Deep-learning data processing of spectral PC-CT longitudinal studies to design and optimize combined Immuno-anticancer Treatments in liver cancer mouse models

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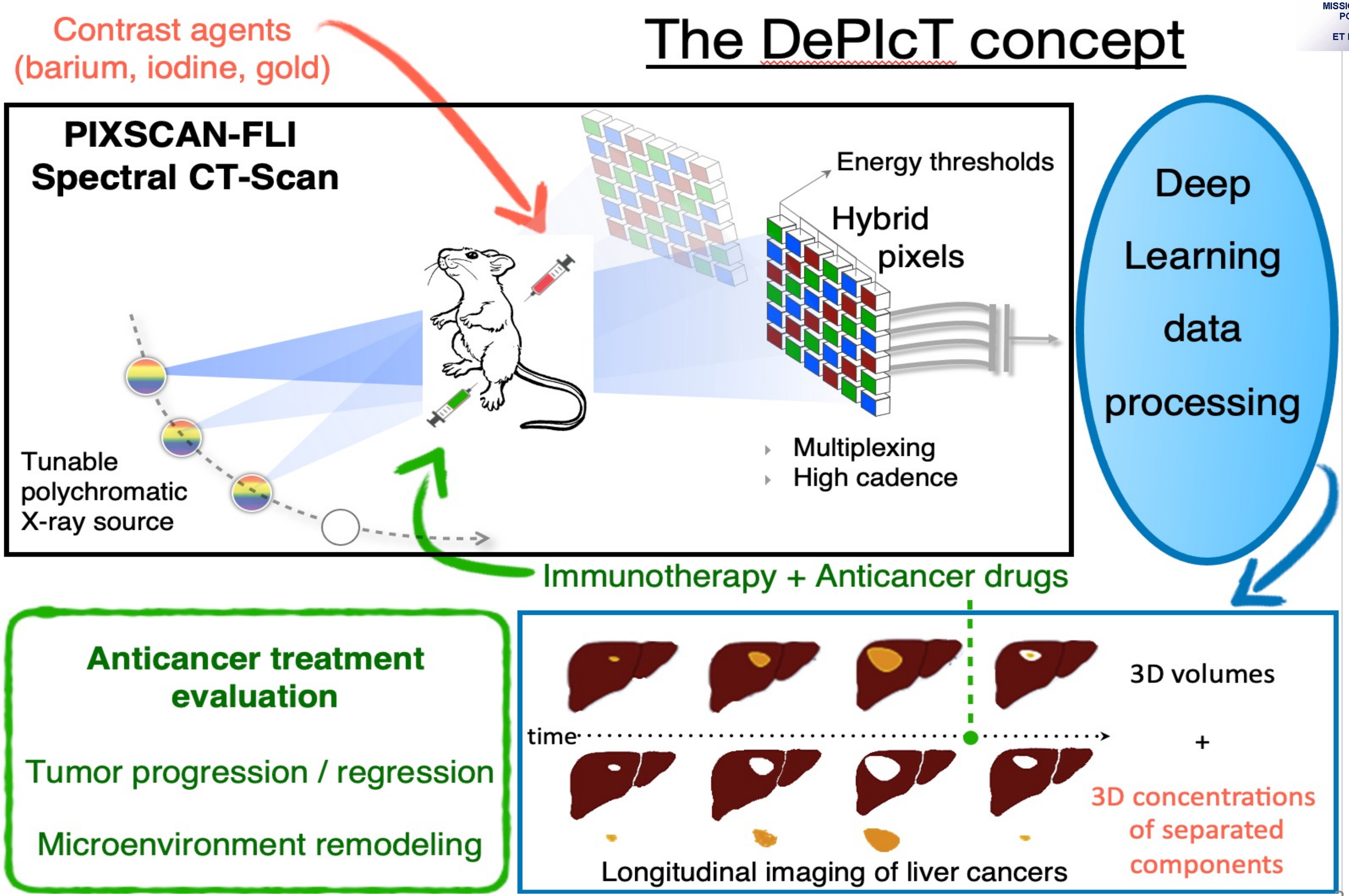
Summary

- Introduction
- Longitudinal studies results with the PIXSCAN-FLI
- Introduction to spectral imaging with K-edge
- Primary results with the new detector

Context and objectives

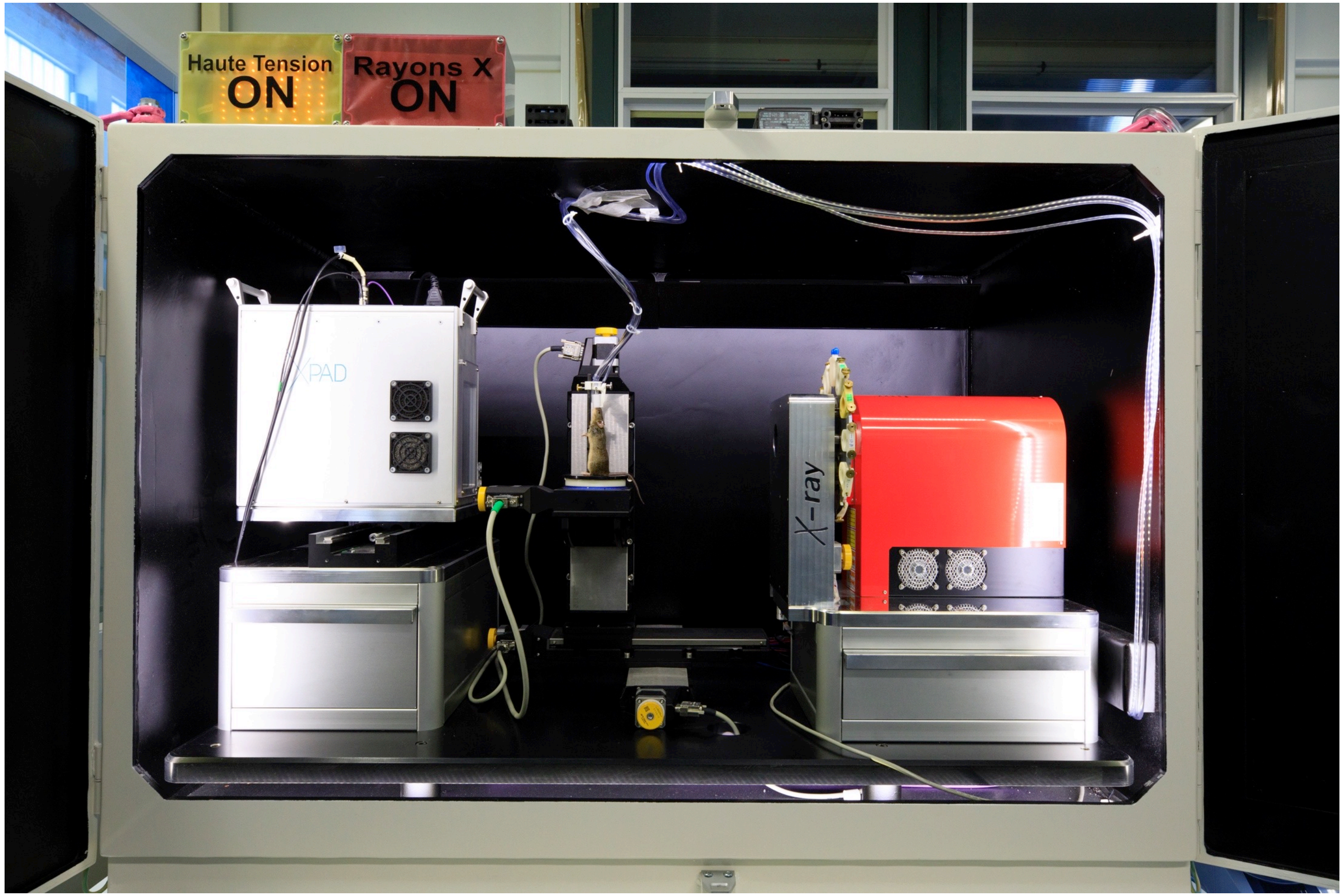
Hepatocellular carcinoma:
- 3rd most deadly cancer in the world
- limited effects of current therapy

The DePIcT concept



http://imxgam.in2p3.fr/depict.php

The PIXSCAN-FLI



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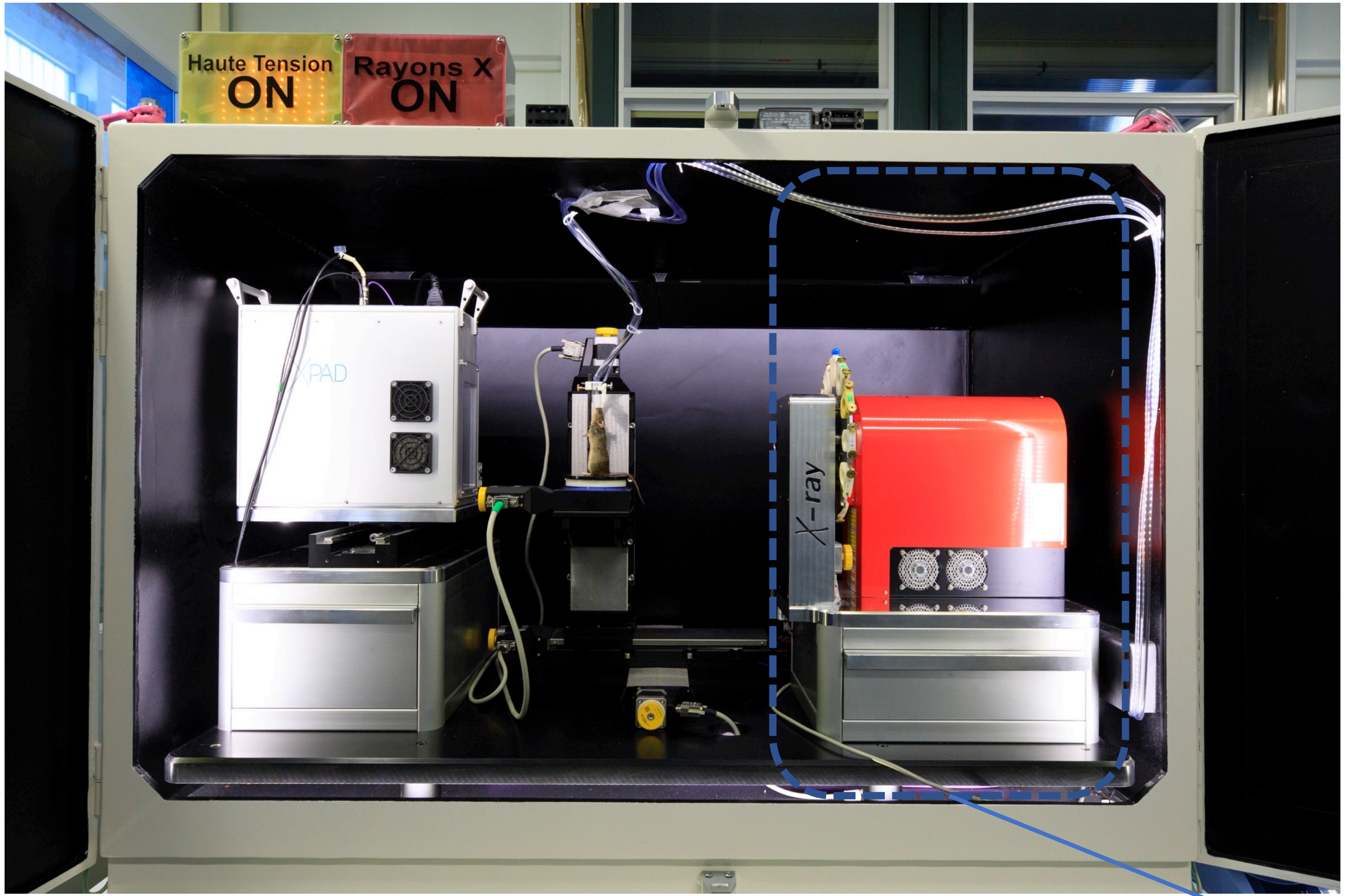
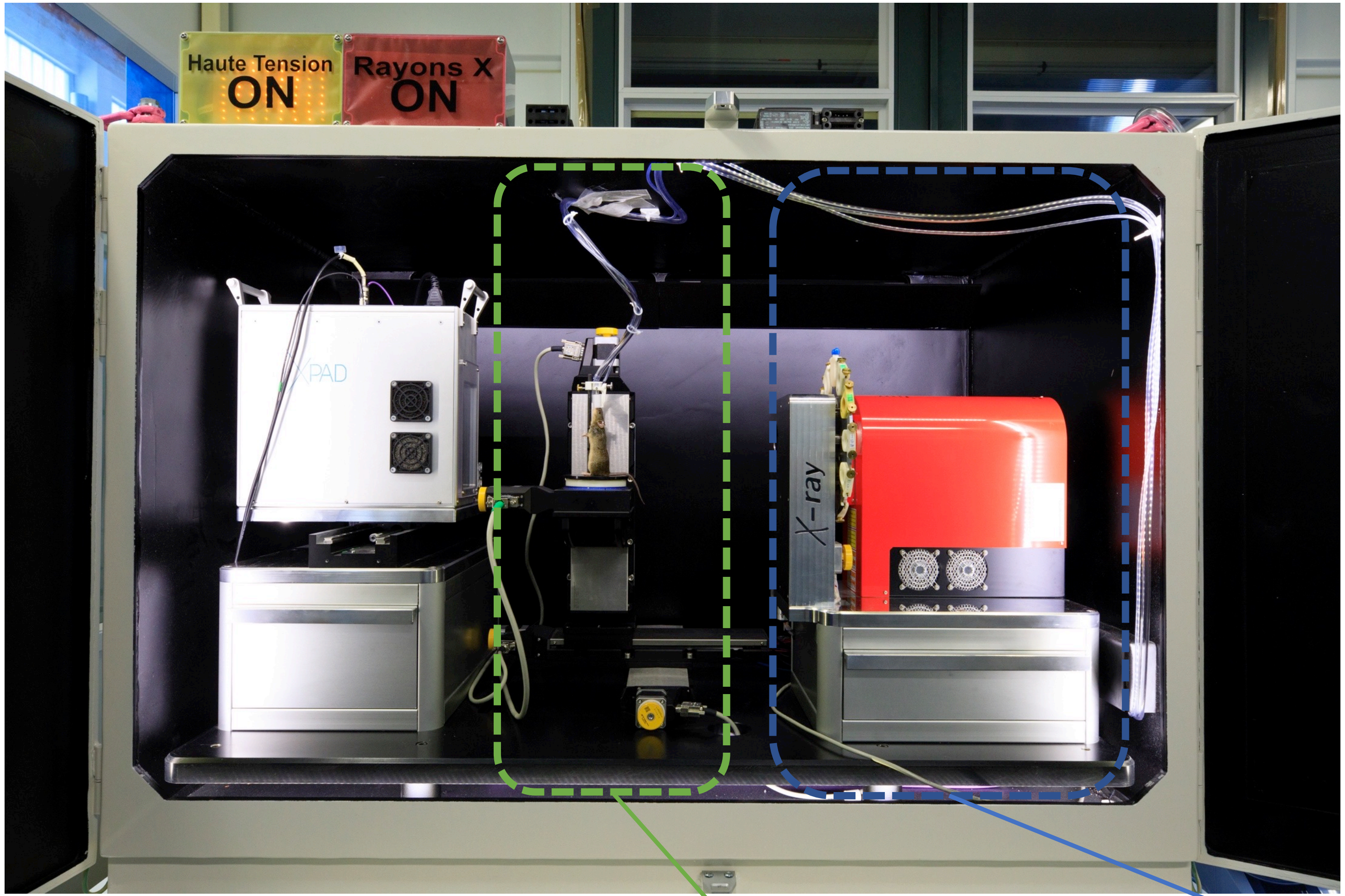


