SPECT imaging of ^{161}Tb and ^{155}Tb and impact of ^{156}Tb pollution on image quality

M. Hussein[a,b], M. Bouteculet[a,b], M.-A. Duval[a,b], S. Gnesin[c], S. Medici[c], D. Viertl[d], C.-O. Bacri[a,b], M.-A. Verdier[a,b].

a: Université Paris-Saclay, CNRS/IN2P3, IJCLab, 91405 Orsay, France.
b:Université Paris Cité, IJCLab, F-91405, Orsay, France.
c: Department of Nuclear Medicine and Molecular Imaging, University Hospital of Lausanne, Lausanne, Switzerland.
d: Institute of Radiation Physics, University Hospital of Lausanne, Lausanne, Switzerland.

Vectorized internal radiotherapy and Theranostic approach

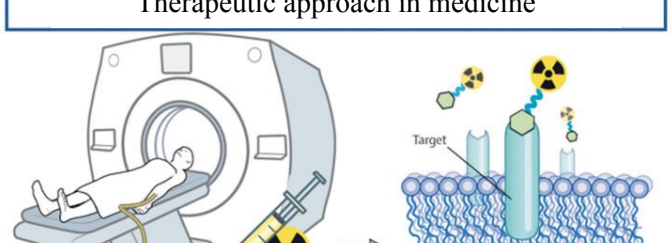
- Vectorized internal radiotherapy (VIR) involves injecting radionuclide isotopes to target and treat cancer.
- To develop new VIR radiotracers, particularly those enabling a theranostic (therapeutic + diagnostic) approach.
- Terbium (Tb) features four key isotopes ideal for theranostic applications in nuclear medicine[1].

Isotope	Diagnosis	Therapy	1/2 life
^{149}Tb	? β+ 14.2% , γ	α	4.118 h
^{152}Tb	β+ (PET)		17.5 h
^{155}Tb	γ (SPECT)		5.32 d
^{161}Tb	Low energy γ (47.5 keV, 74.6 keV)	β-	6.89 d

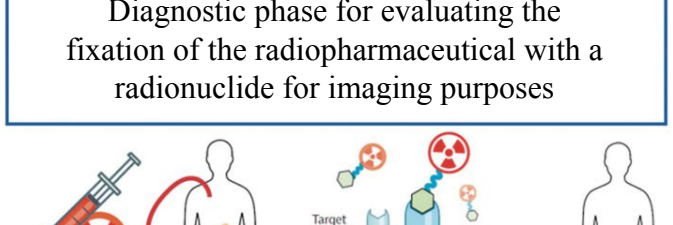
Potential theranostic pair

Potential theranostic pair

Therapeutic approach in medicine



Diagnostic phase for evaluating the fixation of the radiopharmaceutical with a radionuclide for imaging purposes



Therapeutic phase with injection of a radiopharmaceutical with a radionuclide for tumoricidal purposes

La radiothérapie interne vectorisée, nouveau pilier contre le cancer, O. HUILLARD (M.D, Ph.D, E23)

[1] Naskar N, Lahiri S. Theranostic Terbium Radioisotopes: Challenges in Production for Clinical Application. Front Med (Lausanne). 2021 May 31;8:675014.

- PRALINE project: Production RAdioisotopes et Ligants pour l'Imagerie NucléairE
  - Aims to develop new methodologies of radioisotopes production, and develop approaches and methods for nuclear imaging (and new ligands).

- PRALINE-Imaging (SPECT) sub-project Objectives:
  - Study ^{161}Tb SPECT imaging capability.
  - Evaluate the impact of ^{156}Tb contamination (co-produced with ^{155}Tb) on quantitative ^{155}Tb SPECT imaging (same $T_{1/2}$), and acceptable contamination limit in ROI [60, 125] keV.

- Methodology:
  - SPECT imaging experiment of ^{161}Tb.
  - SPECT imaging exp. of: pure (^{155}Tb) and contaminated (^{155}Tb+^{156}Tb).
  - Monte Carlo simulation validated by the experiments.

Gamma rays (keV)		
^{161}Tb	^{155}Tb	^{156}Tb
25.65(23.2%)	86.54 (32%)	88 (18%)
48.92 (17.0%)	105.3 (25.1%)	199.2 (41%)
74.56 (10.2)	180.1 (7.5%)	356.3 (13.6%)
	262.3 (5.3%)	534.3 (67%)
		1065.1 (10.8%)
		1154.1 (10.4%)
		1222.4 (31%)
		1421.7 (12%)

Experimental Setup: Albira S108 – BRUKER

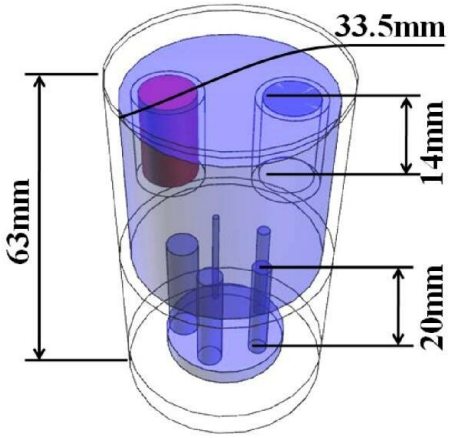
- Detector: ALBIRA S108 small animal PET/SPECT/CT (industrial) imaging system (BRUKER)[1].

