HSTD14 19 Nov, 2025
7. Applications in Astrophysics, Biology, Medicine and Medical Equipments

Development of a high-contrast SPECT for small-animal imaging with high-energy gamma rays

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Outline

1. Introduction	• Background: Imaging of therapeutic drugs • **Activation imaging of gold nanoparticles (AuNPs)** • Imaging devices - Compton camera (CC) - SPECT
2. New imaging system: High-contrast SPECT (HC-SPECT)	• Concept: **Hourglass-hole collimator** • Configuration - Detector configuration - Simulation-based optimization of hole size • Image reconstruction using MLEM
3. Experimental demonstration	• Imaging of activated gold in phantoms - CC vs. Parallel-hole SPECT vs. HC-SPECT - Performance of HC-SPECT • In vivo imaging of radioactive AuNPs (preliminary)
4. Summary	• Summary and future prospects

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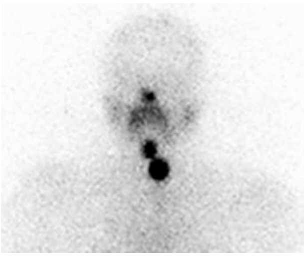
Background

- **Imaging of therapeutic drugs** is essential for effective treatment

^{131}I

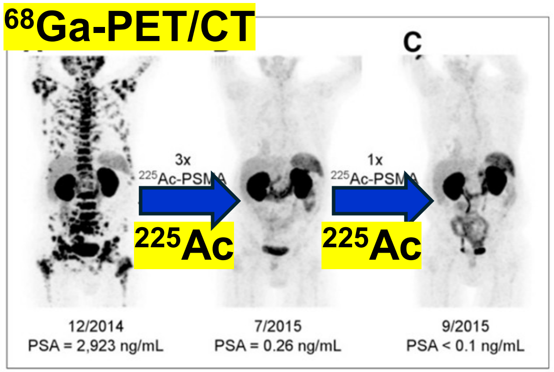
- Thyroid cancer
- β particles
- Gamma ray: **364 keV**



Szumowski et al. Sci. Rep., 2021

^{225}Ac

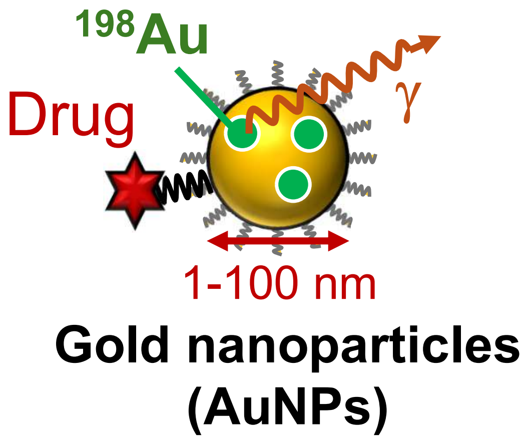
- Prostate cancer
- α particles
- Gamma ray: **440 keV**



Kratochwil et al. J. Nucl. Med., 2016

$[^{198}Au]AuNP$

- Drug carrier
- Gamma ray: **412 keV**

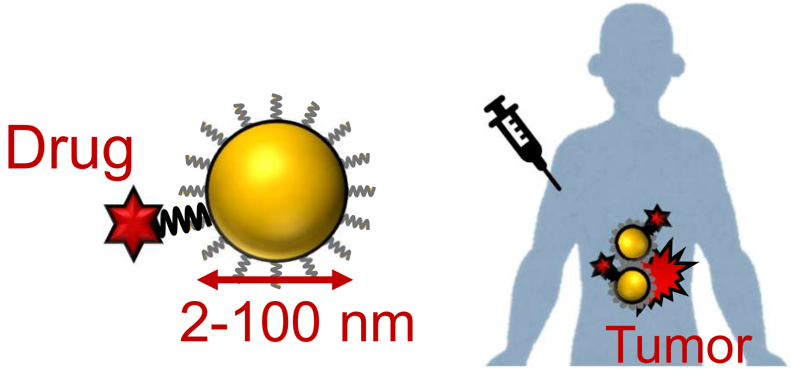


Koshikawa et al., Appl. Phys. Lett., 2022

High-quality imaging with gamma rays
in the range of **several hundred keV** is needed

