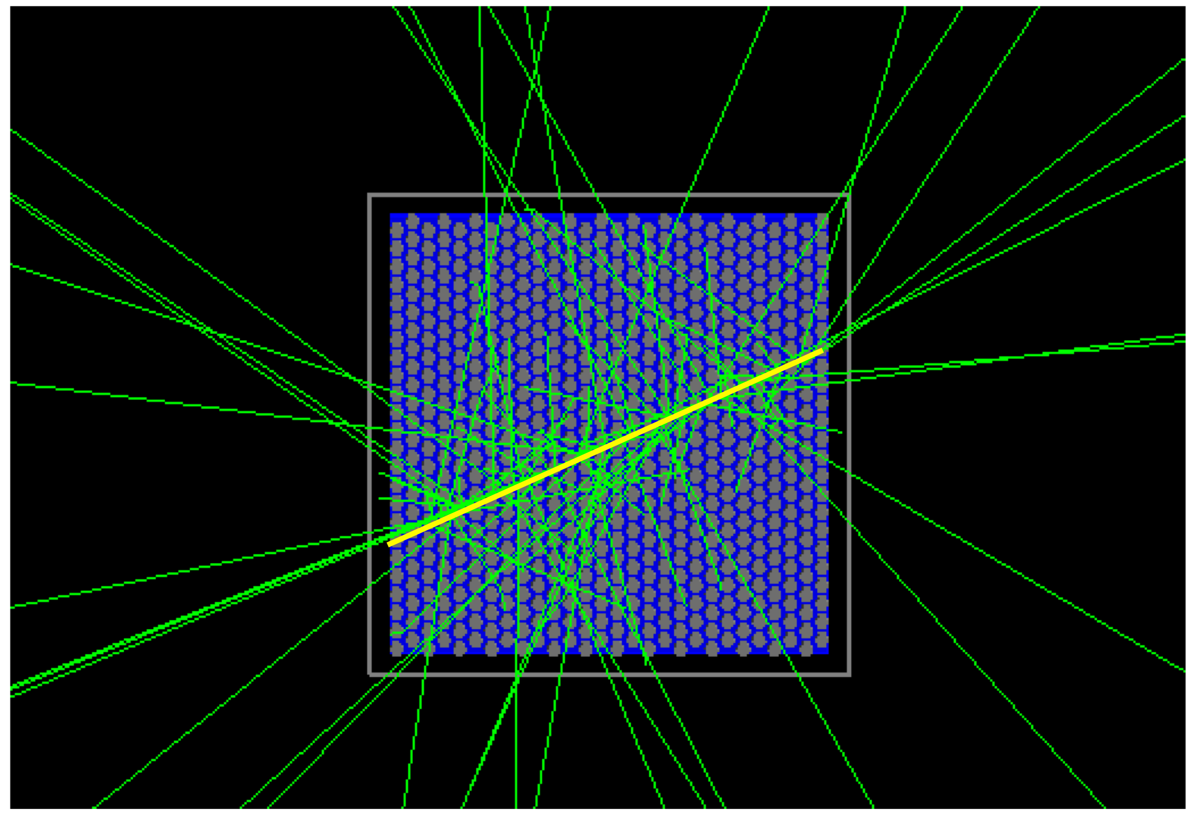
Distortion map

Neural Network

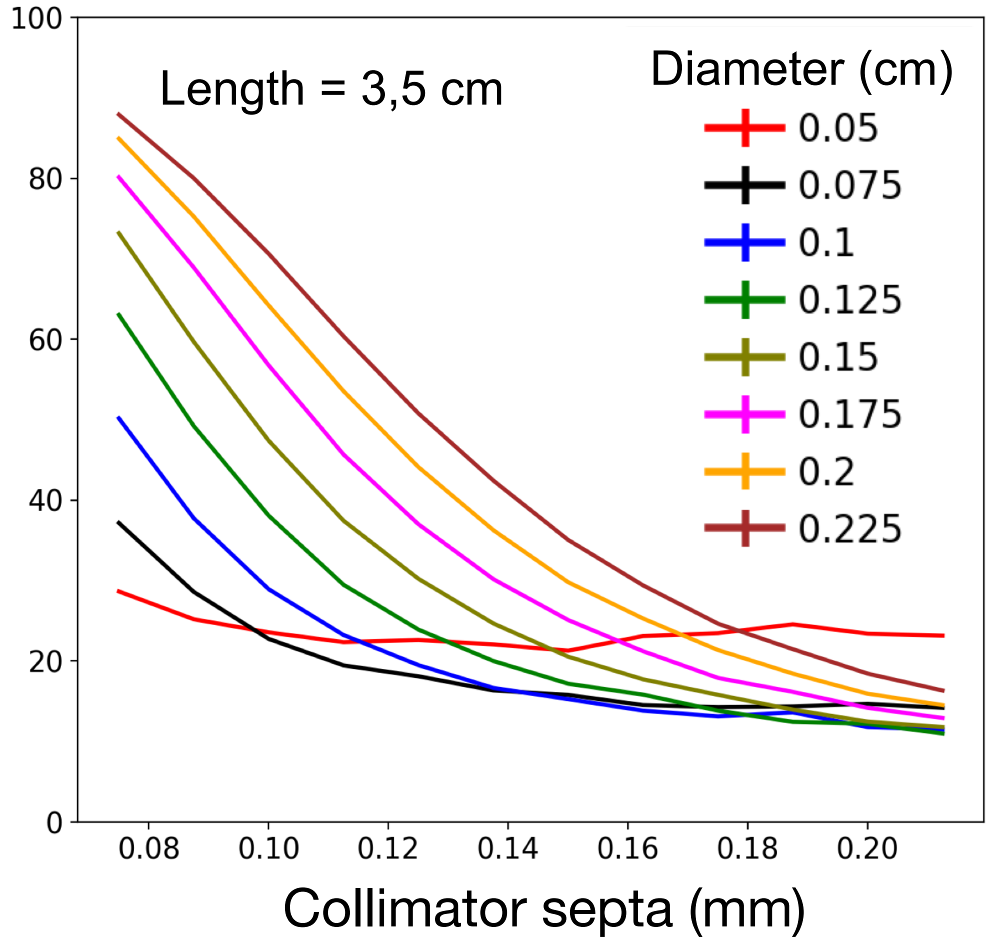
Reconstruction of a 100x100 scan (1mm step)

