

# Whole-body imaging of mice administered At-211 using a high-resolution X-ray and gamma-ray camera for small animals

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## Abstract

In recent years, targeted radioisotope therapy (TRT) using alpha-particle-emitting radiopharmaceuticals, such as At-211, has attracted attention. To confirm the therapeutic efficacy of these agents, it is important to visualize the distribution of At-211 in the body with high accuracy. In animal experiments, At-211 imaging is typically performed using human SPECT, which have a typical spatial resolution of approximately 5-10 mm. However, the resolution is insufficient for animal imaging experiments because of small sample sizes. Therefore, we developed a high-resolution X-ray and gamma-ray camera with a  $10 \times 10 \text{ cm}^2$  imaging area specifically designed for mouse imaging and conducted animal experiments. At-211 AuNPs were locally administered to tumor-bearing mice, and images were acquired targeting the 79 keV X-rays emitted from At-211. Furthermore, by applying a sub-pixel shift method in some of the imaging, the accumulation of At-211 was confirmed with high resolution. The imaging results obtained the day after administration showed that accumulation in the salivary glands and thyroid gland, which could not be visualized with a human SPECT, was successfully visualized.

## Introduction

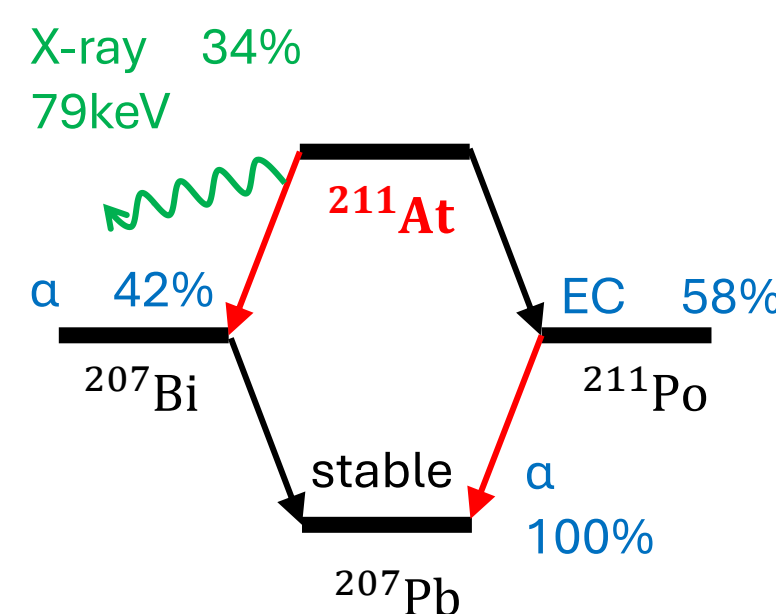
### ◆ Targeted Radioisotope Therapy (TRT)

- Expectations for  $\alpha$ -ray emitting radionuclides
- $\alpha$ -ray emitting radionuclides : Short range and high energy deposit
- $\Rightarrow$  Effective and localized treatment

### ◆ $\alpha$ -ray emitting radionuclides At-211

- Actual 100% alpha-ray emitting nuclide
- Can be produced in Japanese cyclotrons
- Emits 79 keV X-rays that can be imaged

- At-211 is particularly promising in nuclear medicine
- Visualize the distribution of At-211 is important



### ◆ Radiological imaging in animal experiments

- Resolution of human SPECT (5-10mm) is not sufficient  $\Rightarrow$  higher resolution is needed
- To confirm drug distribution in vivo  $\Rightarrow$  whole body imaging of animals at once

- Development of a high-resolution, large-area gamma camera
- Animal experiments were conducted using At-211.