Activation imaging of gold nanoparticles (AuNPs)

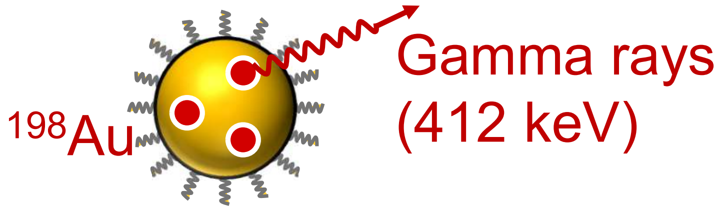
- Gold nanoparticles (AuNPs)
  ...Promising **drug carrier**



✓ **Accumulation in tumors**
✓ High biocompatibility
✓ Easy surface modification

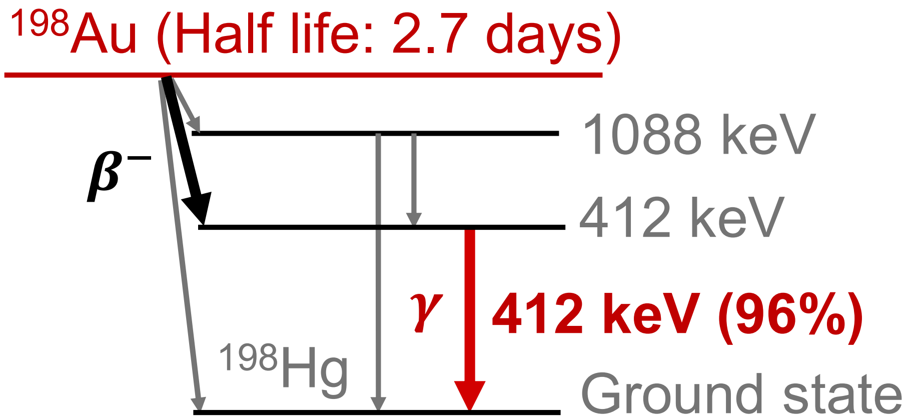
Distribution varies with size, shape, etc.
→ **Visualization of AuNPs** is important

- **[^{198}Au]AuNPs**



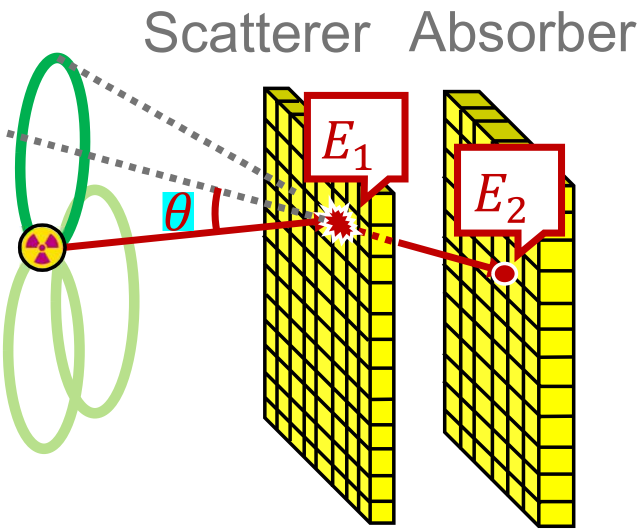
Koshikawa et al., *Appl. Phys. Lett.*, 2022