X-ray tube:
- from 40 to 150 kV
- filter wheel

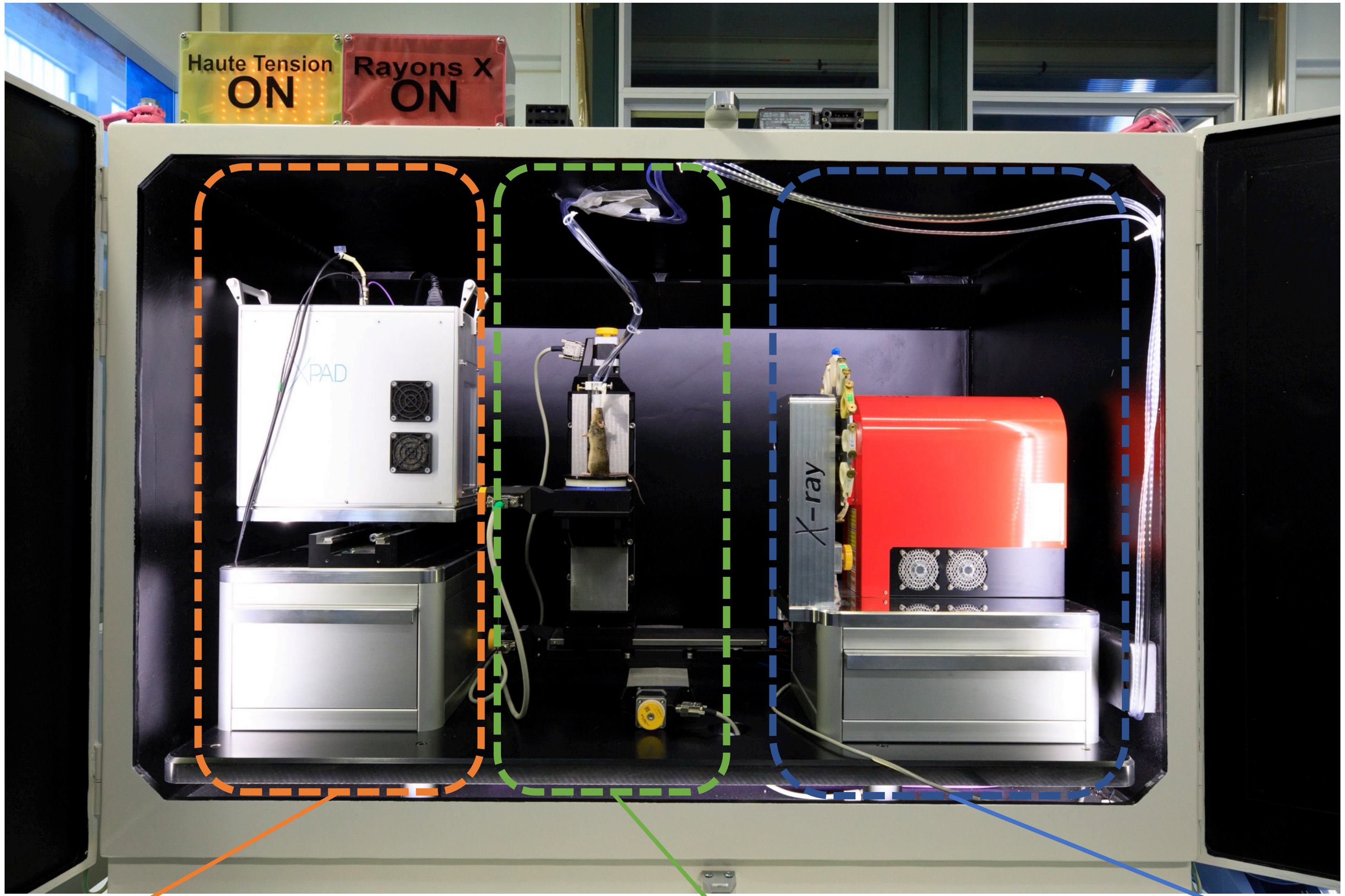
The PIXSCAN-FLI



Animal support:
- 3-axis motion + rotation
- gas anesthesia system

X-ray tube:
- from 40 to 150 kV
- filter wheel

The PIXSCAN-FLI

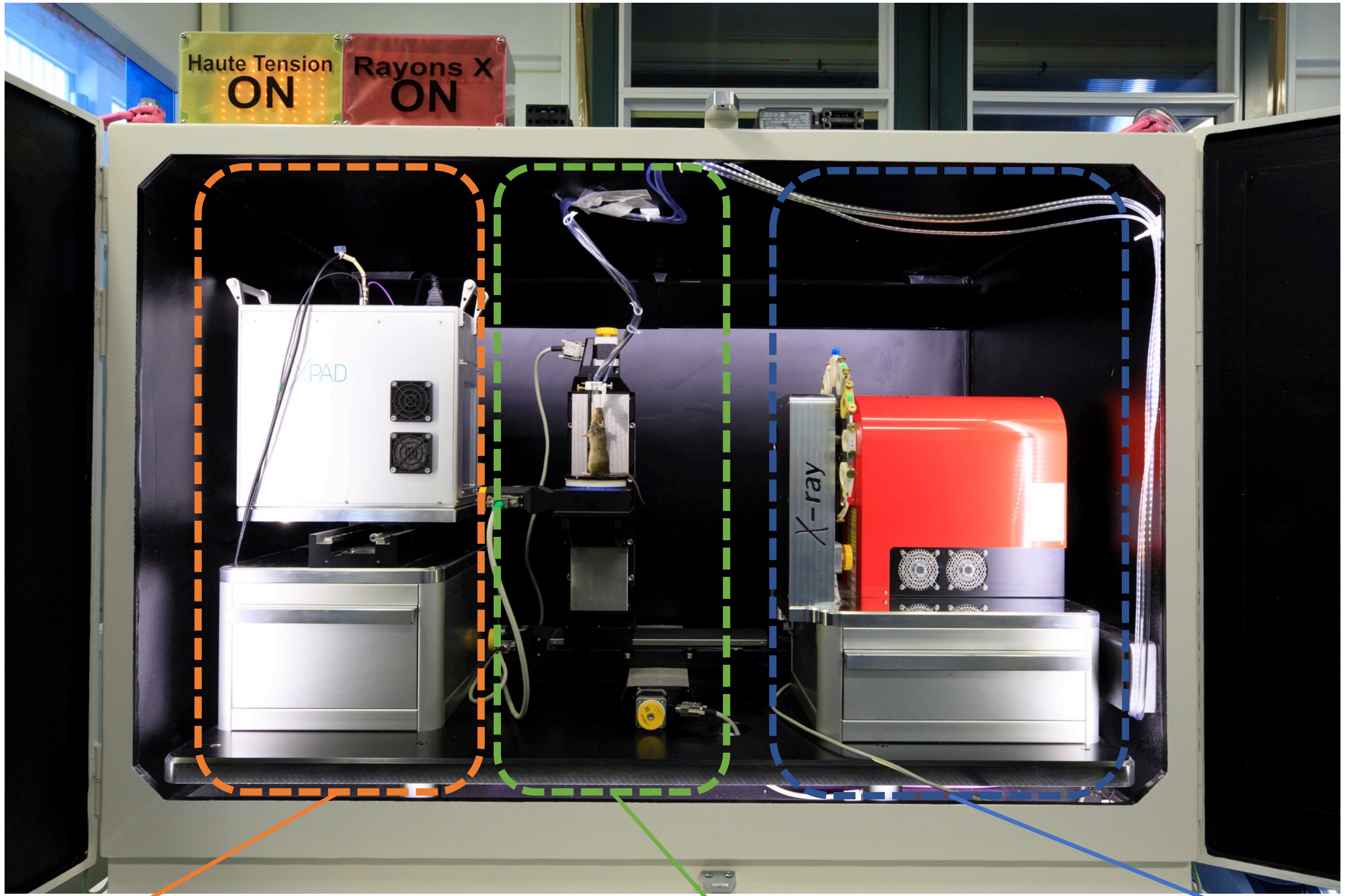


Detectors:
- Si 500 µm or GaAs 1000 µm
- hybrid pixels 130x130 μm^2

Animal support:
- 3-axis motion + rotation
- gas anesthesia system

X-ray tube:
- from 40 to 150 kV
- filter wheel

The PIXSCAN-FLI



Imaging protocol with Si detector:

- standard absorption imaging
- 50 kV/500 µA/0.6 mm Al
- Pose duration: 198 ms
- 1440 projections
- 110 mGy/scan
- hepato-specific contrast agent (ExiTron nano 12000®, barium nanoparticles)