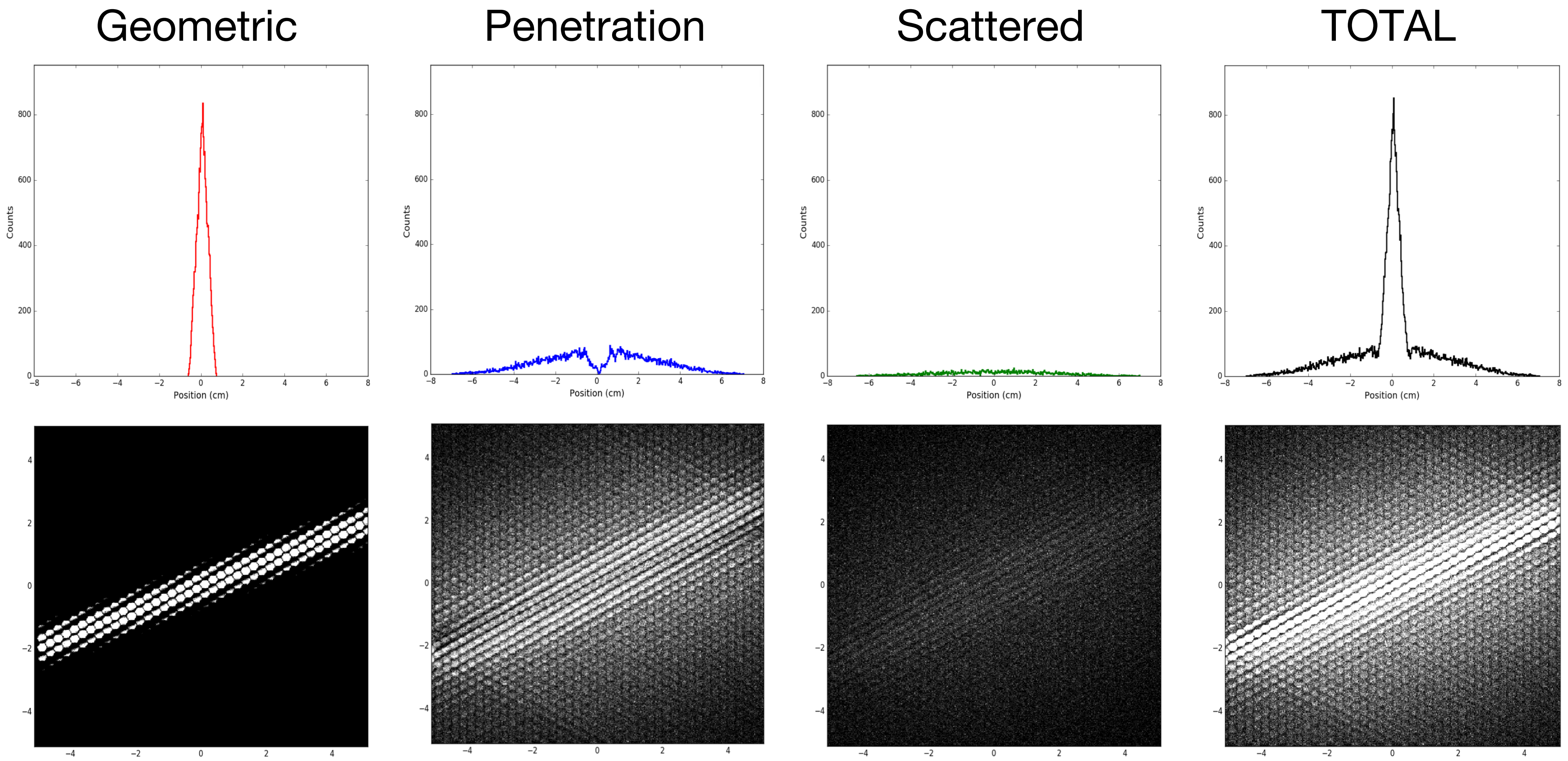
SR (FWHM mm) CFOV	1.15±0.06
SR (FWHM mm) /CFOV	1.54±0.55
Distortion (mm) CFOV	0.11±0.05
Distortion (mm) /CFOV	0.35±0.66
Differential uniformity CFOV	2.39%
Differential uniformity /CFOV	2.47%