Neutron + **^{197}Au** → **^{198}Au**
Stable **Radioactive**



Imaging devices

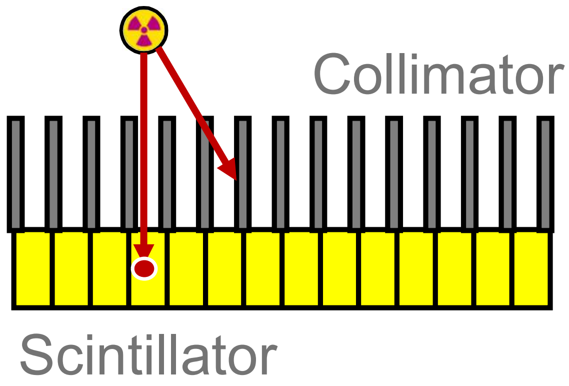
■ **Compton camera**



$$\cos\theta = 1 - m_e c^2 \left(\frac{1}{E_2} - \frac{1}{E_1+E_2}\right)$$

✔ Imaging in the hundreds of keV range
✔ No collimator required → Wide FOV
✖ Limited spatial resolution

■ **SPECT (Single-photon emission computed tomography)**



✔ High spatial resolution
✔ Widely used in clinical settings
✖ **Imaging in high-energy region**
→ Thick collimator required
→ Sensitivity decreases

Imaging devices

- **Compton camera**

Scatterer Absorber

Objective:
Develop a **high-resolution (a few mm), high-sensitivity SPECT detector** for imaging gamma rays in the **several-hundred keV range**.

$$\cos\theta = 1 - m_e c^2 \left(\frac{1}{E_2} - \frac{1}{E_1+E_2}\right)$$

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✓ No collimator required → Wide FOV
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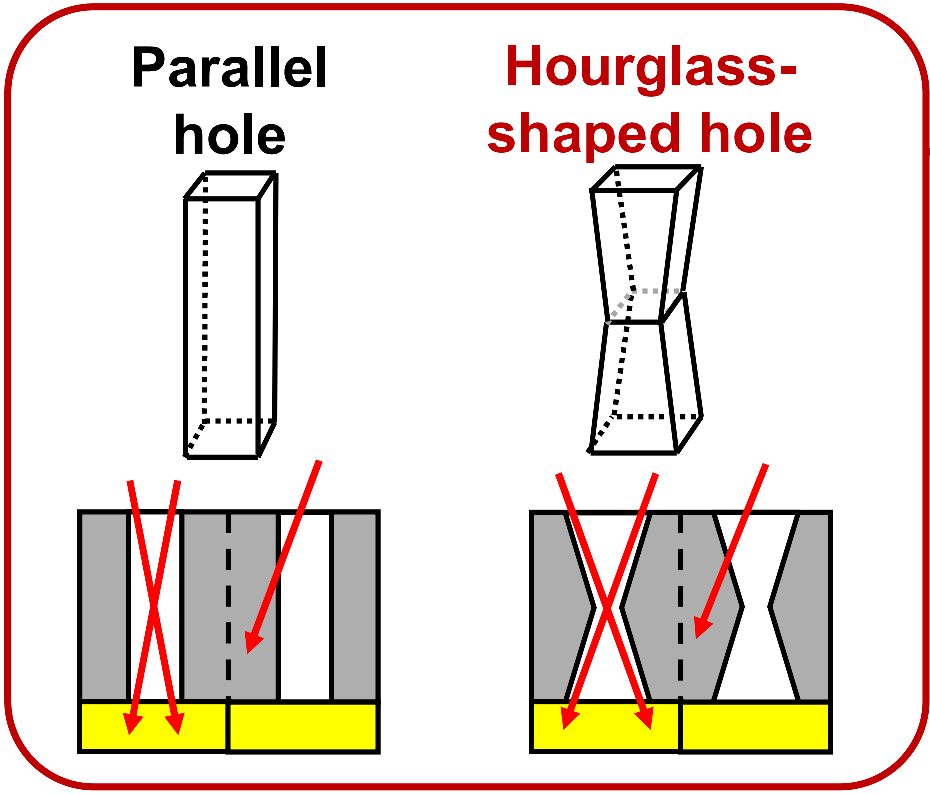
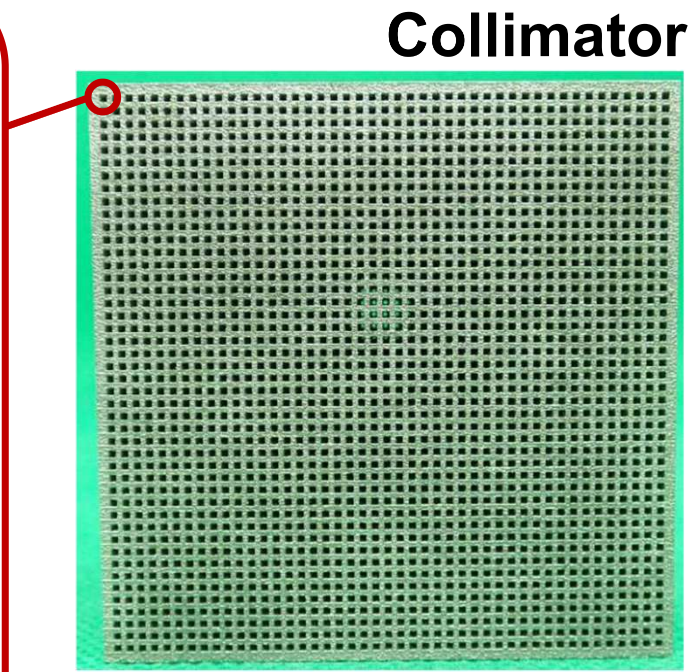
Hourglass hole collimator