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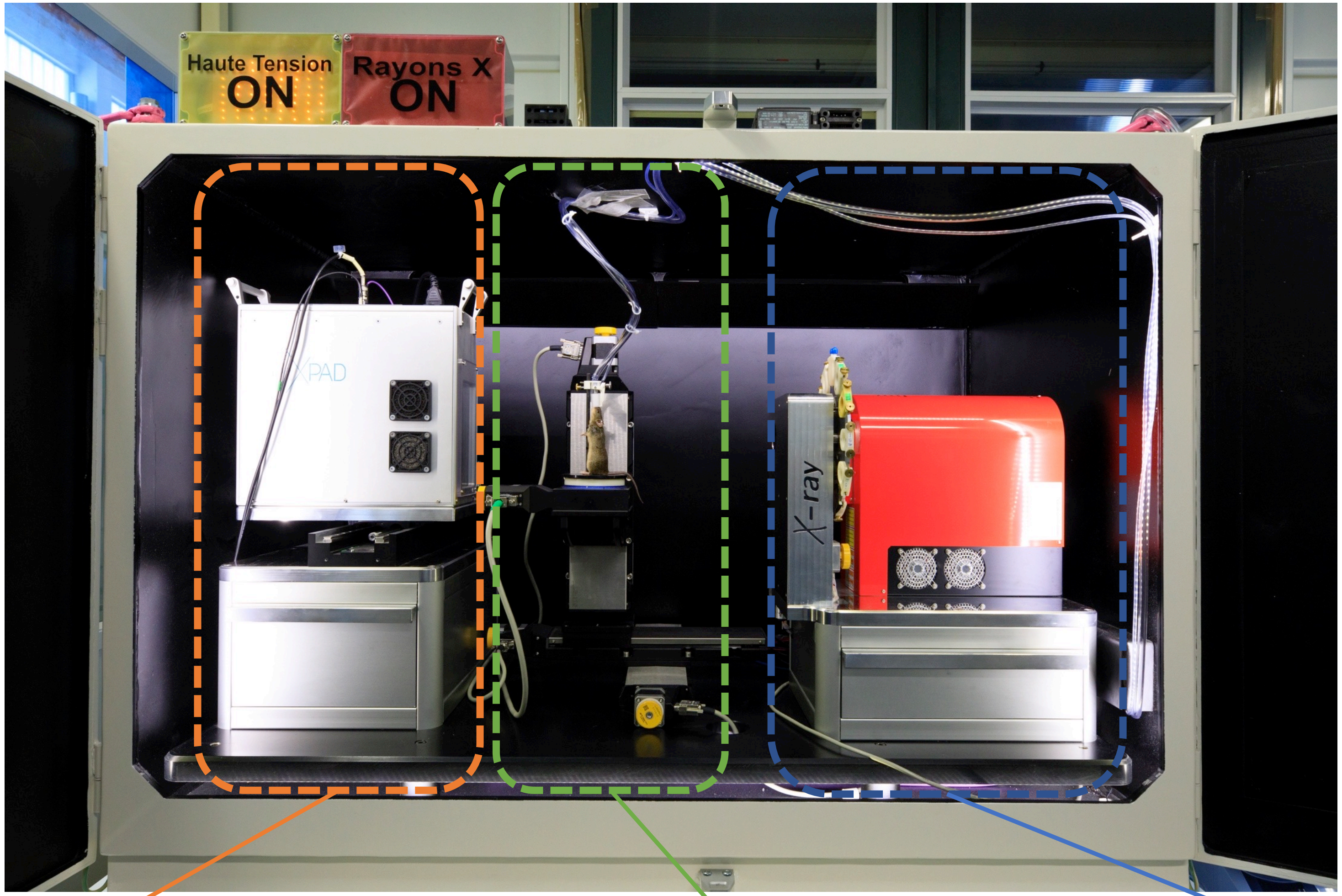

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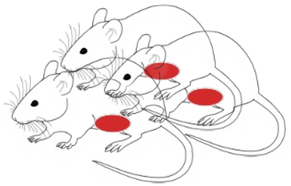
- gas anesthesia system

X-ray tube:
- from 40 to 15
- filter wheel

Longitudinal studies to follow tumor evolution



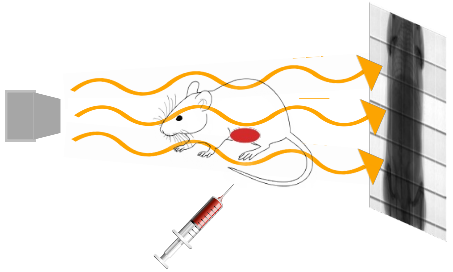
D0* D10* D20*

Treatment injection

Flow cytometry

- Immune cells population analysis

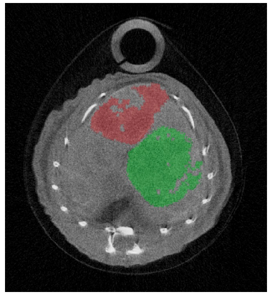
*** Longitudinal study with PIXSCAN-FLI prototype**



Contrast agent

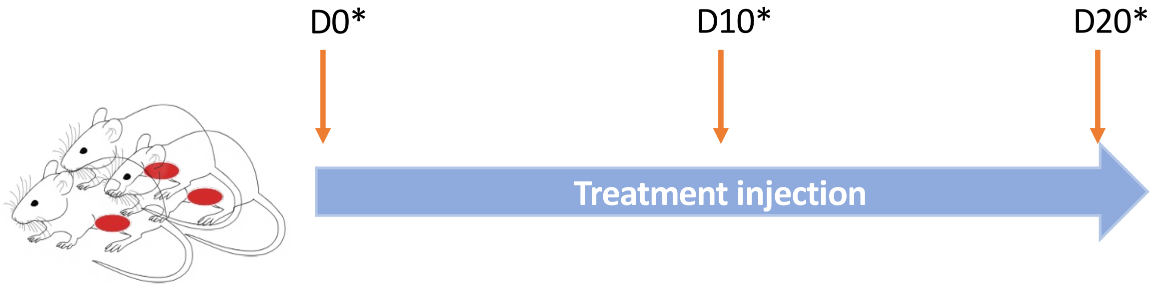
- Tumor evolution
- Microenvironment remodeling

Tumoral volume quantification



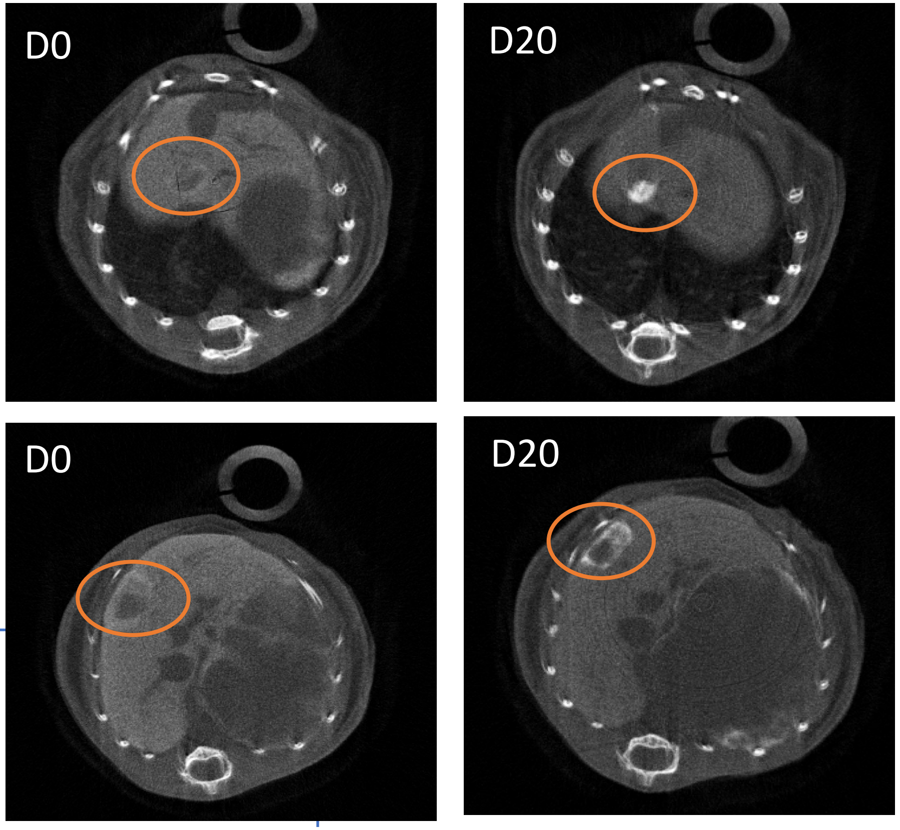
- Volume measurement

Longitudinal studies to follow tumor evolution



Flow cytometry

- ➢ Immune cells population analysis

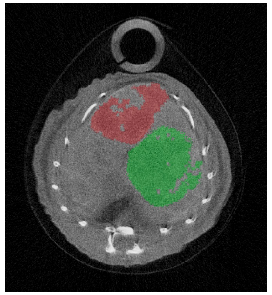


Tumor evolution examples (at D0 in the left and D20 in the right)

*** Longitudinal study with PIXSCAN-FLI prototype**

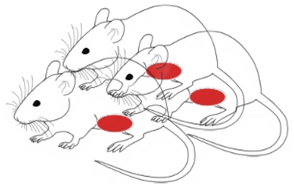
- ➢ Tumor evolution
- ➢ Microenvironment remodeling

Tumoral volume quantification



- ➢ Volume measurement

Longitudinal studies to follow tumor evolution

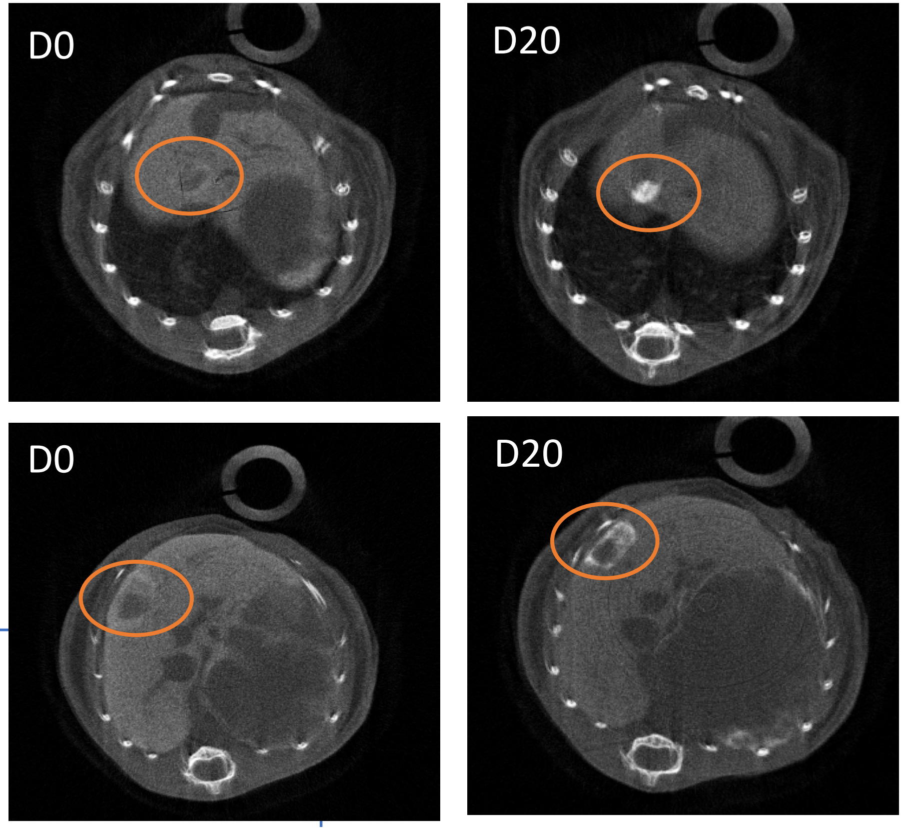


D0* — D10* — D20*

Treatment injection

Flow cytometry

- Immune cells population analysis



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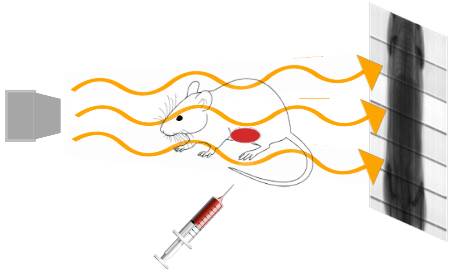
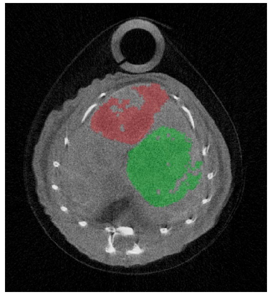
*** Longitudinal study with PIXSCAN-FLI prototype**