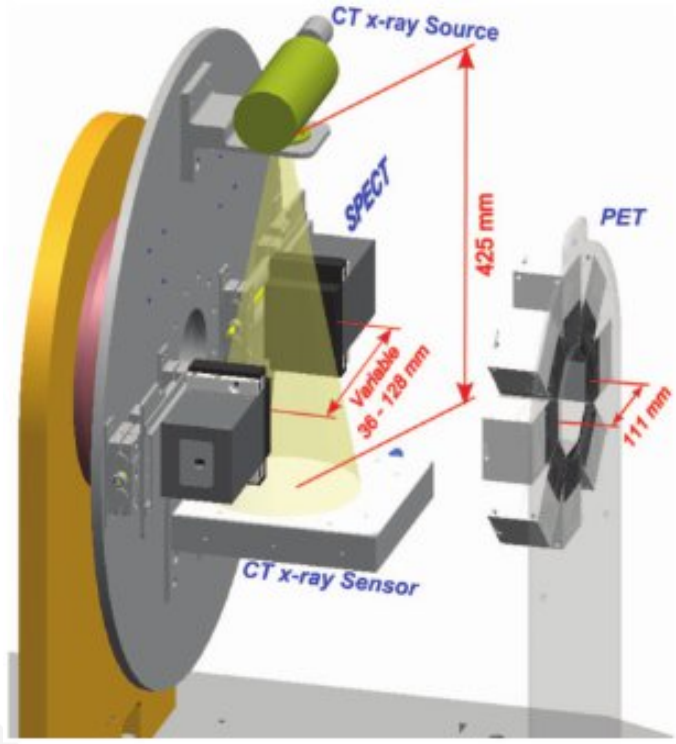
- 2 rotating SPECT heads, 30 positions/camera (6°).
  - Camera optimized for ^{99m}Tc (140 keV).
  - Single pinhole collimator (2 mm W).
  - Spatial Res.(FWHM) : ~1.5 mm (BRUKER).

- Tomo-Reconstruction program implemented.

- Phantom: NEMA NU 4-2008 phantom[2].

➢ **Study and understand camera performance, include corrections in reconstruction.**





[1] Sánchez et al. Med. Phys, 40, No. 5, May 2013.

[2] NEMA Standards Publication NU 4-2008 Performance Measurements of Small Animal Positron Emission Tomographs National Electrical Manufacturers Association 1300 N. 17th Street, Suite 1752 Rosslyn, VA 22209.

Experimental Setup: Tomographic reconstruction and MC simulation

- Monte Carlo simulation: GATE[1] 10 Platform (Geant4 based)

- Tomographic Reconstruction:

  - Ordered Subset Expectation Maximization (OSEM) algorithm, a Faster MLEM variant used for reconstruction.

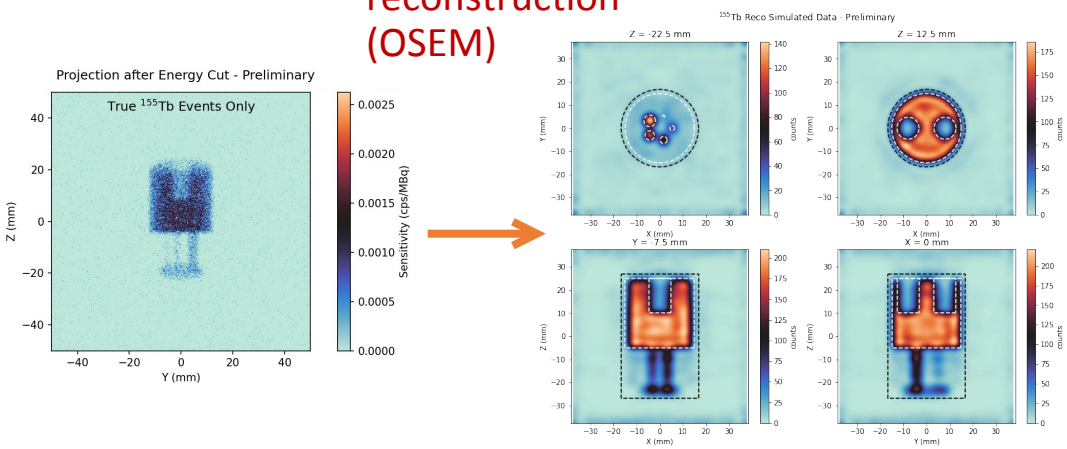
  - CASToR[1] platform used for reconstruction, camera implemented and parameters optimized within it.

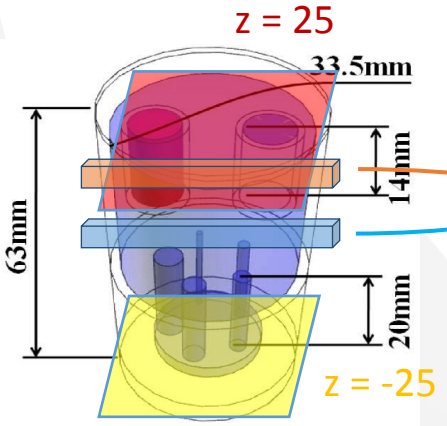
    - Different parameters was optimized.
    - Corrections factors implemented.

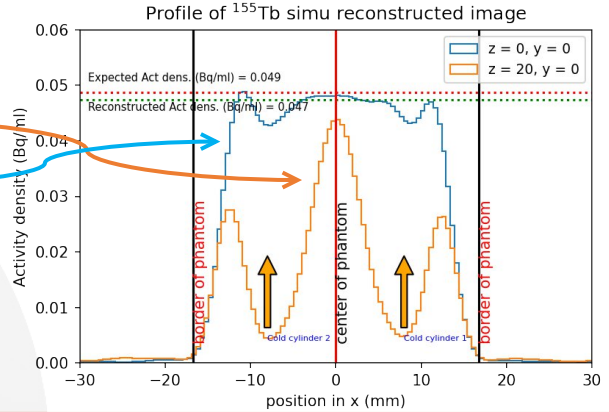
a. 2D Projection

b. 3D image reconstruction (OSEM)

c. 3D reco. image







[1] David Sarrut et al 2021 Phys. Med. Biol. 66 10TR03.
[2] CASToR: a generic data organization and processing code framework for multi-modal and multi-dimensional tomographic reconstruction, Thibaut Merlin et al., 2018.