The high energy parallel-hole collimator



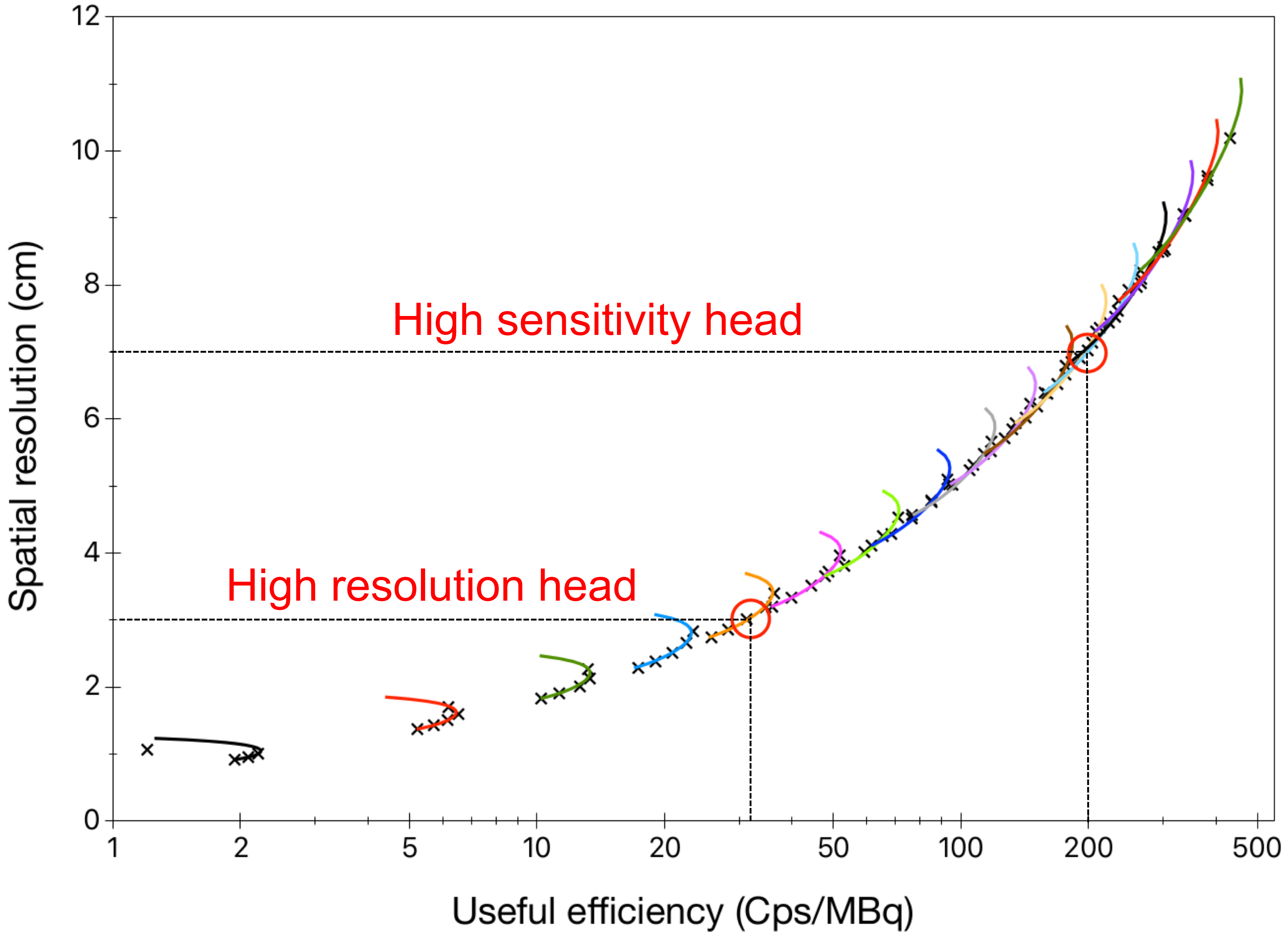
Effective septal penetration (%Total events)





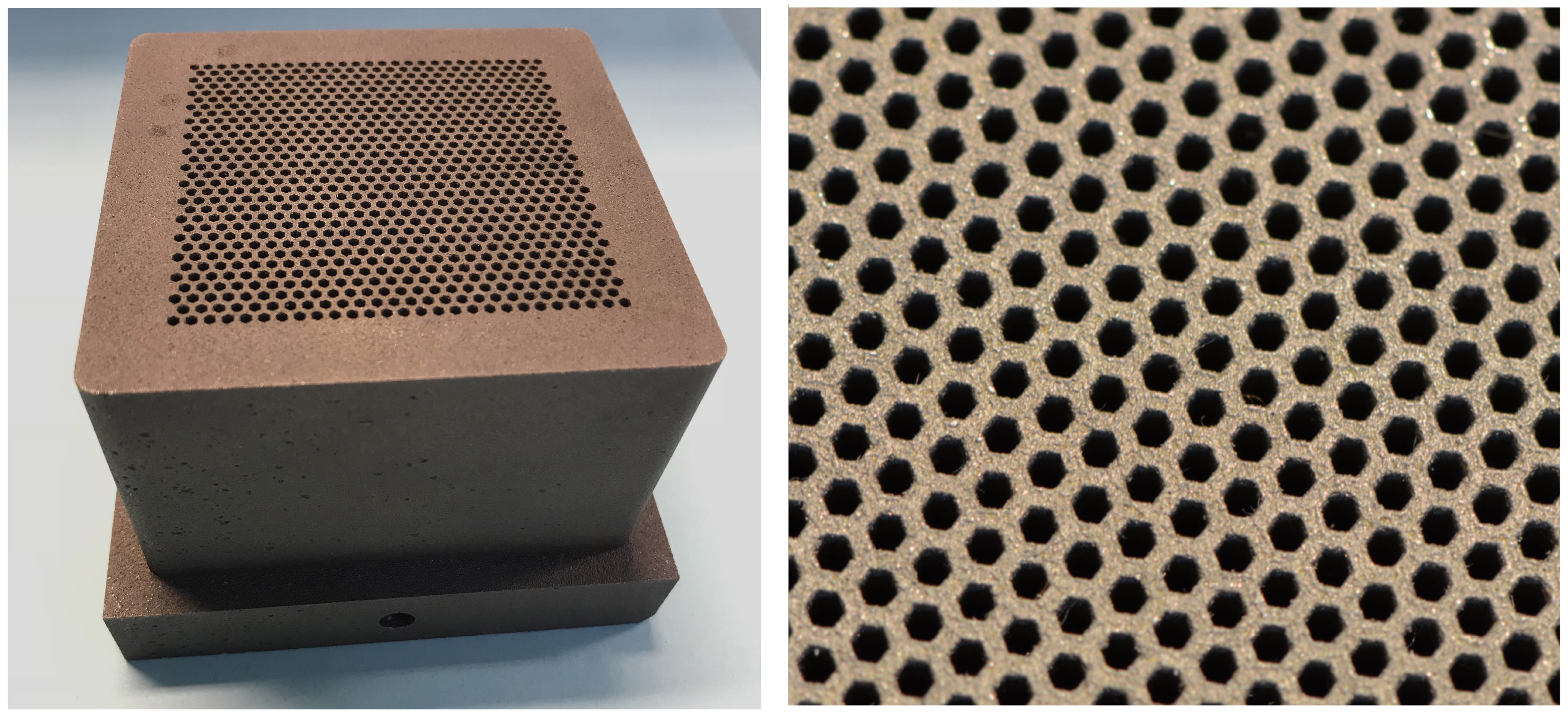
Optimization study based on Monte Carlo simulations (GATE) and analytical models