- Tumor evolution
- Microenvironment remodeling

Tumoral volume quantification



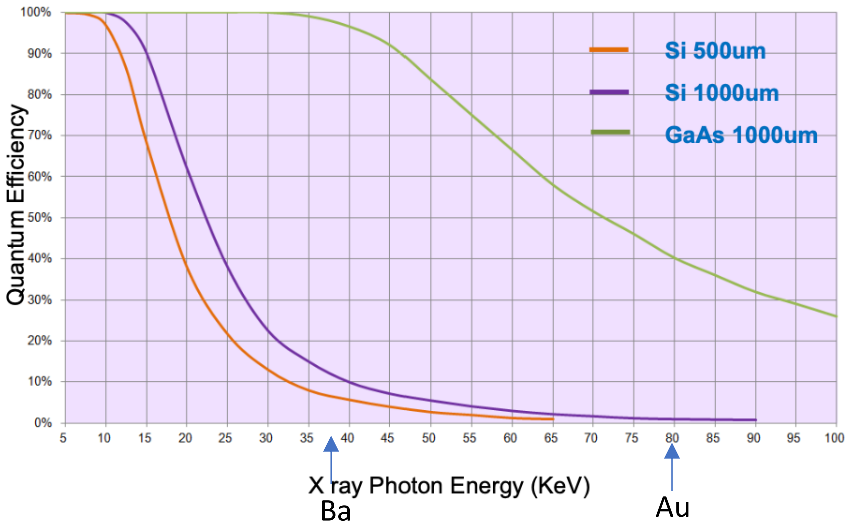
- Vo…

Dissociate Barium from other materials in order to have the immune cells cartography (and thus, tumor cells on the other side)

GaAs hybrid pixels

Characteristics:

- Material: GaAs
- 1 chip = 9600 pixels
- Pixel size: 130 x 130 µm^2
- Hybrid pixel: one threshold in energy



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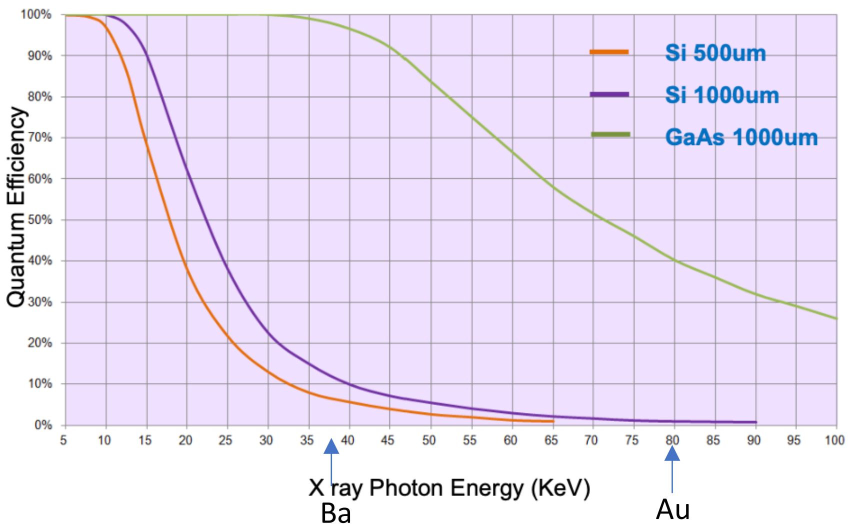


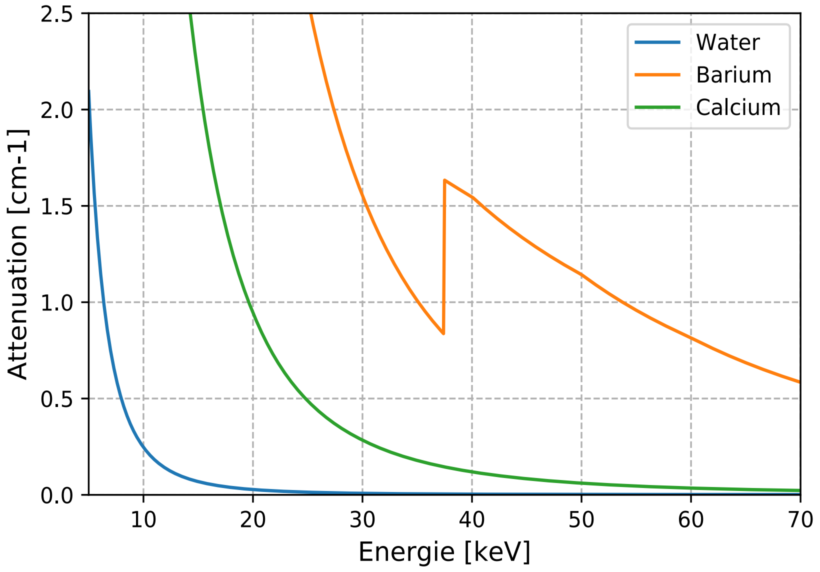
Parameters (DAC) to fit:

- **ITH**: *Intensity Threshold*, global adjustment around a given energy to all the pixels of the chip
- **DACL**: *Digital to Analog Converter Local,* adjust the threshold of each individual pixel
- **ITUNE**: set the ITH and DACL step

Threshold = (ITH - DACL) x ITUNE

Spectral imaging

- K-edge energy: jump in its photoelectric attenuation coefficient at the level of the binding energy, E_K, of the electron of the K layer



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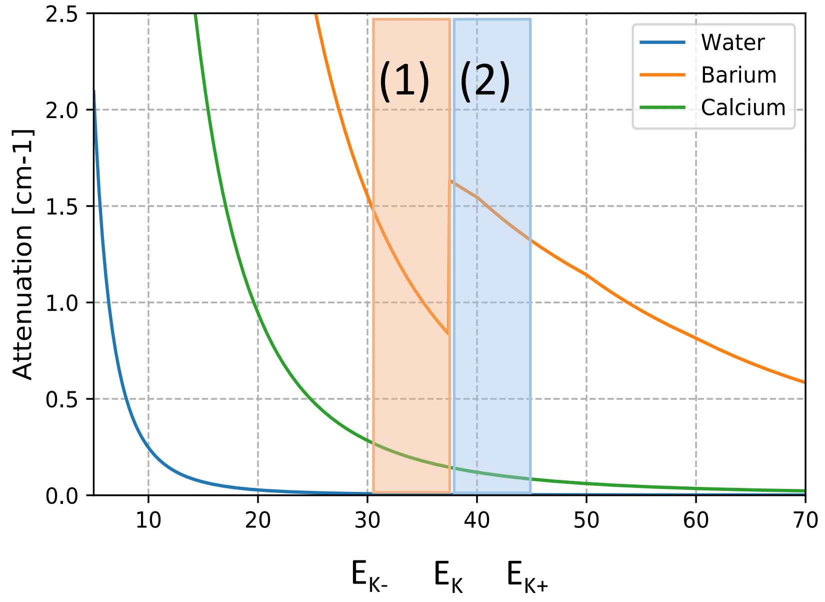

3 images:

- At the K-edge energy (E_K)
- Before K-edge (E_{K-})
- After K-edge (E_{K+})

$\mu(1) = E_K - E_{K+}$
$\mu(2) = E_{K-} - E_K$

Spectral imaging

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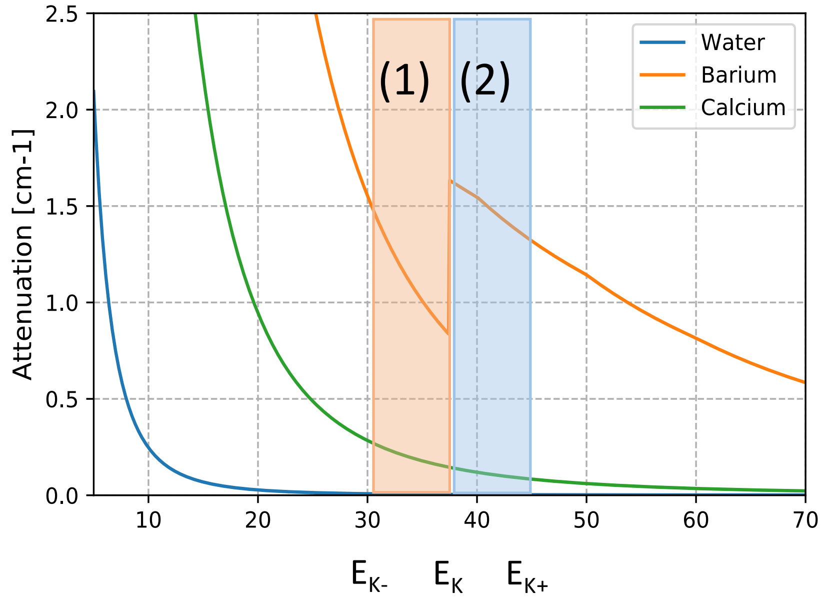

3 images:

- At the K-edge energy (E_K)
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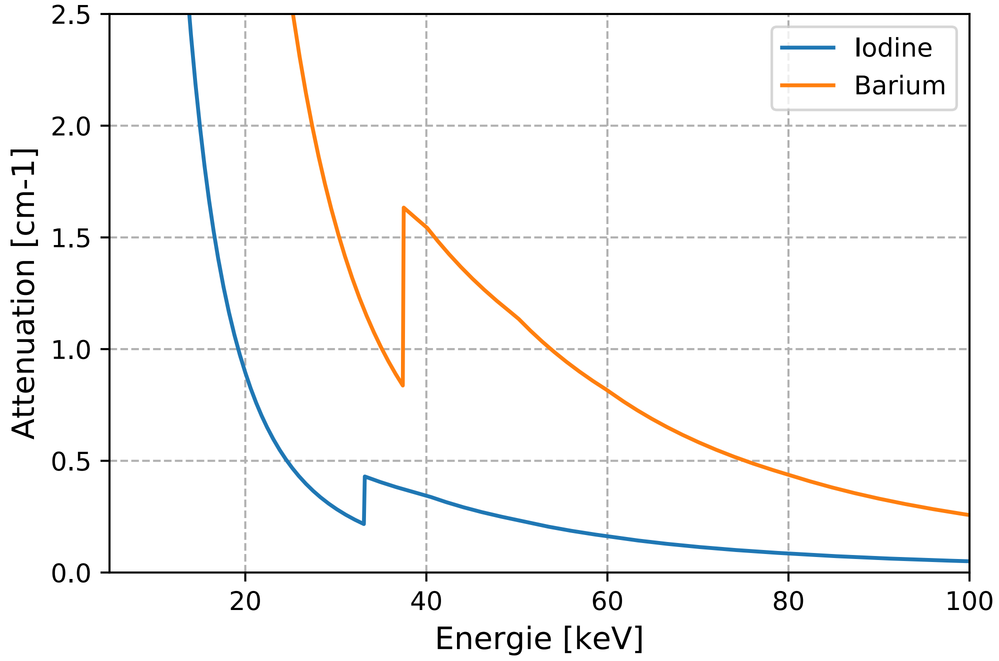
$\mu(1) = E_K - E_{K+}$
$\mu(2) = E_{K-} - E_K$

→ $\mu(2) - \mu(1) > 0$ only for the calibrated material

Iodine/Barium calibration



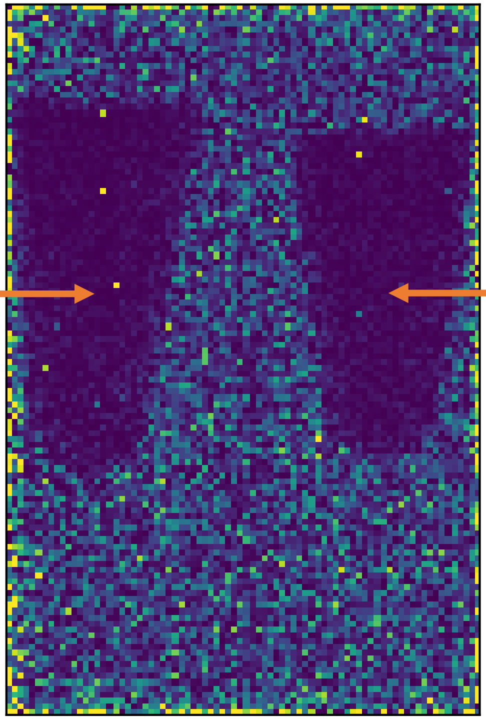
	Iodine	Barium
K-edge energy	33.2 keV	37.4 keV
ITUNE	50	
ITH	82	
DACL step (estimated)	0.7 keV	
Number of pixels calibrated	8151	8787
Number of pixels miscalibrated	1098	1340
% of the detector well calibrated	73.5 %	77.6 %