- Experiments: 3 experiments at CHUV, Lausanne for simulation calibration:
  - 7 MBq of ^{155}Tb ($T_{1/2}$: 5.32 d) phantom (12 h acquisition) – Produced by MEDICIS/CERN .
  - 32.4 MBq (~89%-8%) ^{155}Tb -^{156}Tb phantom (12 h acquisition) – Produced by PSI. (+3% ^{154}Tb)
  - 50 MBq of ^{161}Tb phantom (4 h acquisition) – Produced by PSI.

Isotope	Half life
^{154}Tb	21.5 h
^{155}Tb	5.32 d
^{156}Tb	5.35 d
^{161}Tb	6.96 d

- To quantify the reconstructed images, multiple factors were calculated:
  - Integral uniformity [%]: $IU = \frac{\sigma_N}{\overline{N}}$
  - Signal to noise ratio: $SNR = \frac{|N_s - N_n|}{N_n}$
  - Contrast factor of the cold cylinders [%]: $Q_{cold} = [1 - \frac{\bar{S}_{cold}}{\bar{S}_{Phantom}}]$

σ_N: Standard deviation of voxels values in ROI.
$\overline{N}$: Sum of counts in ROI averaged by # of voxels.

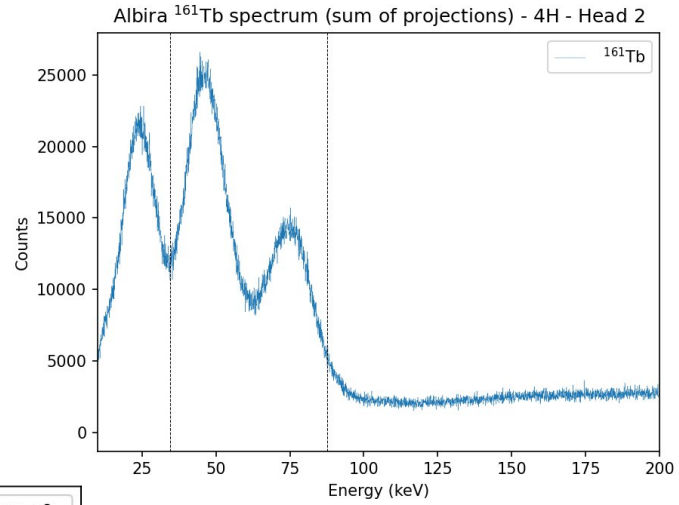
N_s: # of counts considered as signal in ROI.
N_n: # of counts considered as noise in ROI.

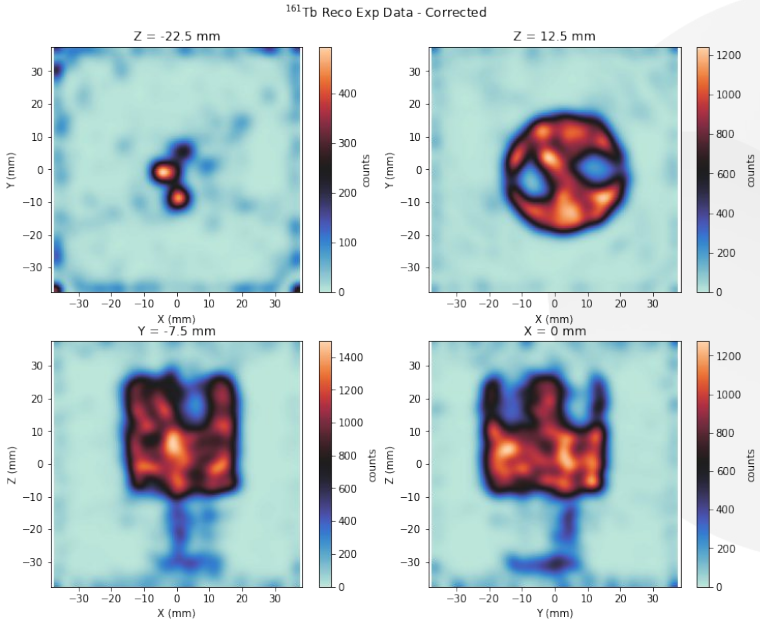
$\bar{S}_{cold}$: average counts in the cold cylinder.
$\bar{S}_{Phantom}$: average counts in the ROI of the phantom.