## Detector configuration

### ◆ Scintillator

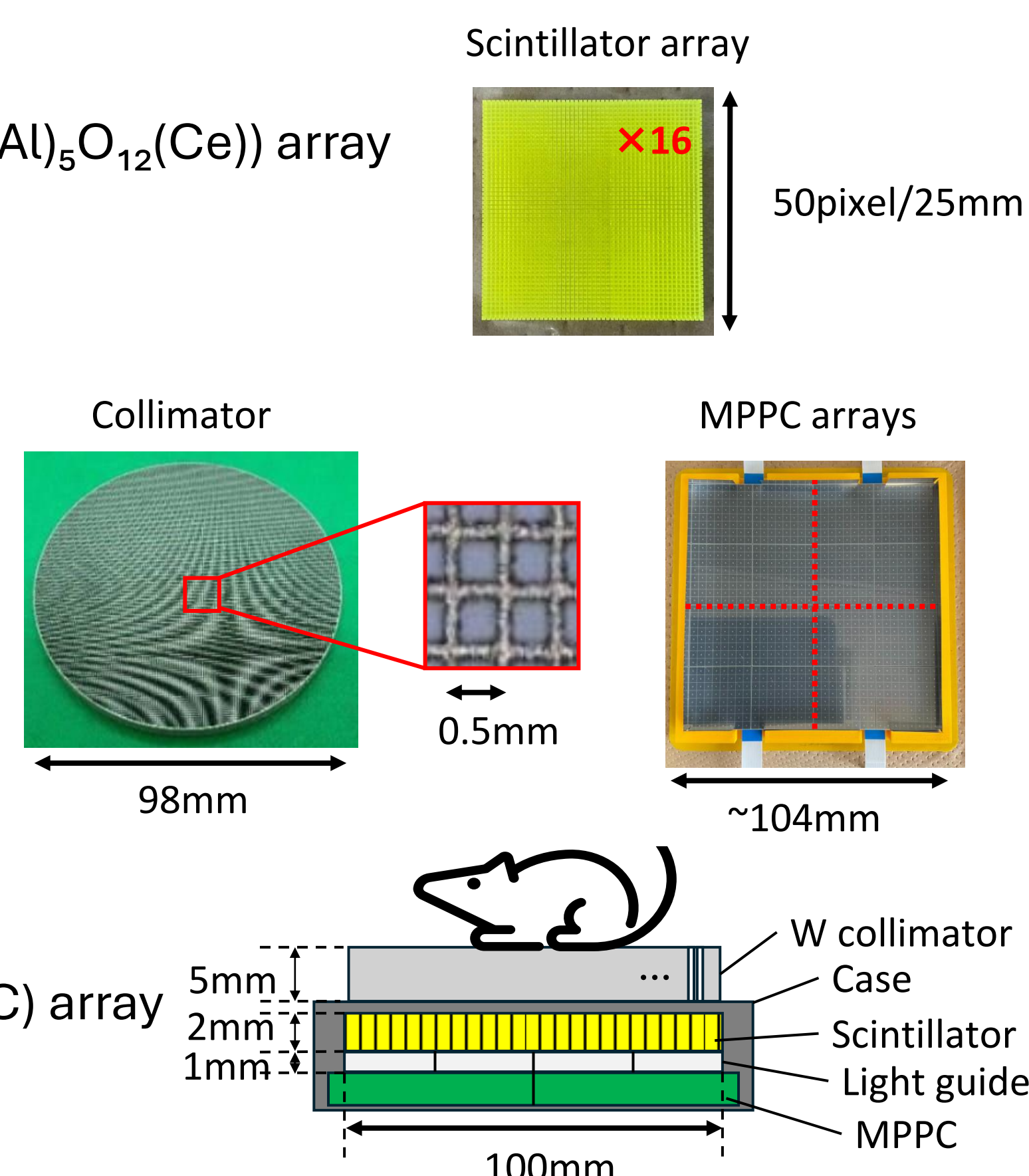
- Dicing Pixelized GAGG(=  $\text{Gd}_3(\text{Ga}, \text{Al})_5\text{O}_{12}(\text{Ce})$ ) array
- 1 pixel:  $0.5 \times 0.5 \times 2 \text{ mm}^3$
- Light guide: 1mm
- $50 \times 50 \text{ pixels/Scintillator} \times 16$