For Iodine, we used Iomeron 350, a contrast agent used in clinic

Iodine/Barium separation

White pixel: uncalibrated

Setup



Iodine

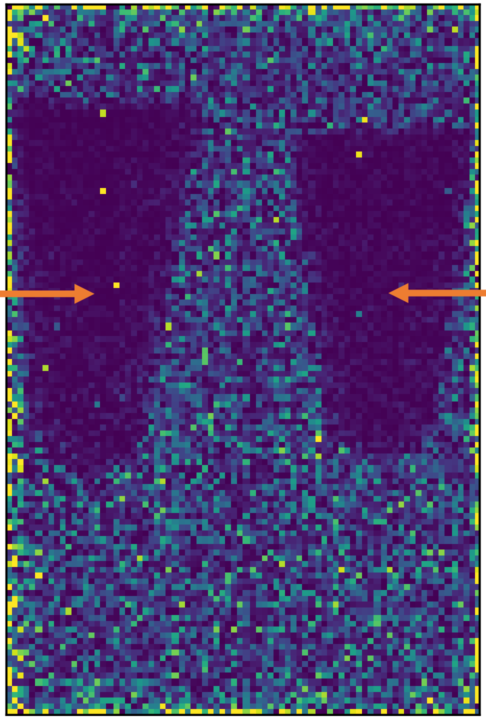
Barium

Iodine/Barium separation

White pixel: uncalibrated

Setup

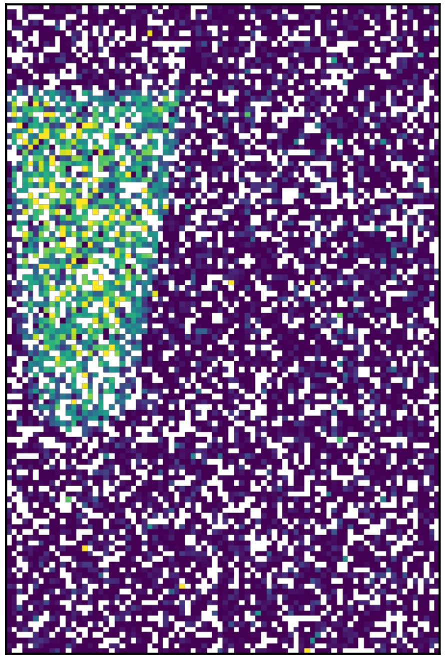
Iodine



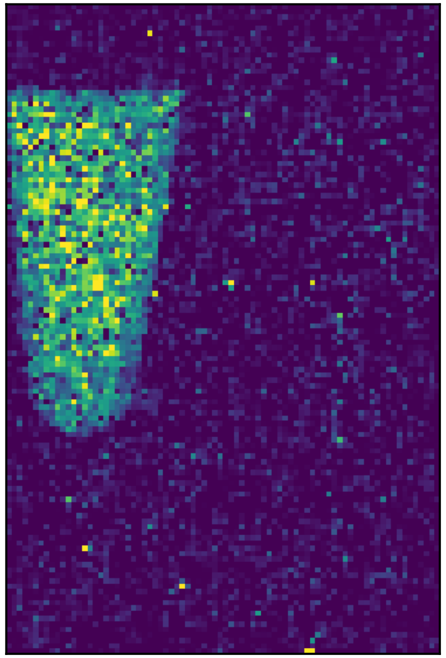
Barium

Iodine separation

With pixels uncalibrated



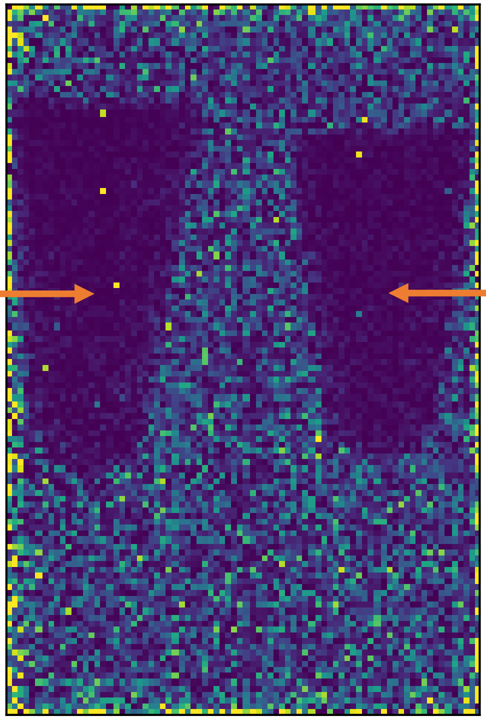
With interpolation



Iodine/Barium separation

White pixel: uncalibrated

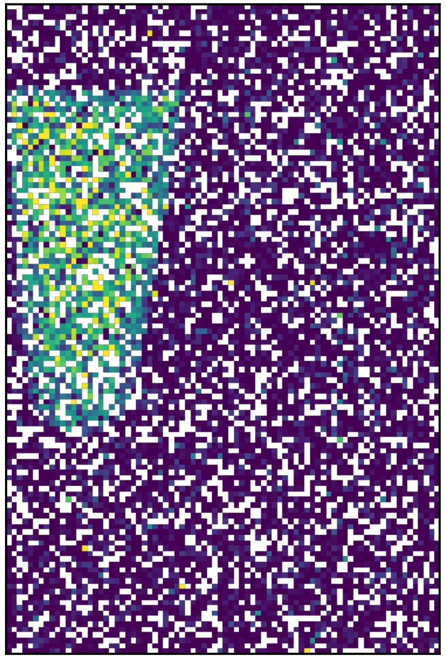
Setup



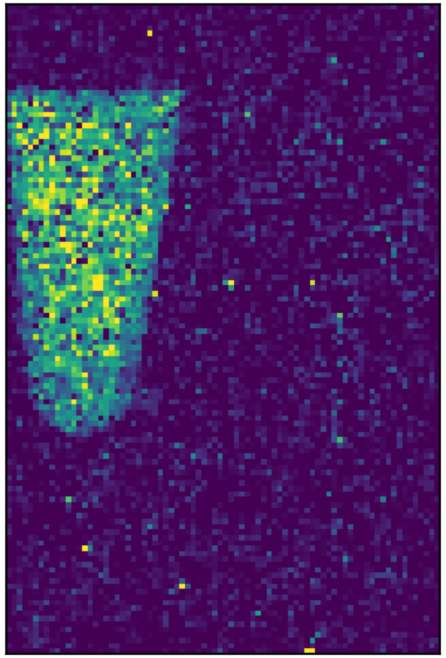
Iodine → ← Barium

Iodine separation

With pixels uncalibrated

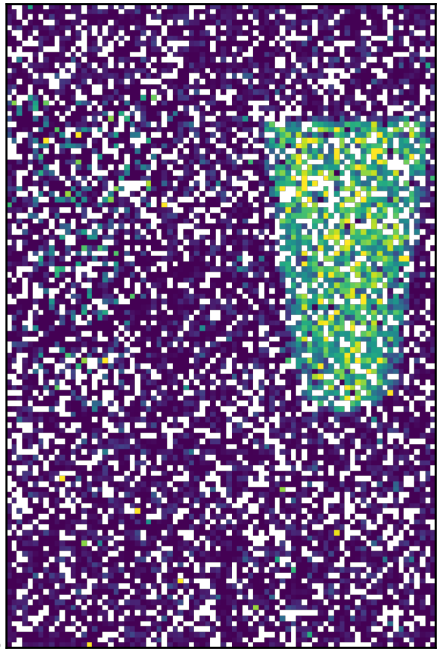


With interpolation

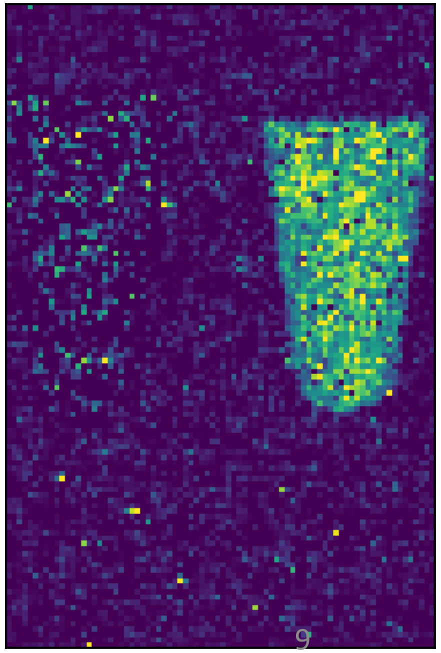


Barium separation

With pixels uncalibrated

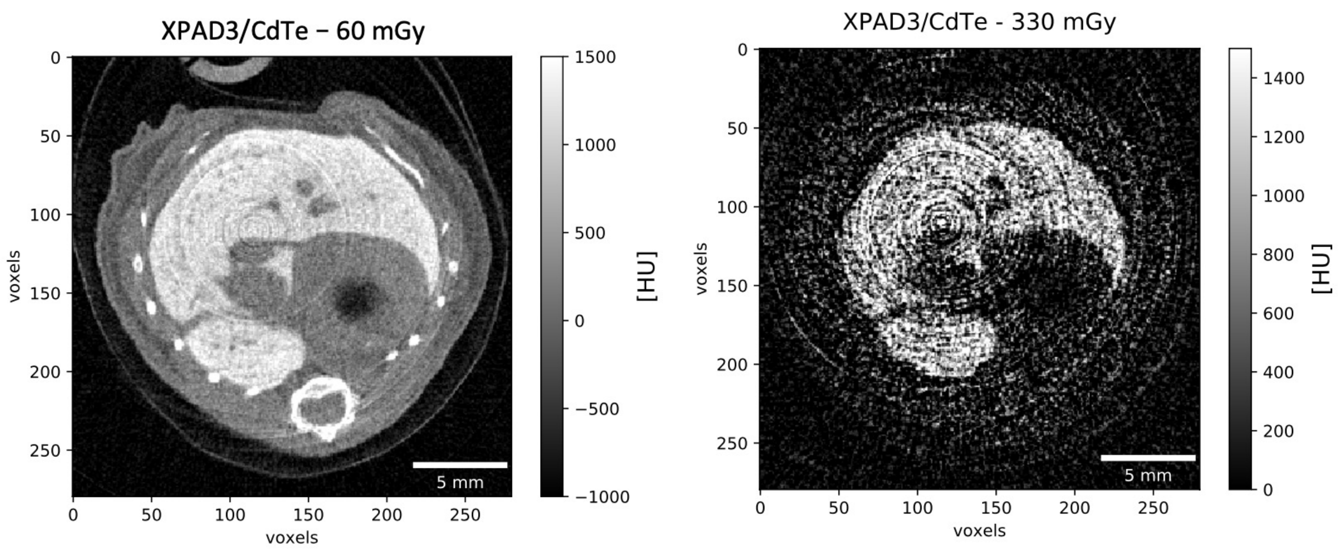


With interpolation



Objective in vivo

- Separation of Iodine and Barium is feasible with this detector, the next aim will be to valid in vivo by using Barium to separate the liver from the rest.