All configurations with effective septal penetration of 7.5 %

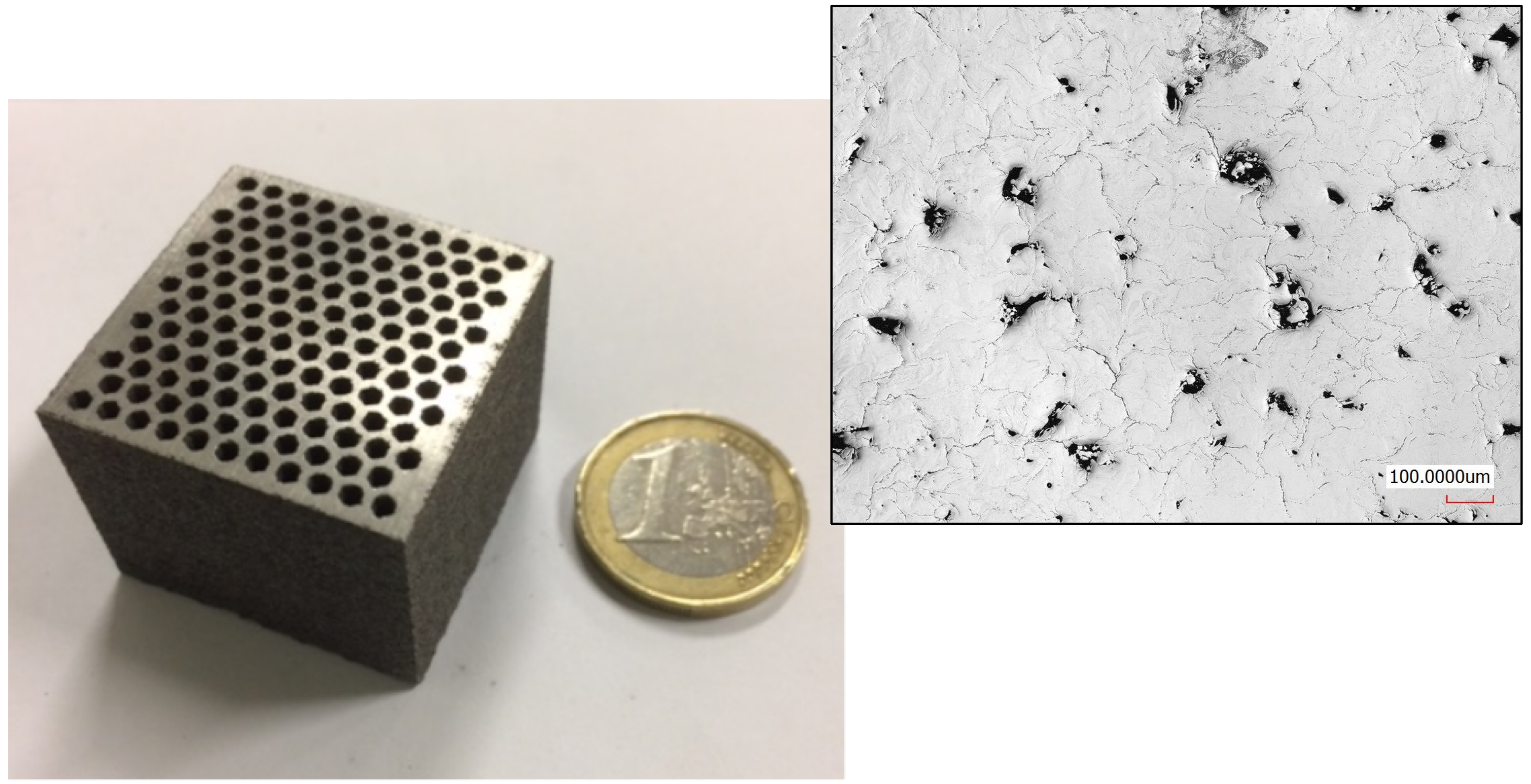


	L (cm)	*d (mm)*	*t (mm)*	*SR (mm) @ 5 cm*	*Efficiency (Cps/MBq) @ 5 cm*
Control	5.87	1.8	0.84	3	32
Planning	5.44	4.02	1.69	7	200

The high energy parallel-hole collimator



Collimator of the Proof of Concept prototype (M&I Materials)



Tungsten sample for 3D printing optimization (UTBM, Belfort)

3D printing with a selective laser melting procedure

Maximal effective density 18,7 $g.cm^{-3}$ compared to 19,3 $g.cm^{-3}$ for bulk tungsten (measured with Mercure intrusion porosimetry, ICB Laboratory)