### ◆ Collimator

- Tungsten parallel collimator
- Produced by 3D printer  $\Rightarrow$  High-definition structure
- $\phi 98 \text{ mm}$
- Pitch: 0.5mm

### ◆ Photodetector

- Multi-pixel photon counter (MPPC) array
- $50 \times 50 \text{ mm}^2 \times 4$
- Signal readout at 4 ends



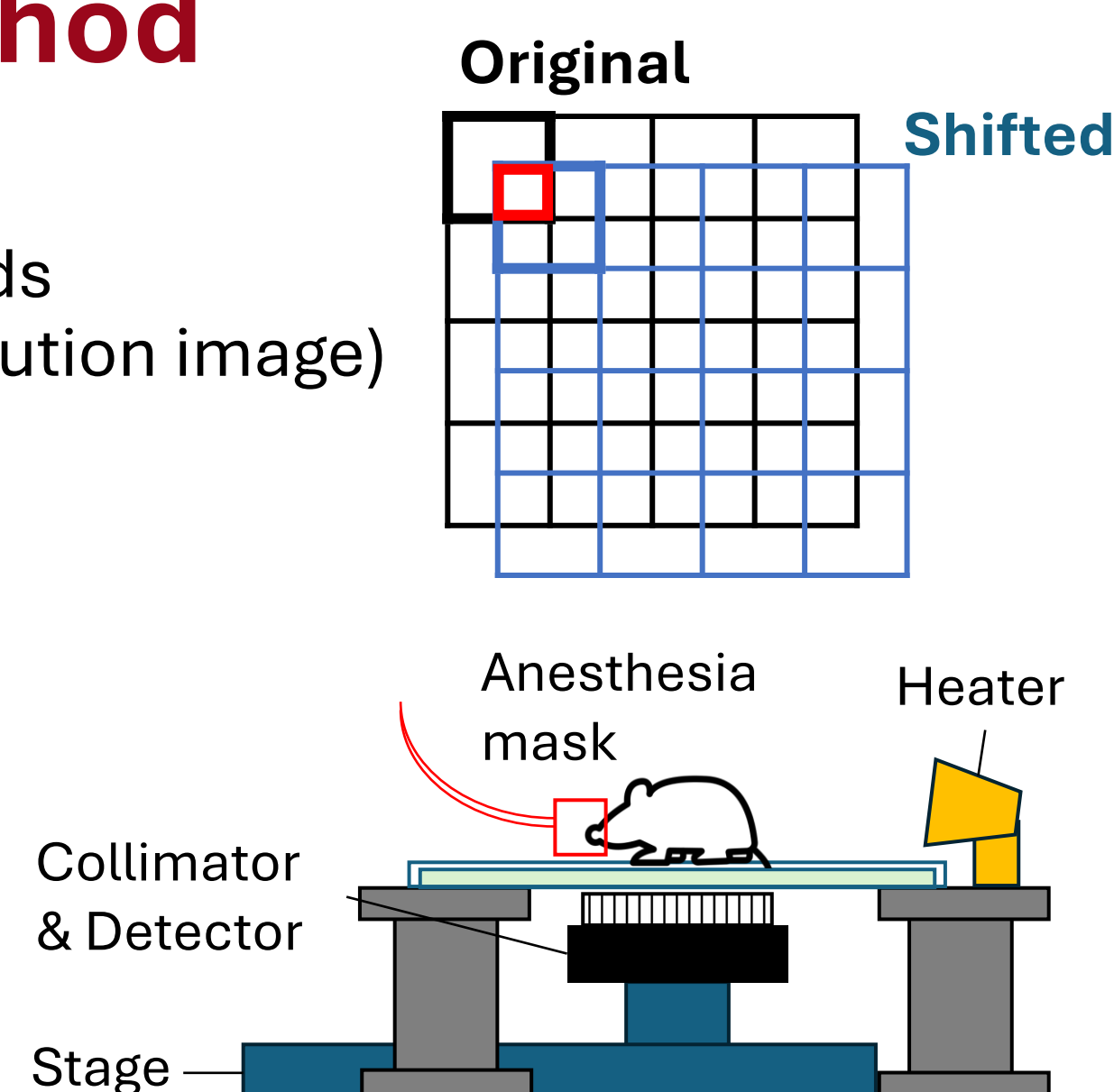
## Image Reconstruction Method

### ◆ Sub-pixel shift

- One of the super