Key feature of High-contrast SPECT

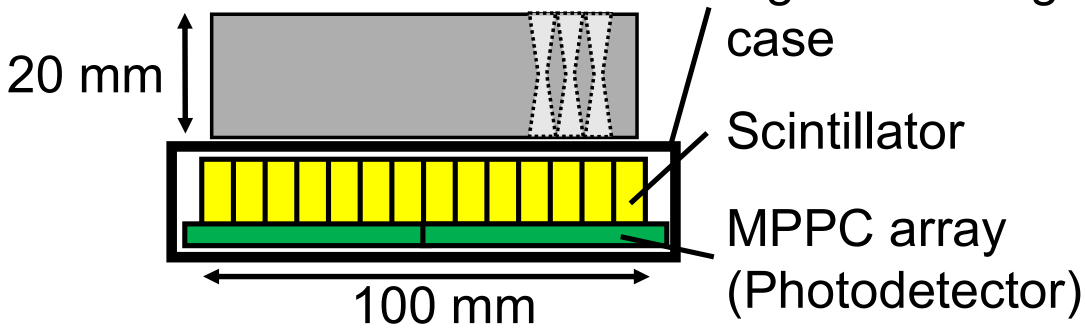




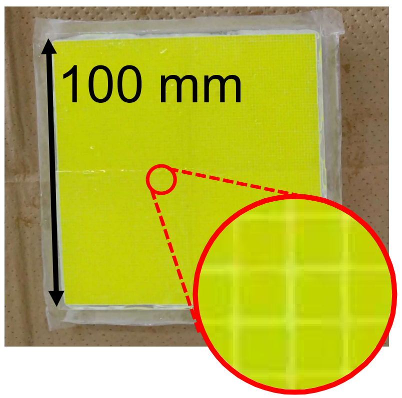
✓ **Achieve high sensitivity while keeping spatial resolution**