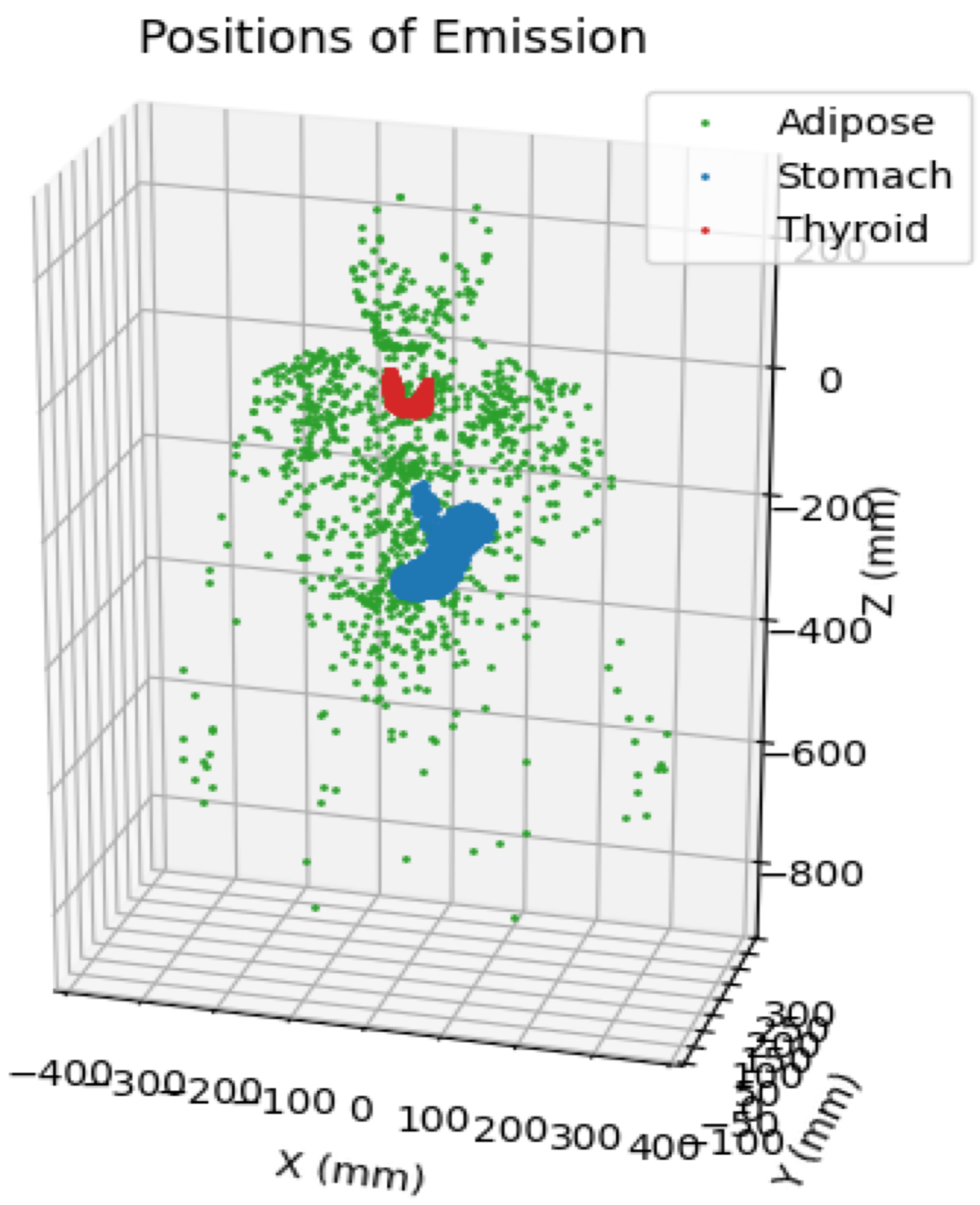
Open/total porosities : 1,8/5% (1.7 to 2.5 µm)

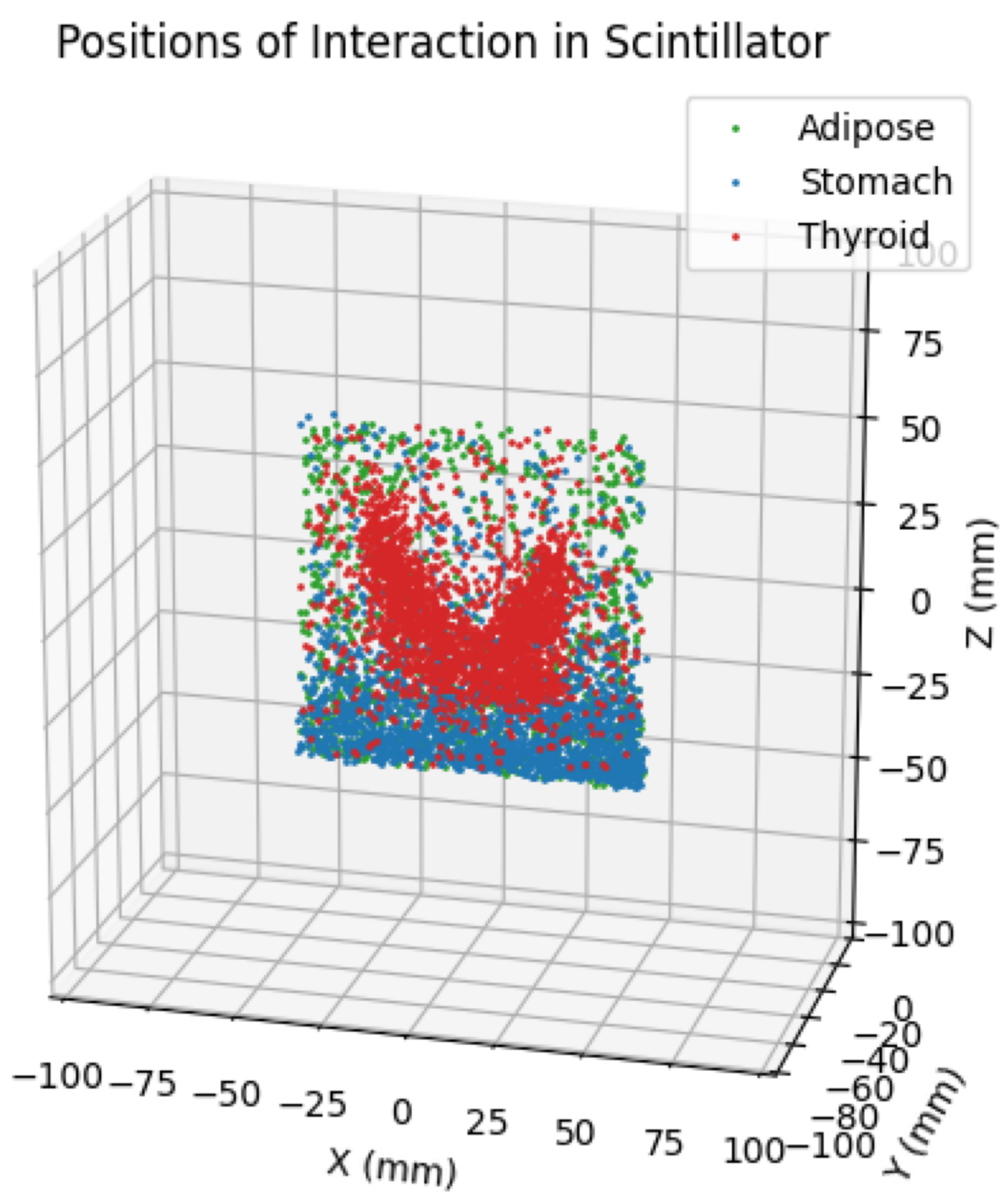
Optimization of shielding through Monte Carlo simulation (Gate)