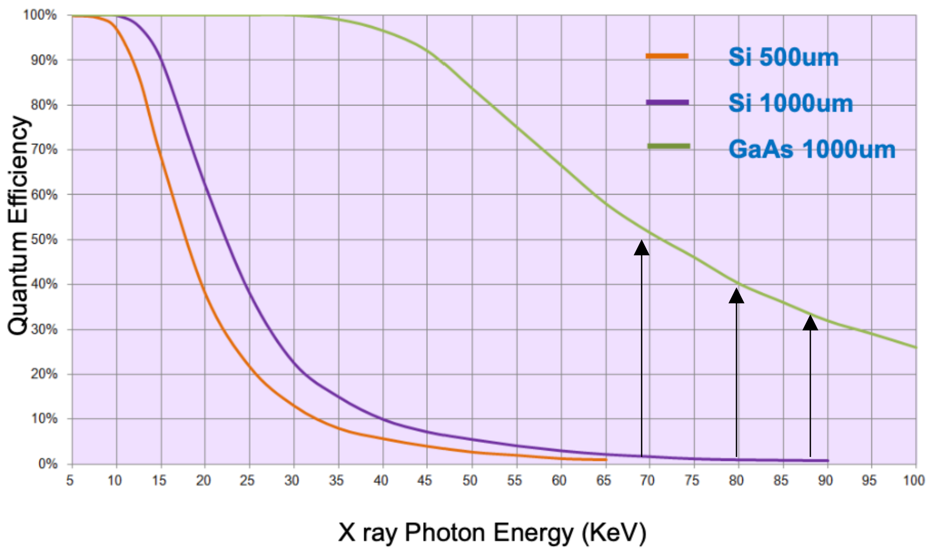


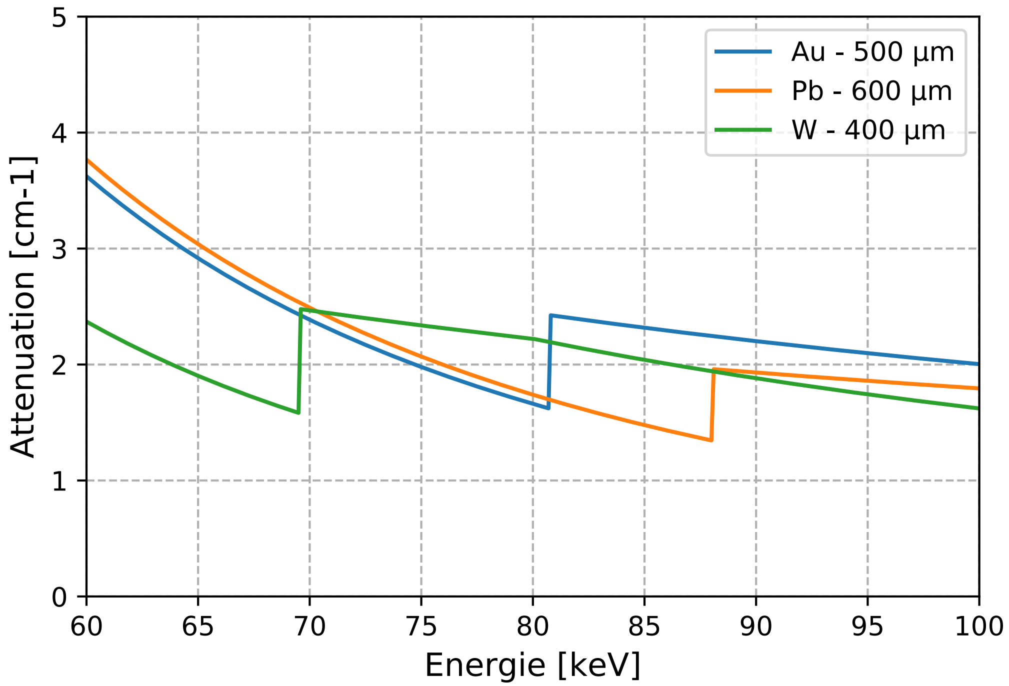
Barium segmentation with cadmium telluride (CdTe) hybrid pixels

[L. Portal, 2018]

What about high energy ?

- GaAs: good efficiency at high energy
- Gold nanoparticles could be used to target cancer cells

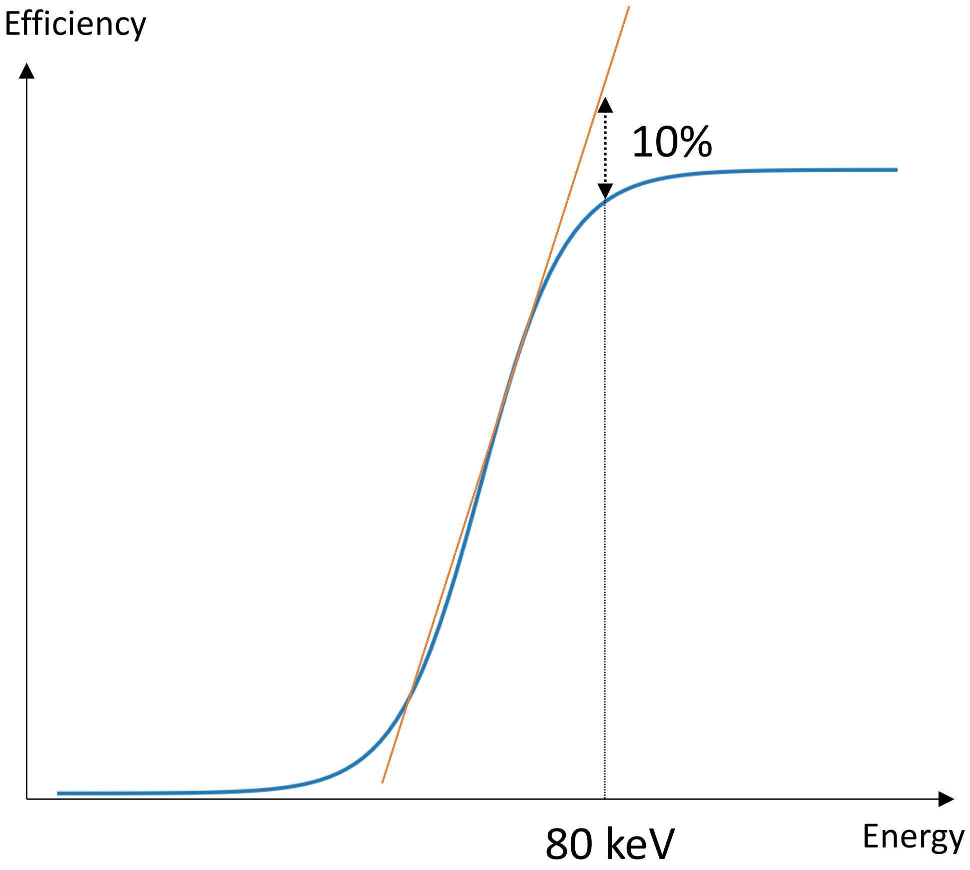




Gold/Tungsten/Lead calibration

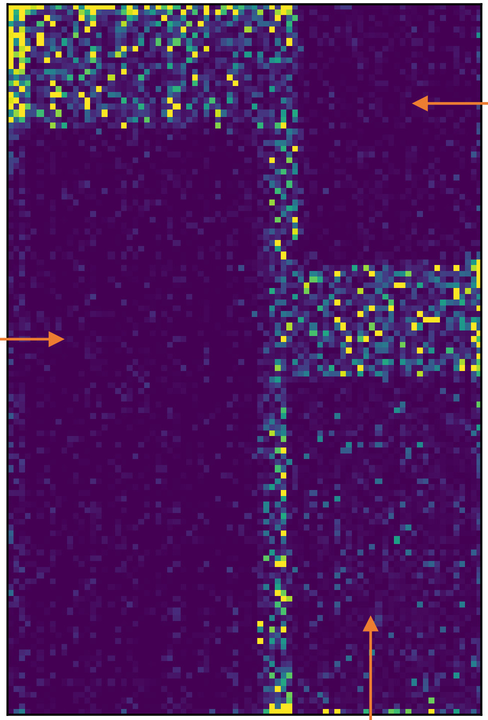
	Tungsten	Gold	Lead
K-edge	69.5 keV	80.7 keV	88 keV
ITUNE	70		
ITH	115		
DACL step (estimated)	Between 1.7 and 2.5 keV		
Number of pixels calibrated	9041	8633	8928
Number of pixels miscalibrated	1579	399	349
% of the detector well calibrated	77.7 %	85.8 %	89.3 %