spatial resolution methods (Several low-resolution images  $\rightarrow$  high-resolution image)

### ◆ Steps

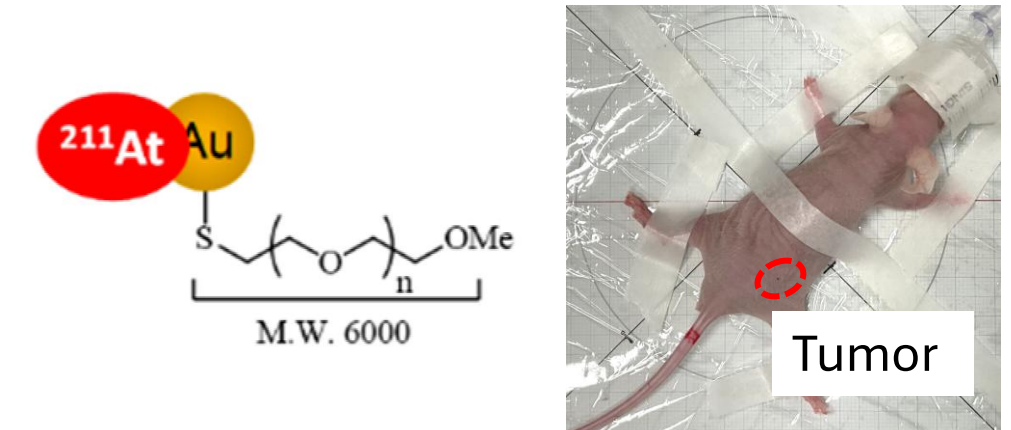
1. Obtain the original image and the shifted image using a **stage** (shifted by half a pixel in both axes)
  2. Calculate the **average value** of the overlapped area of the 2 images
- $\Rightarrow$  Generates an image with half the pixel size