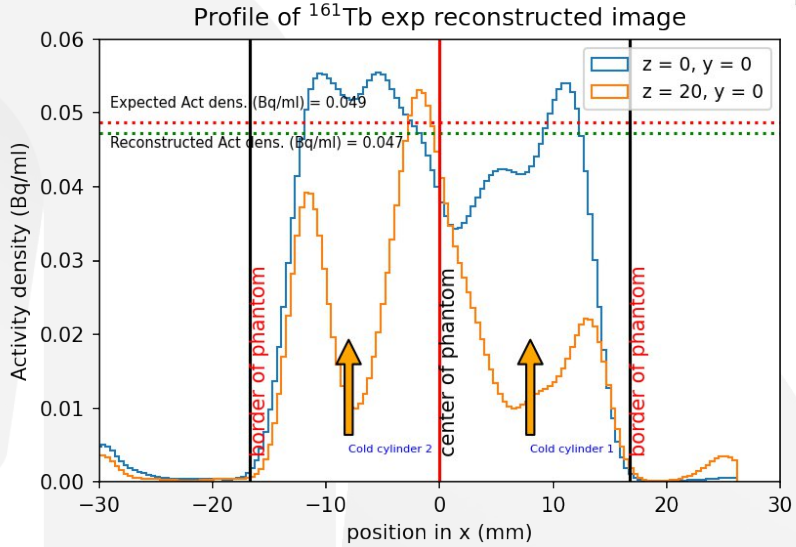
Study ^{161}Tb SPECT imaging capability: Results

- 2 γ peaks (48.9 keV, 74.6 keV) utilizable for SPECT tomographic reconstruction.
- Despite the notable in-homogeneity & non negligible BG, largest rods well-reconstructed.

➡ **Strong potential of ^{161}Tb in imaging clinical application.**







Quantification factor	^{161}Tb Pure
SNR	104.5
IU (%)	16.31
Q_{cold} (%)	88.97

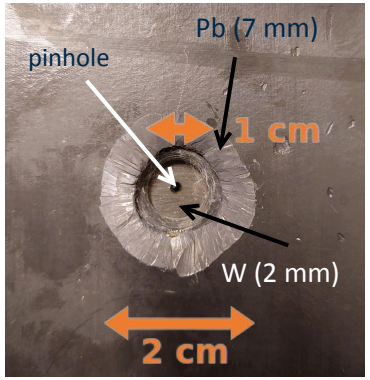
^{155}Tb - $^{154\text{-}155\text{-}156}$Tb experimental results

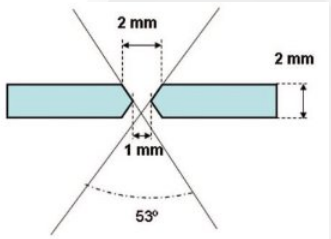
Quant. factor	^{155}Tb exp	$^{154\text{-}155\text{-}156}$Tb exp
SNR	50.86	7.12
IU (%)	8.39	7.54
Q_{cold} (%)	84.48	63.19

➡ ~ 7 times better

- Image immensely polluted with ^{156}Tb .

➡ Shielding and collimation not adapted for these high energies.