Detector configuration

■ Overall configuration

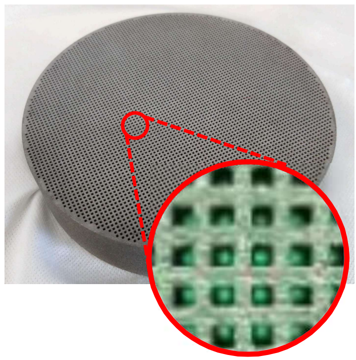


■ Scintillator

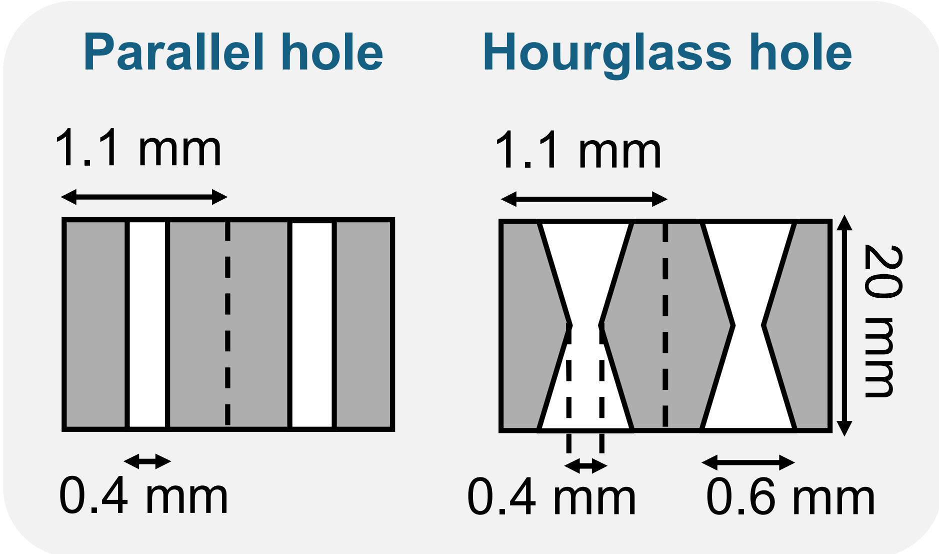


- GAGG ($Gd_3(Ga,Al)_5O_{12}(Ce)$)
- Pixel pitch: 1×1 mm^2
- 90×90 array
- Thickness: 5 mm
- Energy resolution: 7.5%(FWHM)@662 keV

■ Collimator (Toray Precision Co., Ltd)