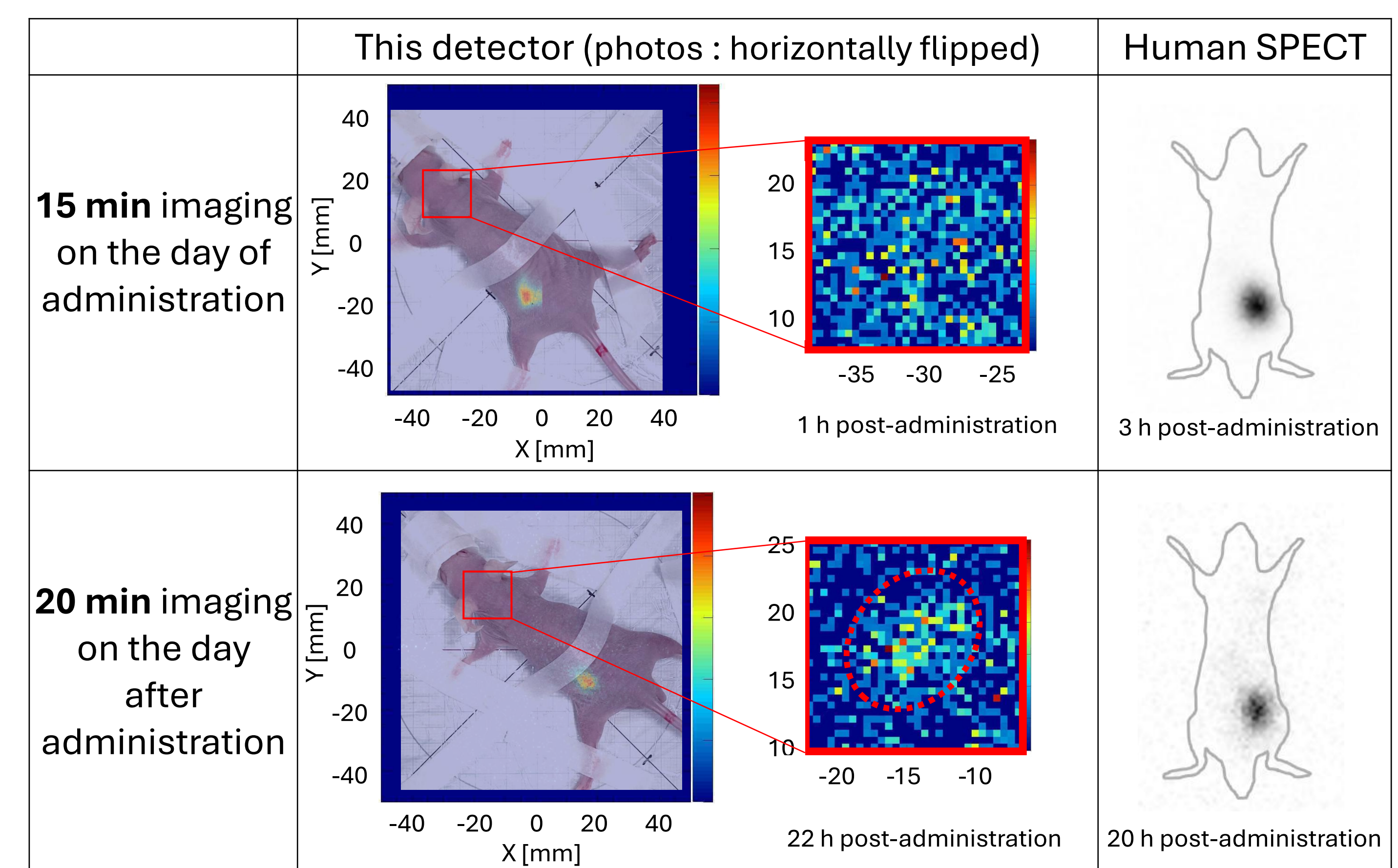
## Results of imaging in mice

### ◆ Condition

- Administration : **intratumoral administration** 0.648 MBq of 5 nm [At-211]AuNP-S-mPEG(5k)
- Tumor : SAS cells @ lower flank