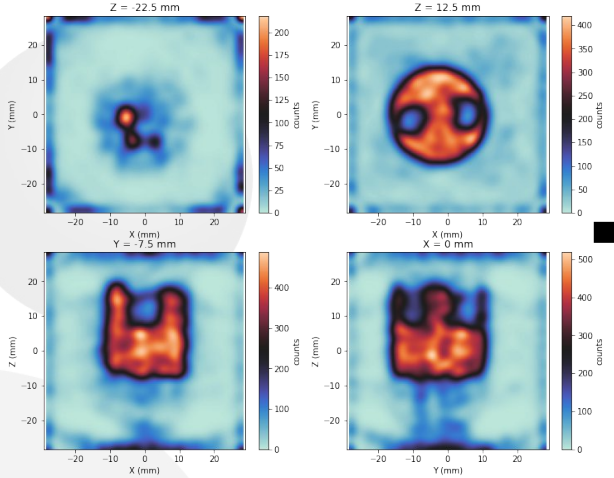


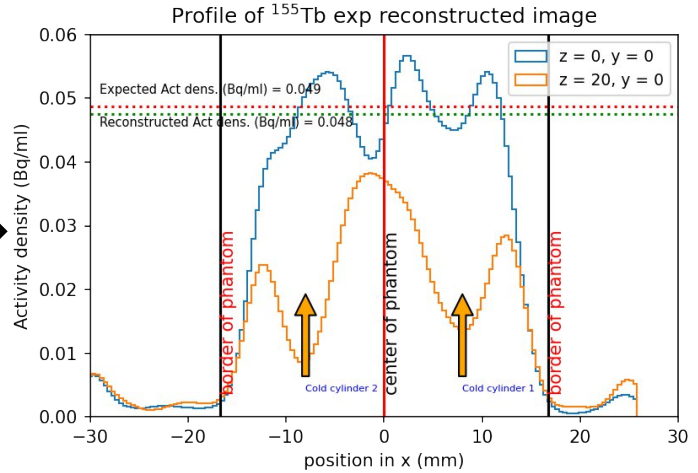


Knife-edge pinhole

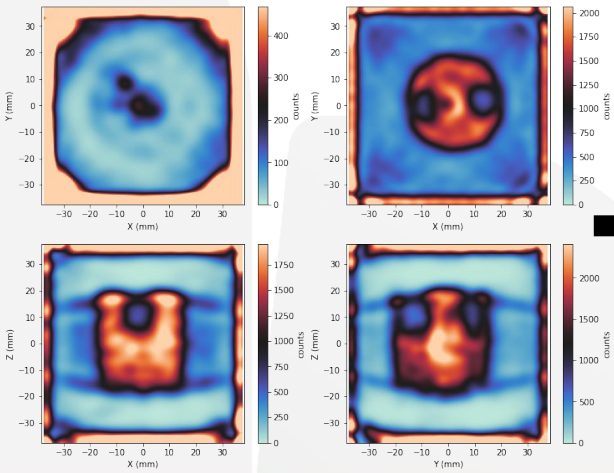
➡ **To study it using simulation.**

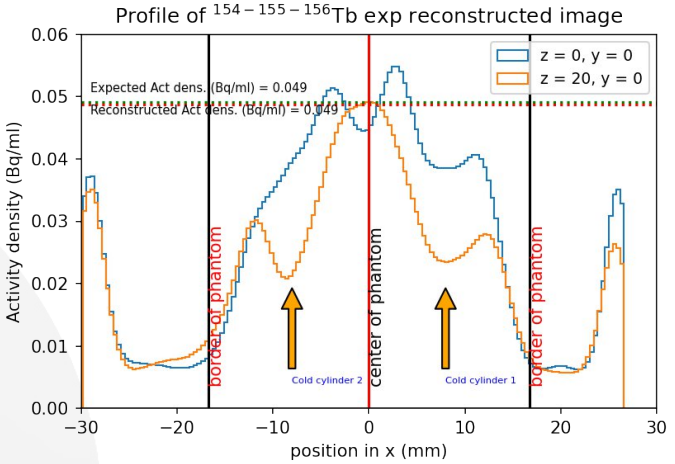
^{155}Tb Reco Exp Data - subtracted and corrected





$^{155-156}$Tb Reco Exp Data





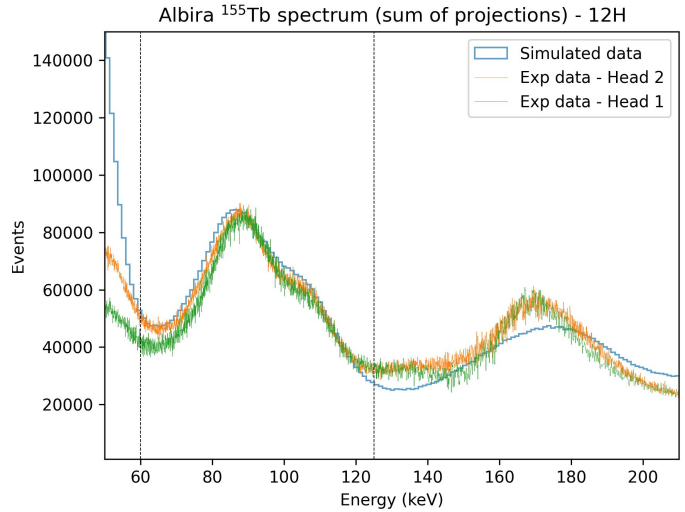
MC simulation: GATE

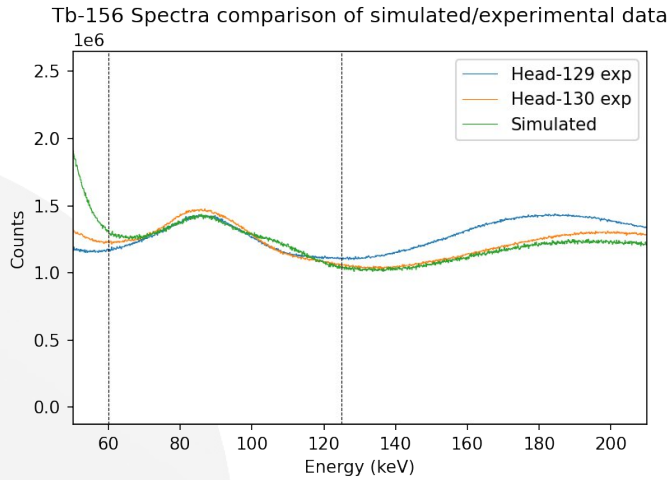
- Objectives of simulation:
  - Accurately replicate Albira and validate the simulation based on experimental data.
  - Determine contamination acceptable limit.
  - Optimize collimation and shielding.

- Methodology:
  - GATE 10 simulation[1] (reproduction) of camera, phantom and all sources (isotopes and contaminants).
  - Simulate different mixtures of isotopes.

- Simulated spectrum approximately reproduce the experimental one in [50, 200] keV.

➢ Reproduction of the camera within ROI [60, 125] keV.





Simulation-experiment comparison

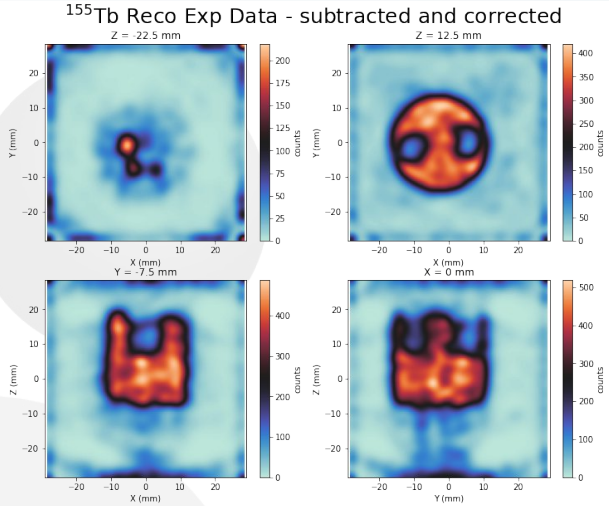
- Simulation reconstructed images are more homogeneous, rods ~ 2 mm SR.
- Successful reproduction of the camera output and effective reconstruction.
- Diffusion at borders of phantom even for simulated data > Reco. effect, scattering?