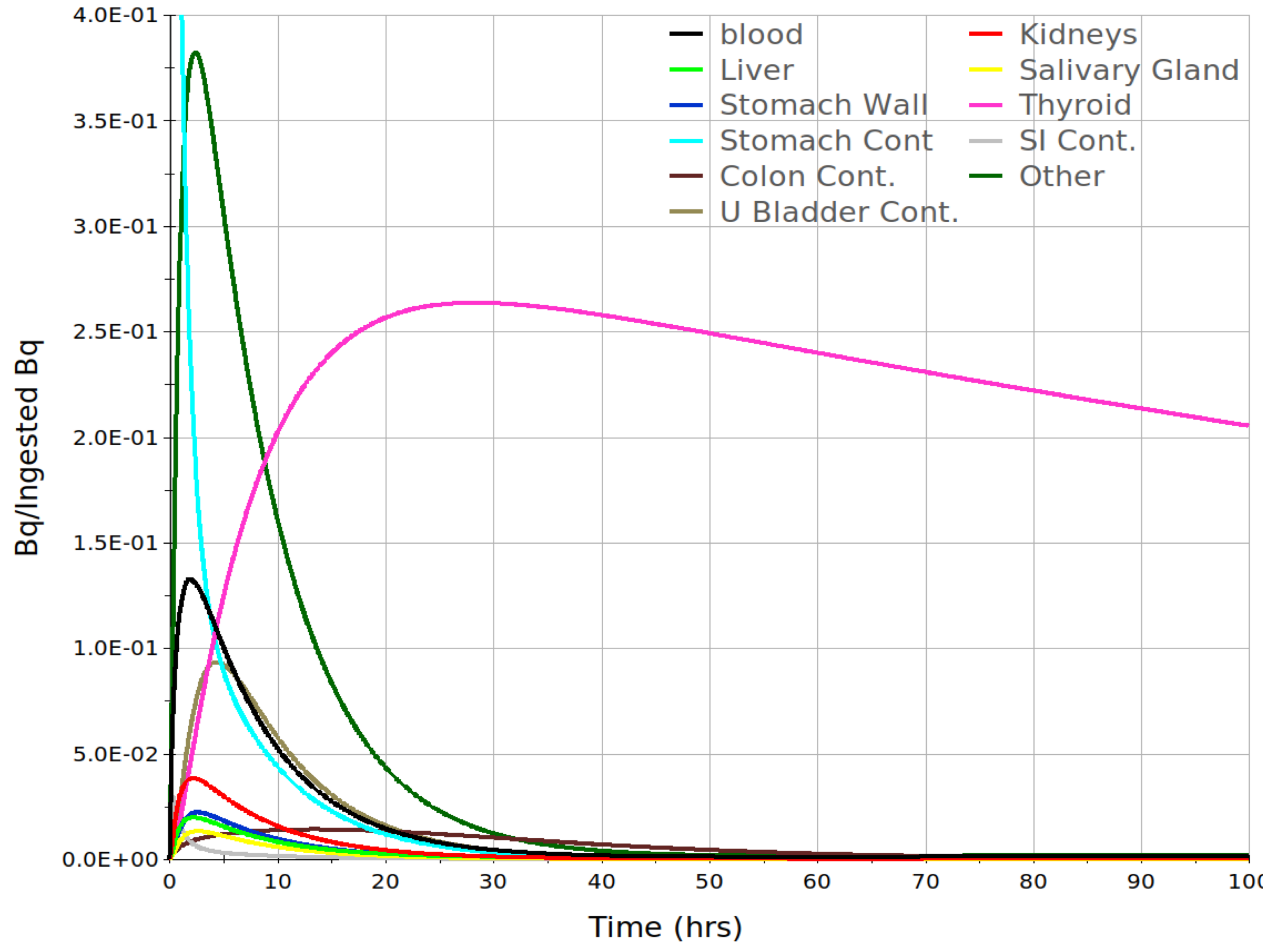
Sensitivity of the camera for each simulated organ + biokinetics given by the Leggett model [1]

Signal (activity coming from the thyroïd) to noise (activity coming from other organs) ratio over time