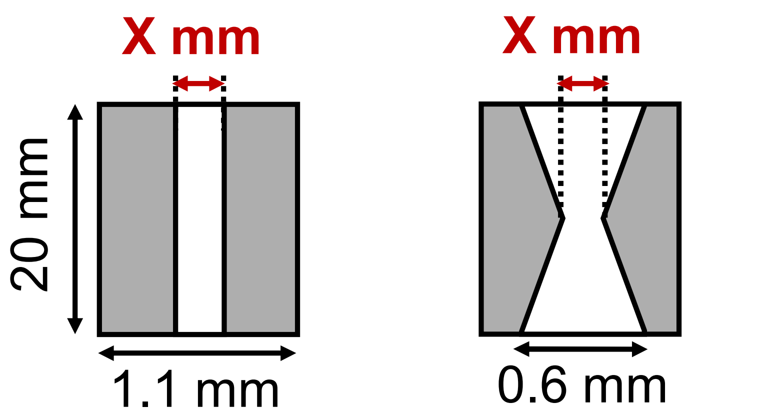


- Tungsten
- Pixel pitch: 1×1 mm^2
- ϕ98 mm
- Height: 20 mm

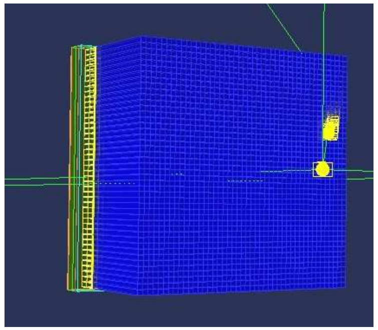


Hole-size optimization

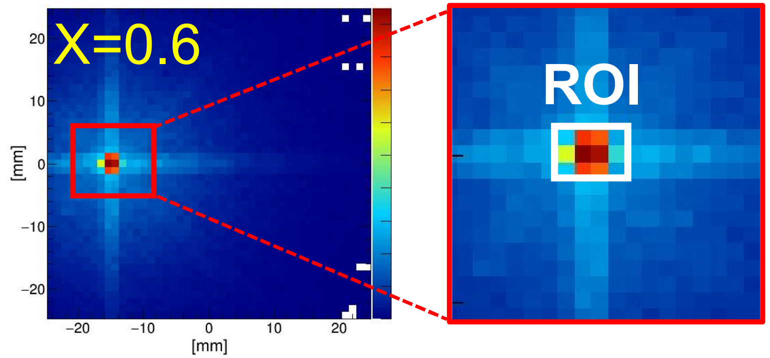
■ **Geant4 simulation**



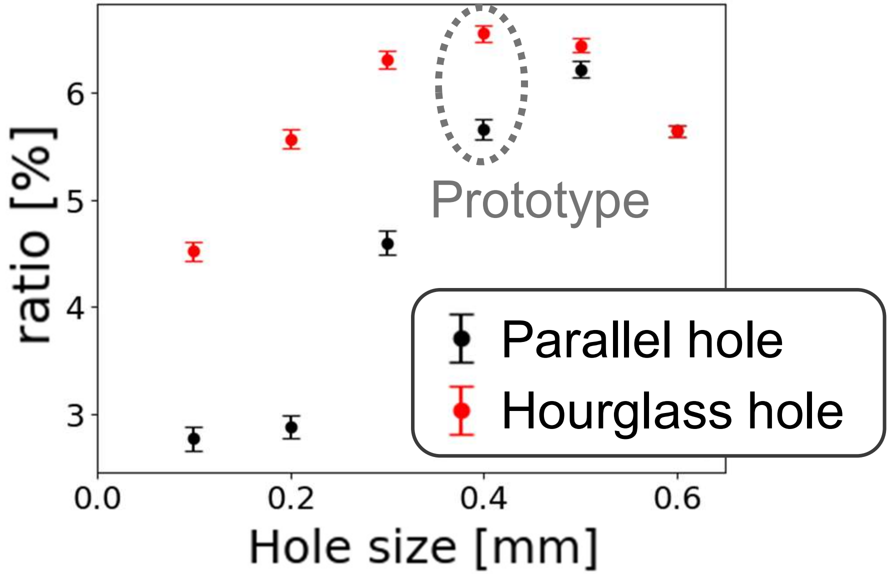
X = 0.1, 0.2, 0.3, 0.4, 0.5, 0.6



Source
Energy: 412 keV
Position: (-15, 0) mm
Size: ϕ3 mm



Pixel value inside ROI / All pixel value



MLEM analysis

Maximum-likelihood expectation maximization

Number of iteration