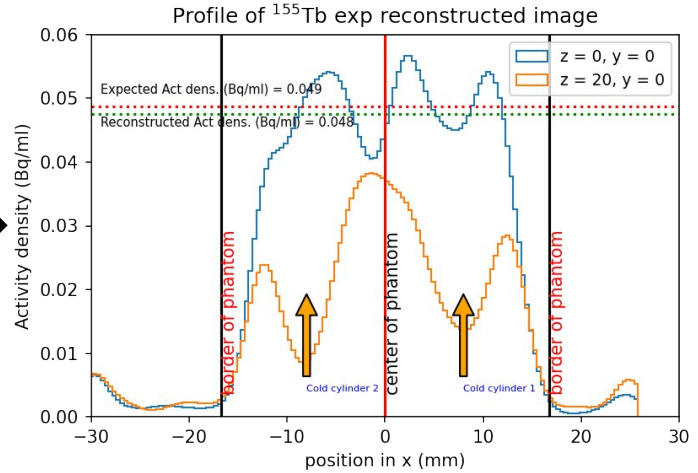
➢ Profiles show that this SPECT camera is not perfectly reproduced by simulation.

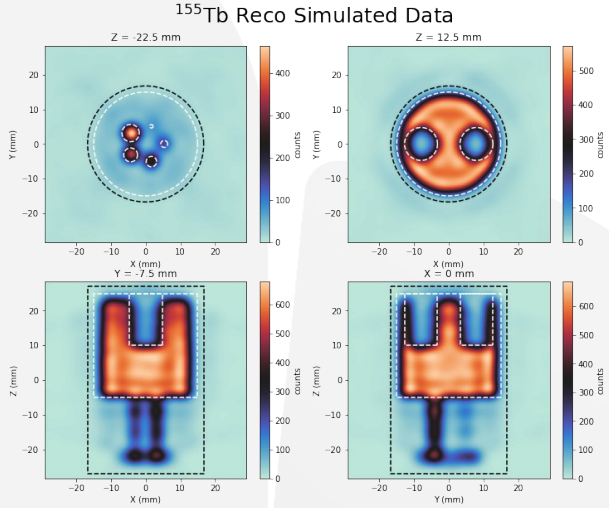
Quantification factor	^{155}Tb simu	^{155}Tb exp
SNR	103.9	50.86
IU (%)	4.49	8.39
Q_{cold} (%)	89.73	84.48