XCAT Voxelized phantom



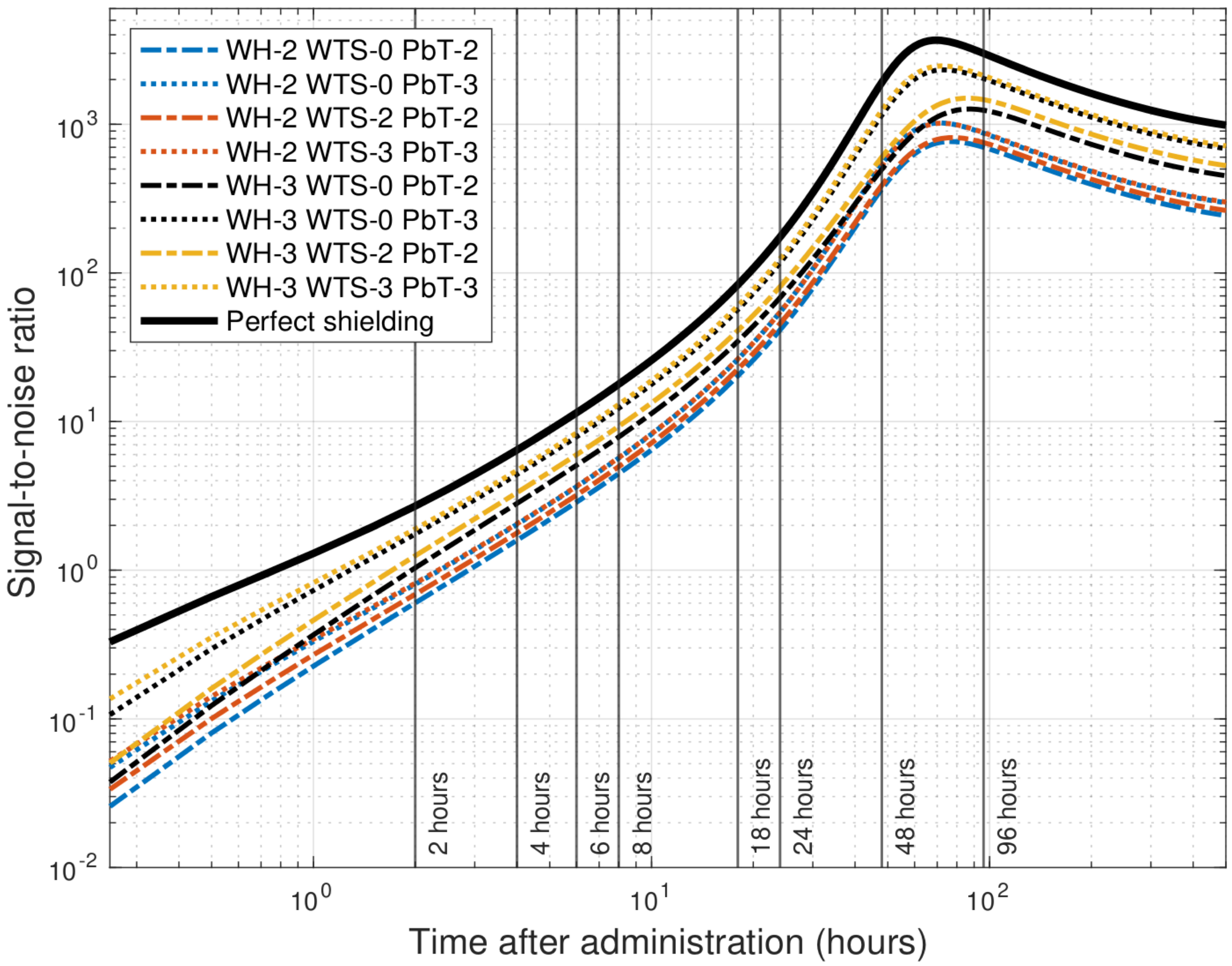




[1] R. W. Leggett, “A Physiological Systems Model for Iodine for Use in Radiation Protection,” *Radiation Research*, vol. 174(4), 2010

The shielding optimization

15% uptake in the thyroid



Best shielding (trade-off between SNR and size/ weight of the mobile camera)

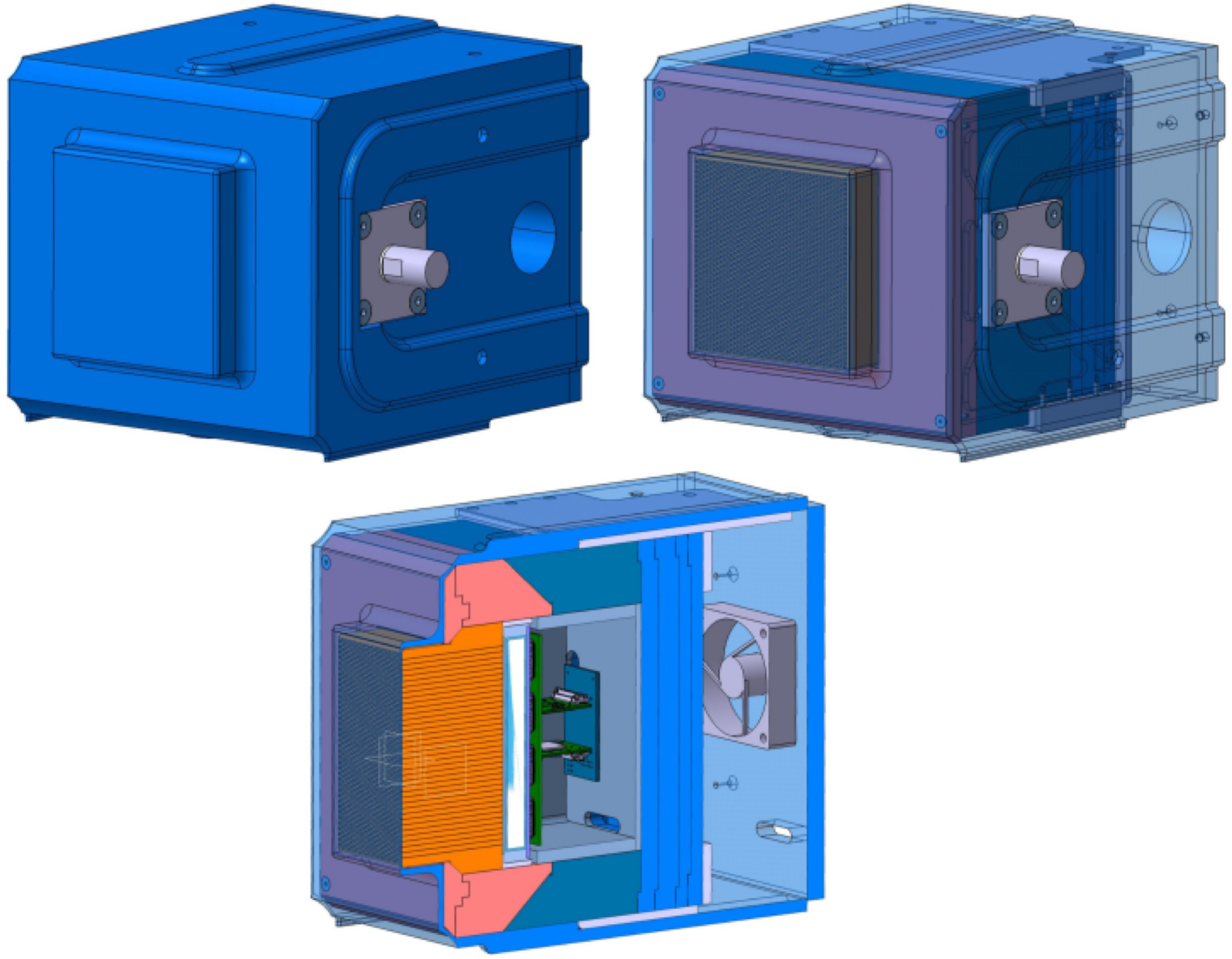
- Front of the camera : 3 cm Tungsten
- Back & sides of the camera : 3 cm Lead