Linearity of the analog chain



Gold/Tungsten separation

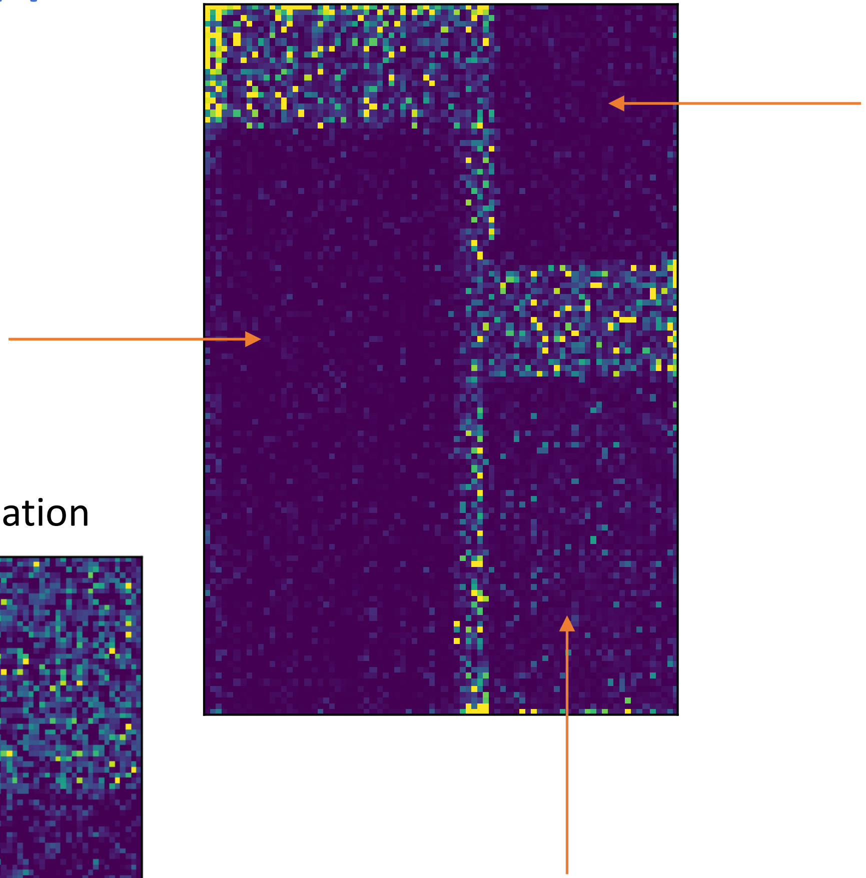
White pixel: uncalibrated



White pixel: uncalibrated

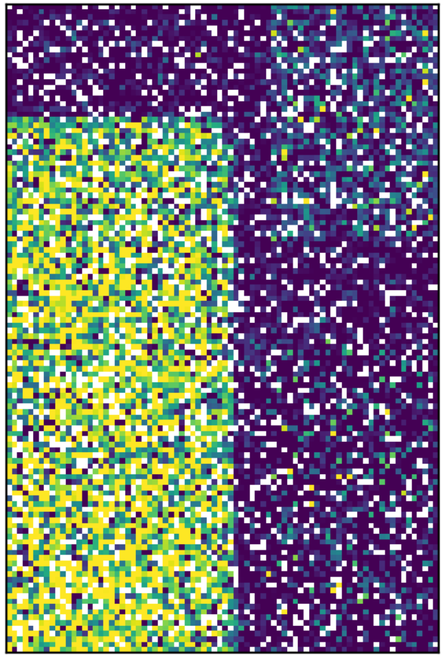
Gold/Tungsten separation

Setup

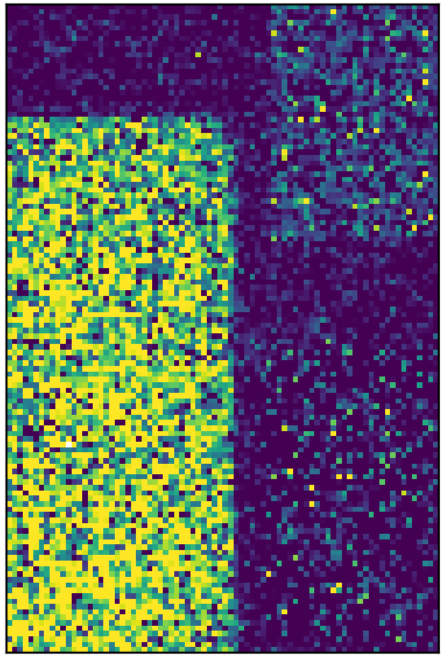


Gold separation

With pixels uncalibrated



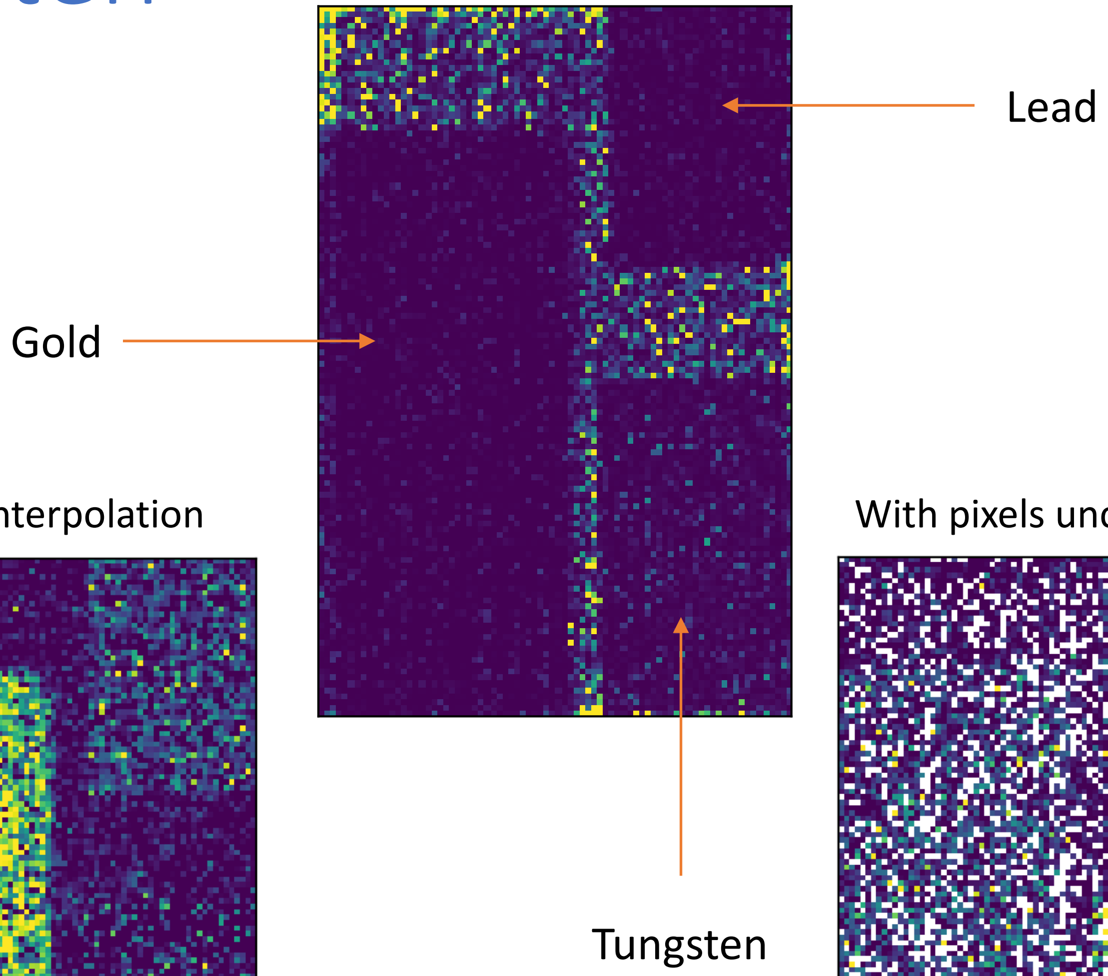
With interpolation



Gold/Tungsten separation

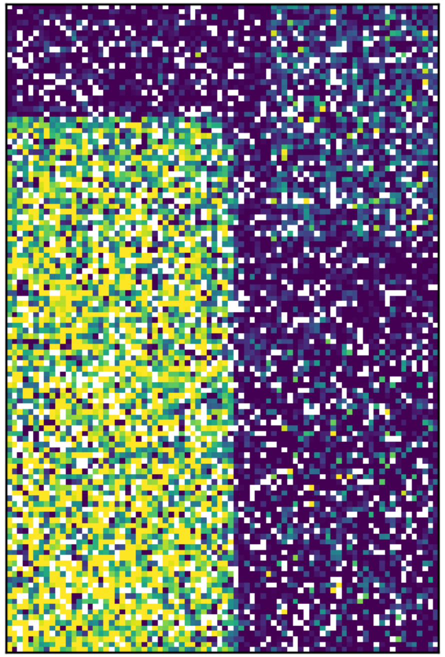
White pixel: uncalibrated

Setup



Gold separation

With pixels uncalibrated



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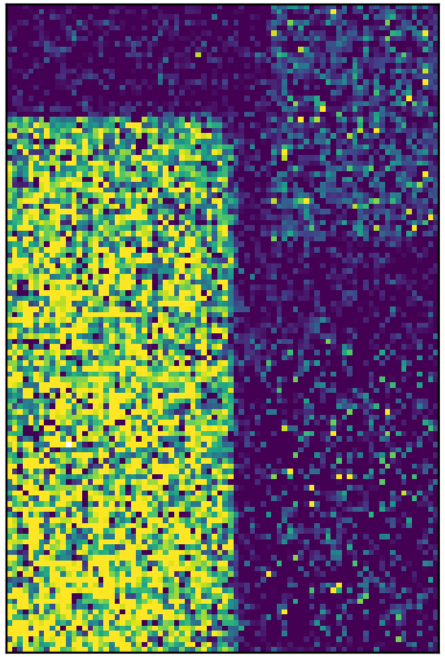
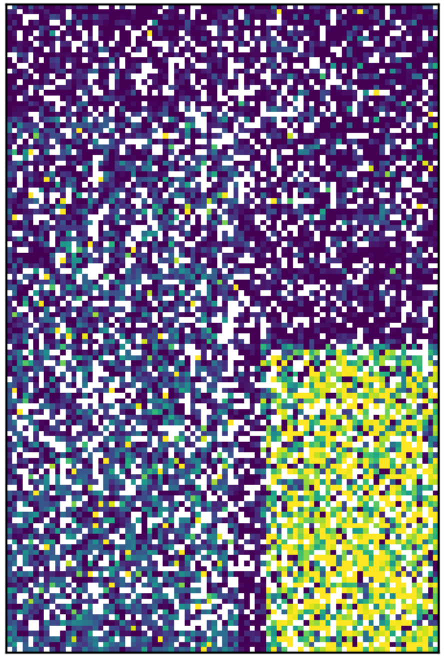


Tungsten separation

With pixels uncalibrated



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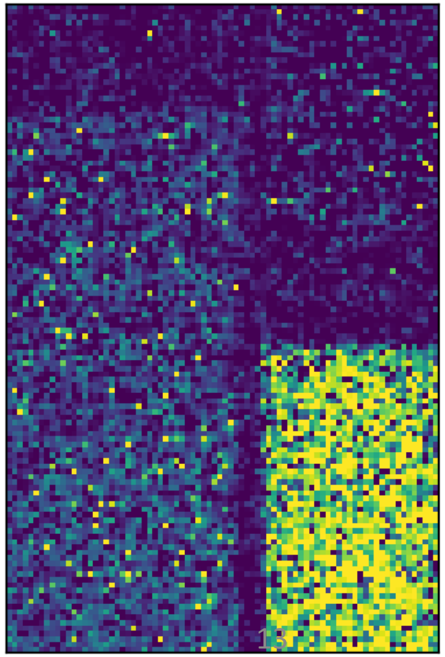
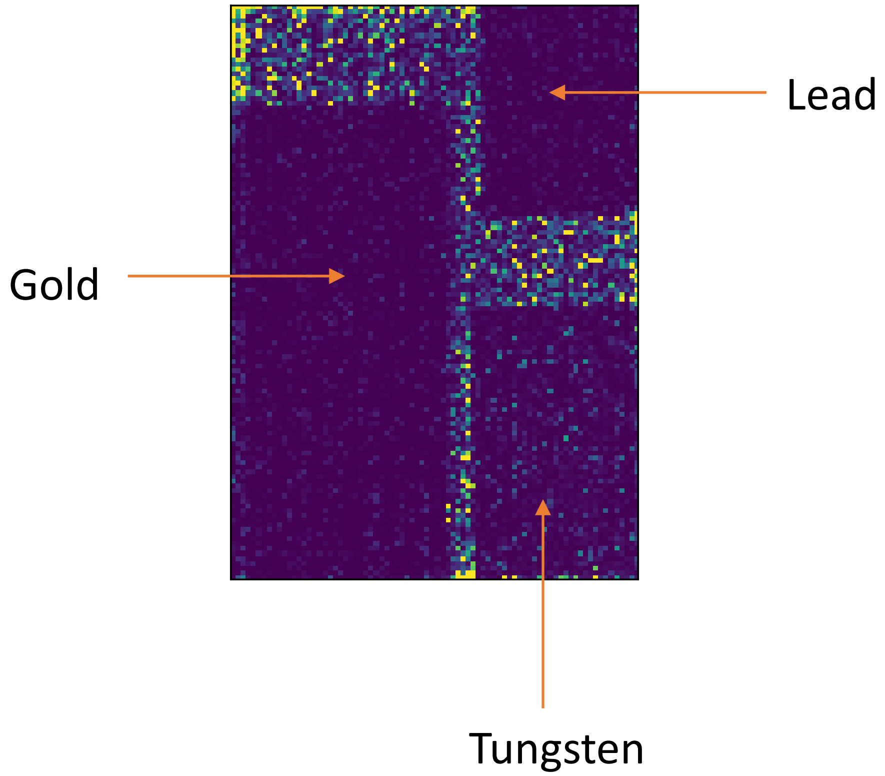
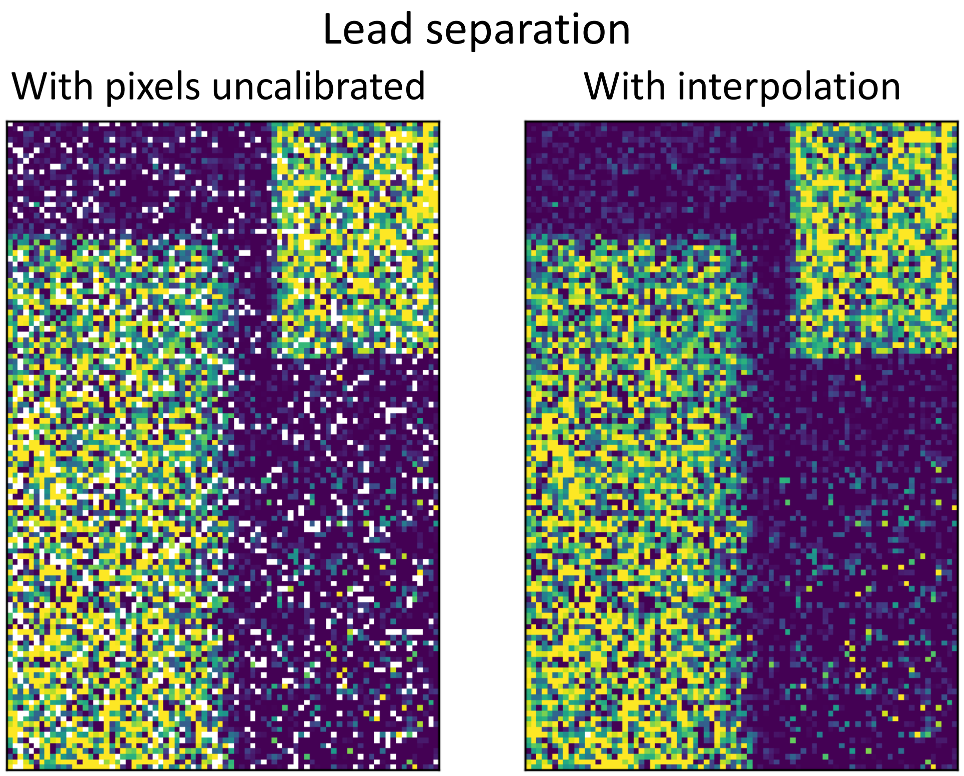


Lead separation limits





At this energy, gold and lead are too close and the electronic non-linearity doesn't allow to separate correctly the lead

Conclusion

- Longitudinal studies allow us to follow tumors throughout treatments experiment
  - ➢ Try to understand the heterogeneity of responses

- We are able to do spectral imaging with GaAs detector and to separate materials (up to gold)
- We have developed an algorithm (ProMeSCT) which is able to quantify the quantity of each material

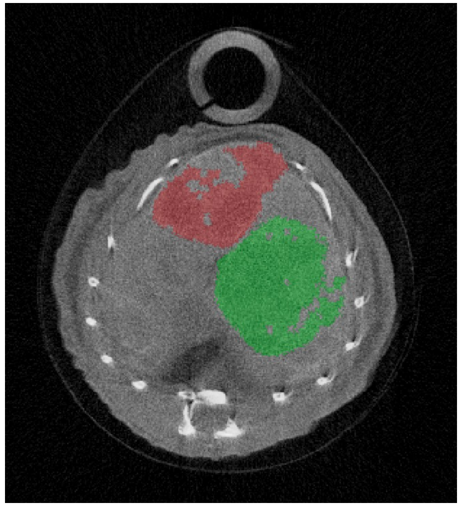
  - ➢ Do a tomographic in-vivo test with a **complete module** from Cegitek