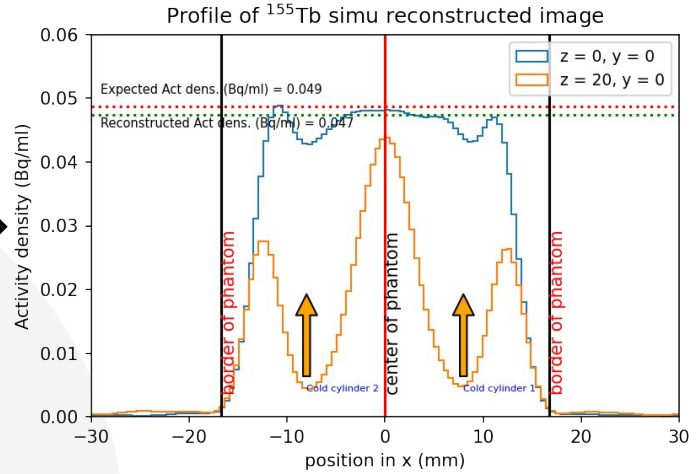
➡ >2 times better

➡ ~2 times better



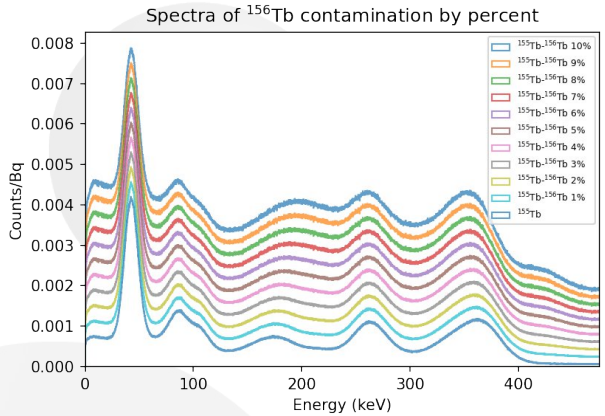


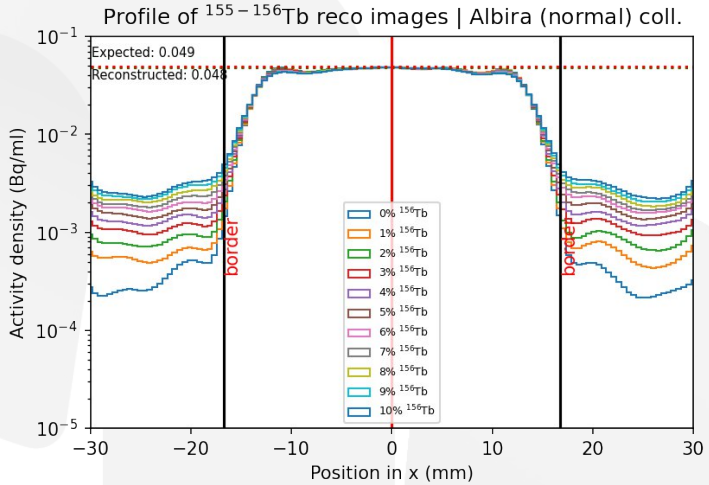


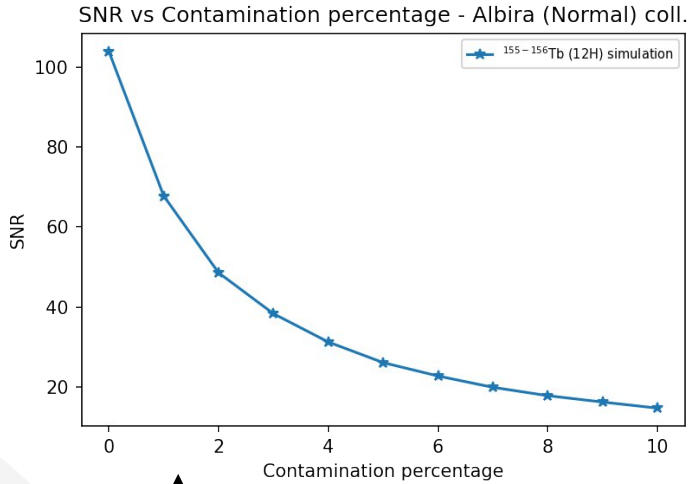


Normal density collimator

- To study the impact of contamination: ^{155}Tb with ^{156}Tb contamination from 0% to 10% was simulated.
- At 2% ^{156}Tb contamination, SNR drop (exponentially) to its half.
- ^{156}Tb detected counts contribution in ROI:
  - At 1% activity cont. = 25.8%
  - At 10% activity cont. = 79.3%



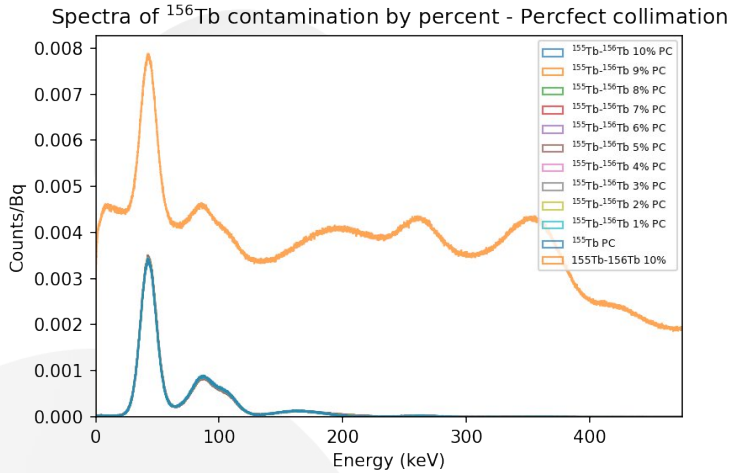




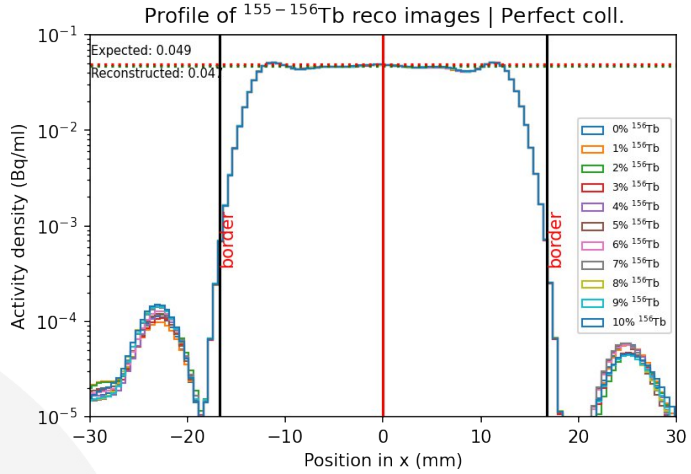
Infinite (Perfect) density collimator

- To study the impact of low collimator thickness & weak shielding: density of collimator and shielding is set into infinity in the simulation.

- Notably ^{156}Tb contribution is negligible if HE collimator is used.
  - ➢ Results are not dependent on the radionuclide alone; it depends on the specific imaging camera used.



- ^{156}Tb detected counts contribution in ROI:
  - At 1% activity cont. = 0.5% detected counts
  - At 10% activity cont. = 4.9%



Conclusion and Summary

- SPECT camera (Albira) was calibrated, studied and implemented in CASToR.
  - Camera has good performance at low energy, however, high energy gammas are not collimated.
- Experiments of ^{161}Tb, ^{155}Tb & $^{155\text{-}156}$Tb were performed.
  - Strong ^{156}Tb contamination due to insufficient collimation.
  - ^{161}Tb and (pure) ^{155}Tb projections reconstructed and quantified $\rightarrow$ confirm imaging capability.
  - ^{161}Tb has strong potential in imaging clinical application.
- Preliminary simulation of MC digital twin of this SPECT camera were done.
- Contamination acceptable limit is dependent on used instrumentation (camera and collimation).
- A well-collimated camera effectively addresses imagery requirements, while dosimetry questions remain under investigation.

- Determine acceptable contamination limit of ^{156}Tb (as a function of collimation) for clinical purposes using simulation.
- Study dosimetric aspects of ^{156}Tb contamination.
- Determine acceptable contamination limit with well-collimated medium energy camera (THIDOS[1]).

(1) Medium energy camera developed in our group, optimized at 370 keV.

Thank You

Thank to PRISMAP[1] European project and CNRS MITI, this project was financed by them.

Thanks to C. Duchemin[a],N. van der Meulen[b], Z. Talip[b]

1: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP)
a: MEDICIS, CERN.
b: Paul Scherrer Institute PSI.

Quantifying The Results of the Reconstruction

➢ To quantify the reconstructed images, multiple factors were calculated:

- Integral uniformity (IU) [%]:

$$IU = \frac{\sigma_N}{\overline{N}}$$

σ_N: Standard deviation of voxels values in ROI.
$\overline{N}$: Sum of counts in ROI averaged by # of voxels.