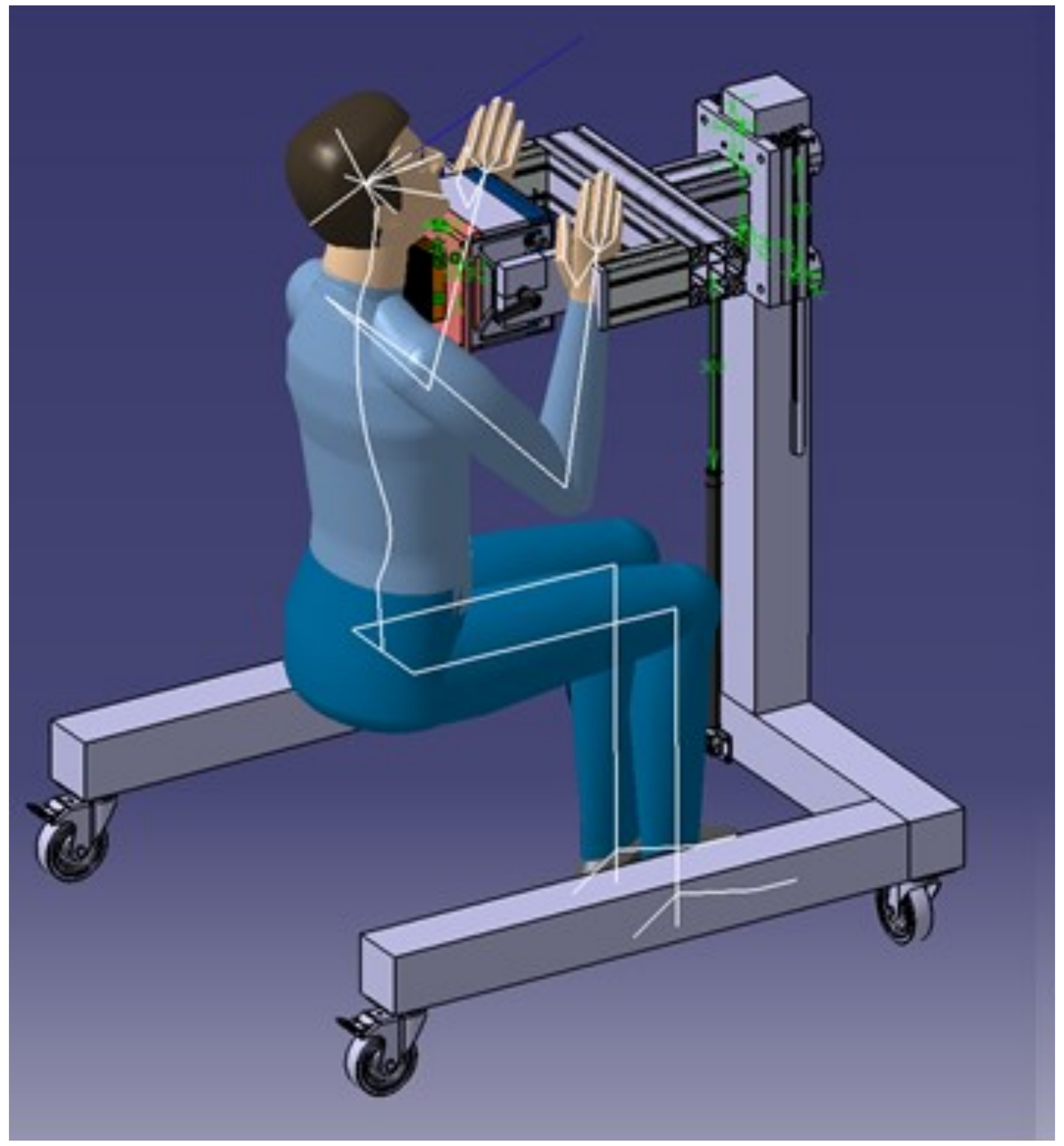
SNR at 6 hours after administration :

- Perfect shielding : 11.5
- Chosen configuration : 8
- Lowest shielding : 1.3

Overall mecanical dimensions

Towards a fully operational clinical mobile gamma camera dedicated to thyroid imaging





- Overall dimensions : 18x18x20 cm^3
- Total weight : 50 kg (including 30 kg lead shielding and 9 kg collimator)

Summary and Conclusion

A 10x10cm^2 field of view clinical prototype is currently under development, dedicated to the patient specific dosimetry in radioiodine treatment of thyroid diseases

- ✓ Energy resolution of 8% FWHM will reduce the influence of scattered events on image contrast and sensitivity
- ✓ Millimetric intrinsic spatial resolution will reduce partial volume effect and leads to better ROI estimation
- ✓ Fastness of Neural Network reconstruction allows to use it for online monitoring

Next steps

- ✓ **Calibration of the camera and evaluation of the accuracy and robustness of the quantification protocol** (correction methods, integration of different angular views, ...) using 3D phantoms
- ✓ **Clinical feasibility** study for the radioiodine treatment of differentiated thyroid cancers and benign thyroid diseases : interest to better correlate the dose delivered to the expected dose, as well as to the observed clinical effects (destruction of tumor remnants, thyroid function, toxicity on salivary glands).
- ✓ Determine the best methodological way to integrate available data (mobile camera, SPECT, counting probe…) in order **to reduce uncertainties of the absorbed dose evaluation. Implementation of innovative propagation methods based on Bayesian networks to estimate dose-related uncertainties.**

Acknowledgments

Carlotta Trigila
Yves Charon
Françoise Bouvet
Laurent Ménard
Laurent Pinot
Marc-Antoine Verdier

Denis Reynet
Harald Ramarijaona
Aurélien Blot

Tiffany Beaumont
David Broggio
Mohamed Bensiali
Estelle Davesnes
Aurélie Desbrée

Olivier Caselles
Laviana Vija
Delphine Vallot

Mathieu Sinigaglia
Slimane Zerdoud

Luis Ammour
Jad Farah
Aurélie Forbes

With financial support from ITMO Cancer AVIESAN within the framework of the Cancer Plan (AAP Physicancer 2019-2023, THIDOS project)