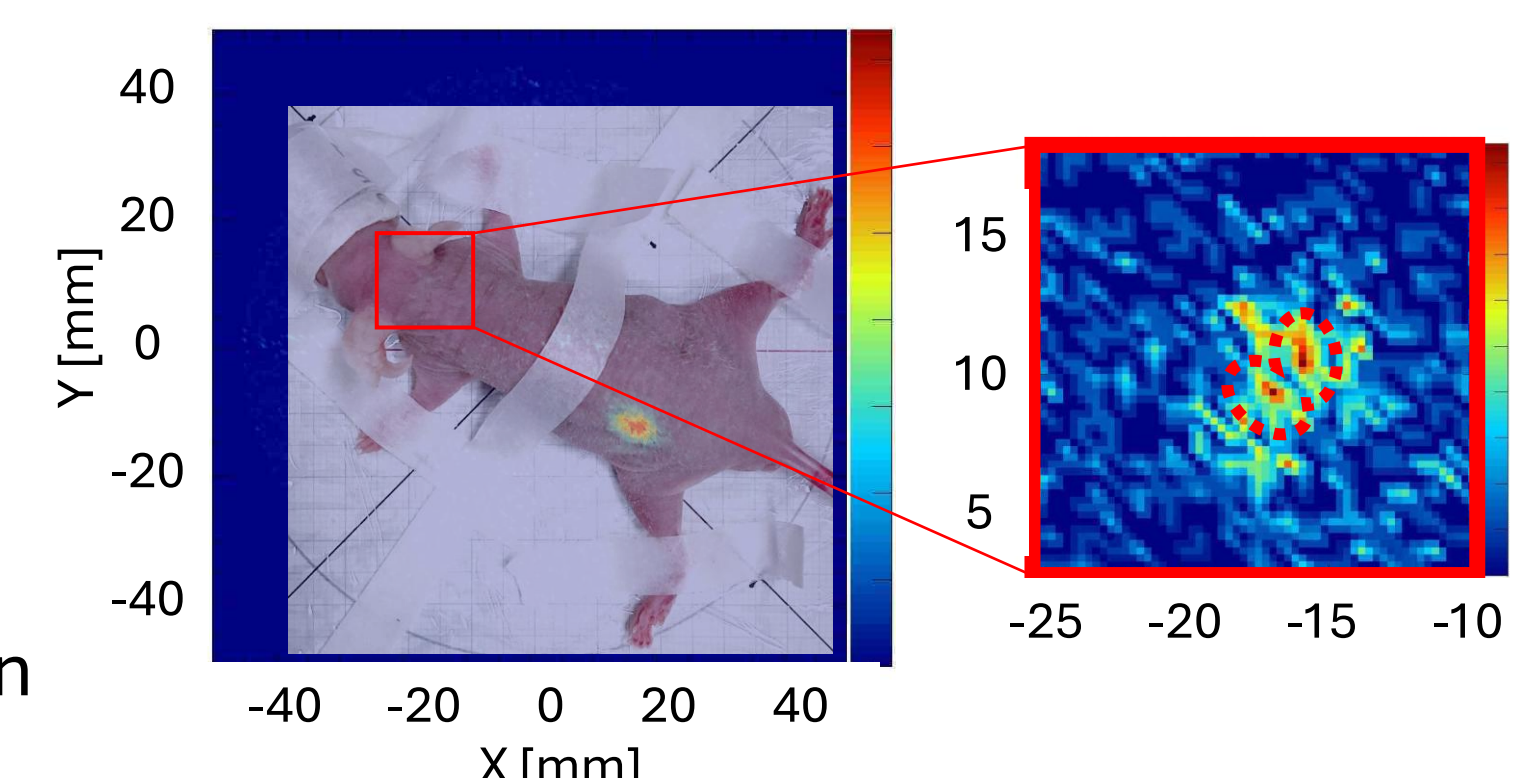
### ◆ Comparison with human SPECT



- The results the day after administration showed accumulation in the **thyroid and salivary glands**, which could not be visualized with SPECT.
- **Autopsy** (24 h post-administration)  $\rightarrow$  Confirmed accumulation in the thyroid and salivary glands.

### ◆ Imaging results with sub-pixel shift

- Total 71 min starting 24 h after administration
- Statistics ...initial position = shifted position



- Although statistics are lacking, **the shape of the thyroid/salivary glands** is becoming clearer. (Red dotted line)
- The accumulation was visualized at a high resolution of **0.25 mm pitch** using sub-pixel shift.

## Conclusion & Future work

### ◆ Conclusion

- ✓ Development of a large-area, high-resolution detector for animal imaging.
- ✓ This detector allowed us to visualize the in vivo distribution of 211-At with **higher resolution and sensitivity** than human SPECT imaging.

### ◆ Future work

- ✓ Imaging of mice that were administered At-211 AuNPs conjugated with a **target molecule** via tail vein injection.
- ✓ Visualization of drug accumulation within tumors following intravenous administration is anticipated.