- Signal to noise ratio (SNR):

$$SNR = \frac{|N_s - N_n|}{N_n}$$

N_s: # of counts considered as signal in ROI.
N_n: # of counts considered as noise in ROI.

- Contrast factor of the cold cylinders (Q_{cold}) [%]:

$$Q_{cold} = [1 - \frac{\overline{S}_{cold}}{\overline{S}_{Phantom}}]$$

$\overline{S}_{cold}$: average counts in the cold cylinder.
$\overline{S}_{Phantom}$: average counts in the ROI of the phantom.

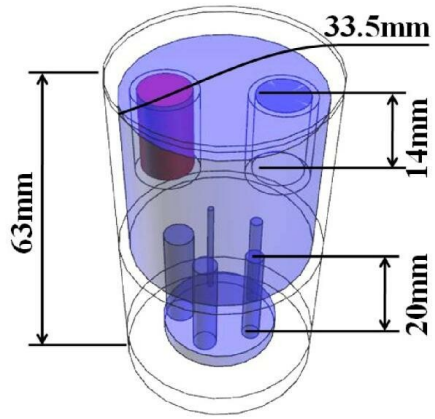
Experimental Setup: Albira S108 – BRUKER

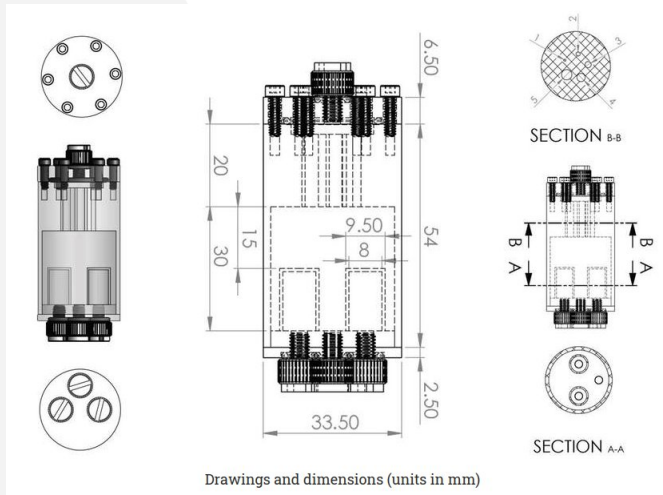
- Detector: ALBIRA S108 small animal PET/SPECT/CT (industrial) imaging system (BRUKER)[1].
- 2 rotating SPECT heads, 30 positions/camera (6°).
  - Camera optimized for ^{99m}Tc (140 keV).
  - Single pinhole collimator (2 mm W).
  - Energy range 30-400 keV (BRUKER).
  - Energy Res. (FWHM) : 13.5% @140 keV (BRUKER).
  - Spatial Res.(FWHM) : ~1.5 mm (BRUKER).
  - Projection image in-uniformity.
- Tomo-Reconstruction program implemented.
- Offer access to List-mode data (x,y,E)

for each projection.

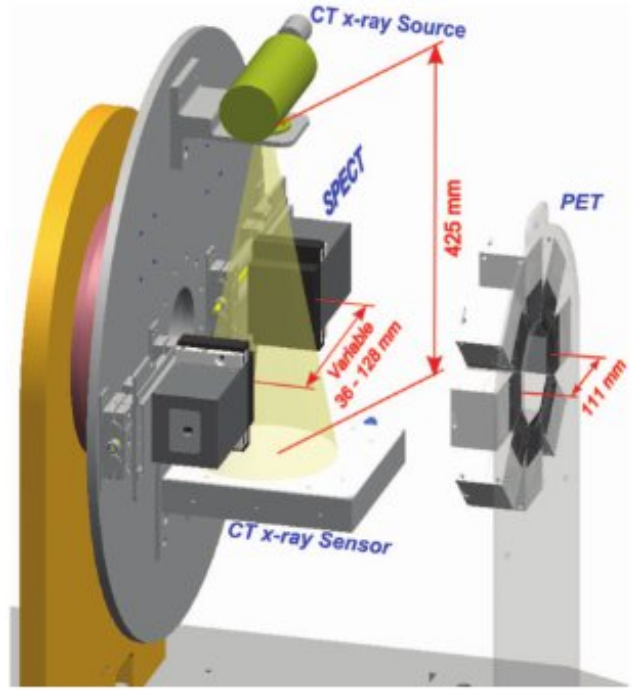
- Phantom: NEMA NU 4-2008 phantom[2].

➢ **Study and understand camera performance.**





Drawings and dimensions (units in mm)



[1] Sánchez et al. Med. Phys, 40, No. 5, May 2013.

[2] NEMA Standards Publication NU 4-2008 Performance Measurements of Small Animal Positron Emission Tomographs National Electrical Manufacturers Association 1300 N. 17th Street, Suite 1752 Rosslyn, VA 22209.

Experimental setup: camera challenges

- Background studying ➡ count rate 30-40 cps (negligible).
- Sensitivity disparity between the two heads + geometrical effect ➡ corrected for each projection.
- Sensitivity drop below ~ 50 keV, and above ~ 200 keV.
- Measured spatial resolution : 17% at 140 keV.
- New calibration, calibration of head 1 is non-linear ➡ Complicate treatment and analysis !
- Projection image non-uniformity cause artifacts in reco images and lower SNR ! ➡ Corrected.
- Very thin collimator : 2 mm W with pinhole ➡ septal penetration.
- Shielding adapted for < 140 keV: 6 mm Pb behind collimator and 2 mm on camera sides
  ➡ high potential scattering.

➢ An external reconstruction performed to include all these corrections.