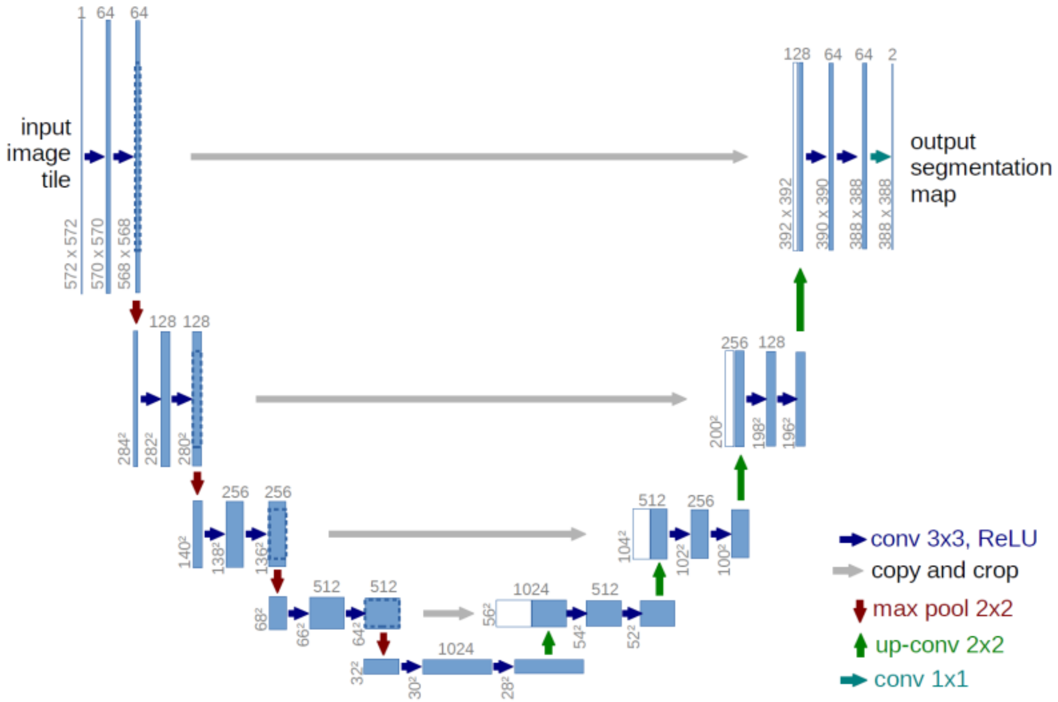
Thank you for your attention

Backup

Deep learning method

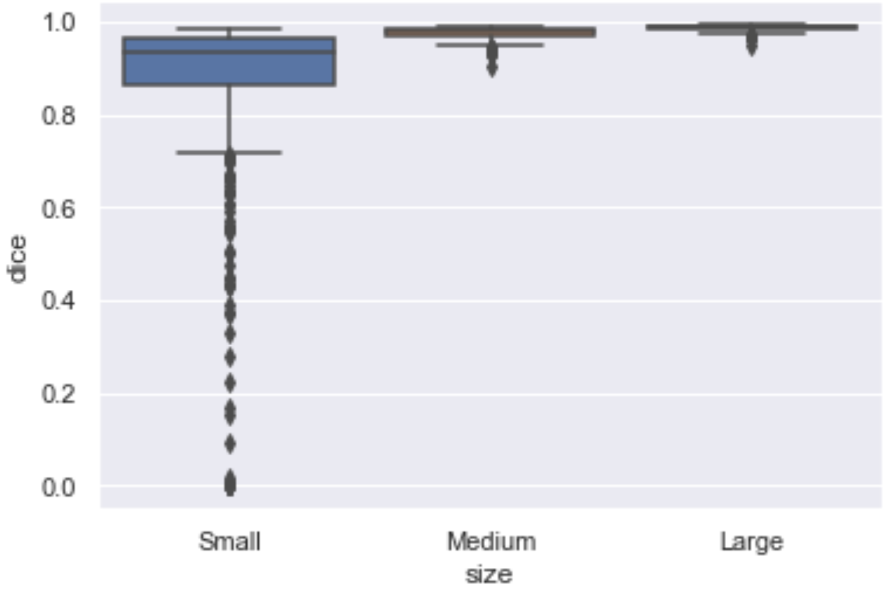
Database: 73 scans + segmentation





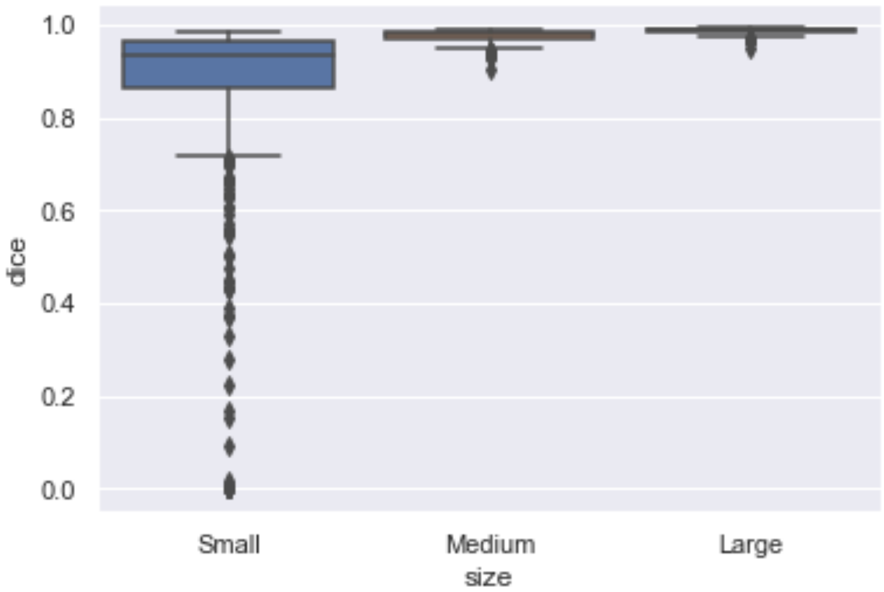
Unet network

Score dice according to the tumor size



Deep learning method

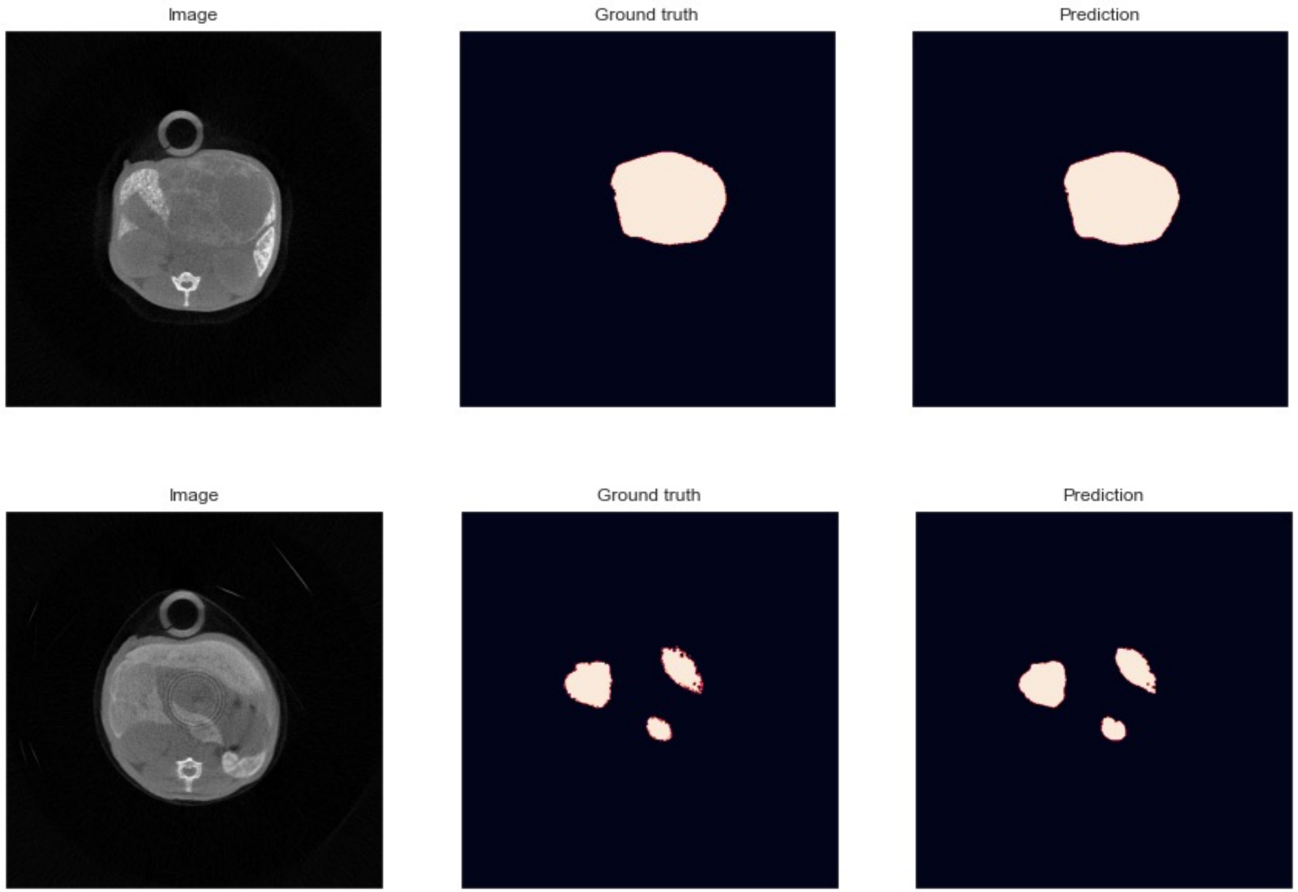
Score dice en fonction de la taille de la tumeur



Performance moyenne : 0.92

Classification des tumeurs :

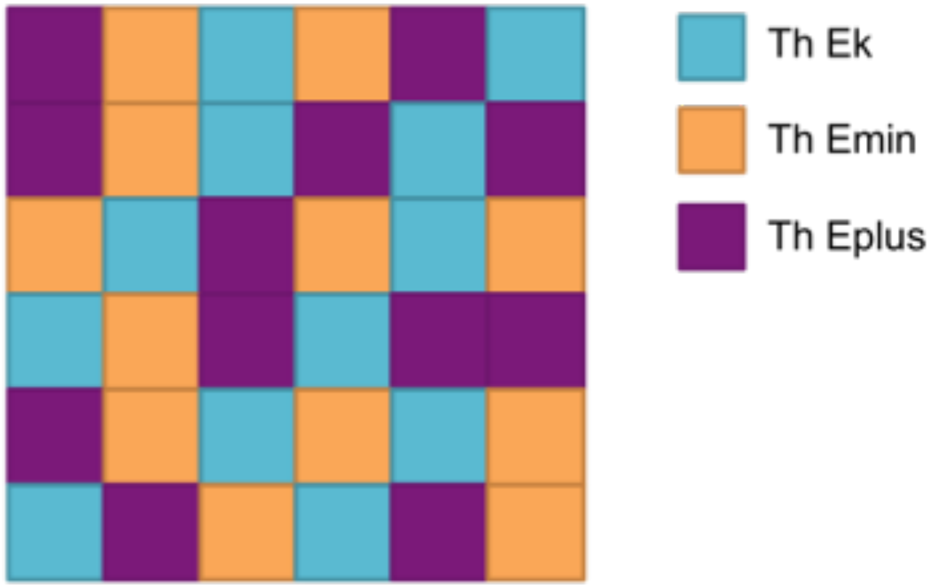
- Small : < 50 mm^2
- Medium : 50 <= tumeur < 100 mm^2
- Large : >= 100 mm^2

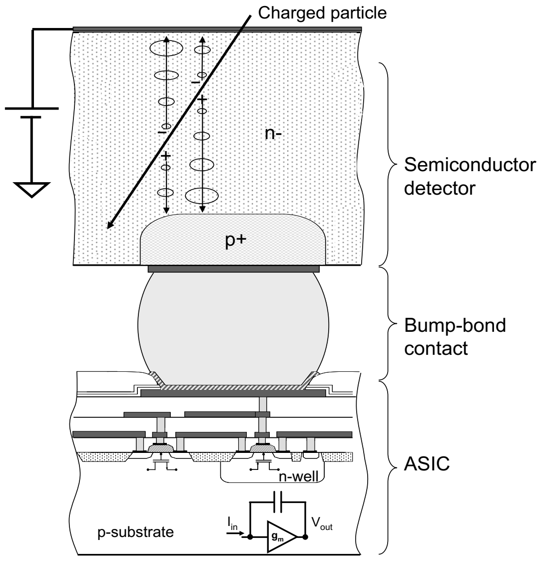


Exemples de prédictions

Composite pixel

Composite pixels:
- Apply an irregular pattern on energy thresholds
- Get the spectral information in a single acquisition
- Reduce the dose





Hybrid pixel scheme