Image

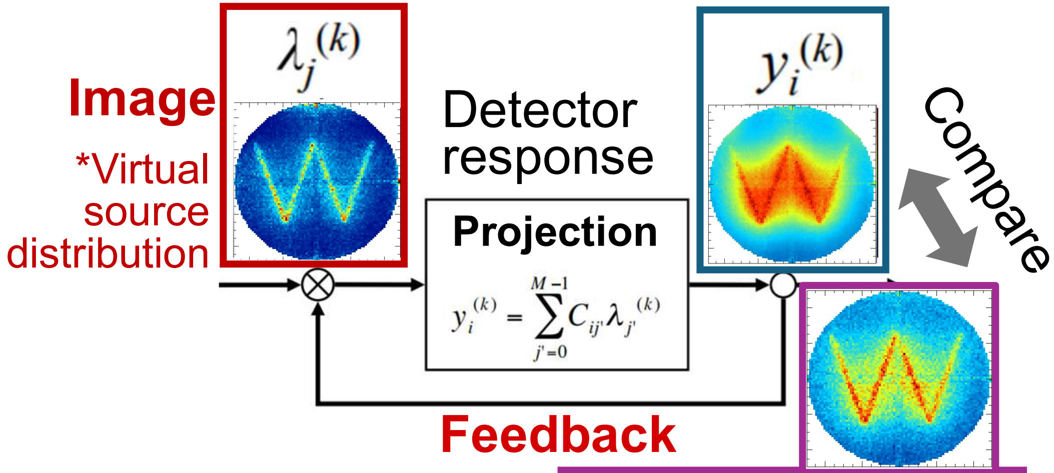
Measured response

$$\lambda_j^{(k+1)} = \frac{\lambda_i^{(k)}}{\sum_{i=0}^{N-1} C_{ij}} \sum_{i=0}^{N-1} \frac{y_i C_{ij}}{\sum_{j'=0}^{M-1} C_{ij'}\,\lambda_{j'}^{(k)}}$$

$y_i^{(k)}$

Sensitivity matrix

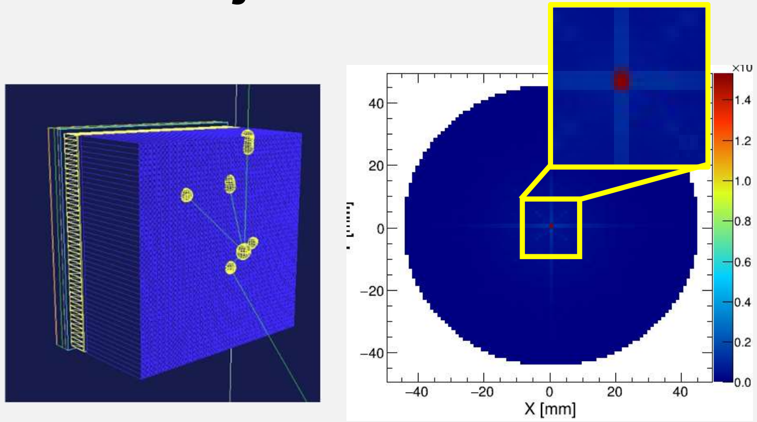
Calculated response

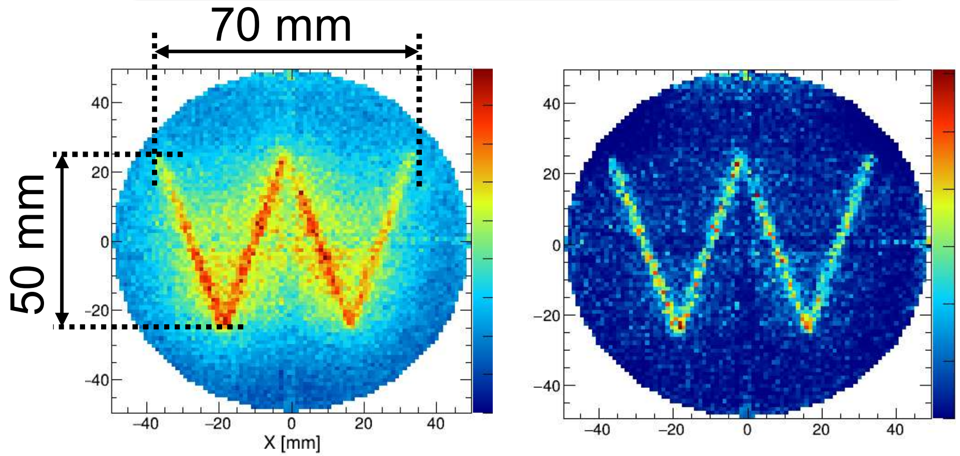


(Comparison w/ measured data=y_i)

Apply MLEM

Obtain Cij w/ Geant4





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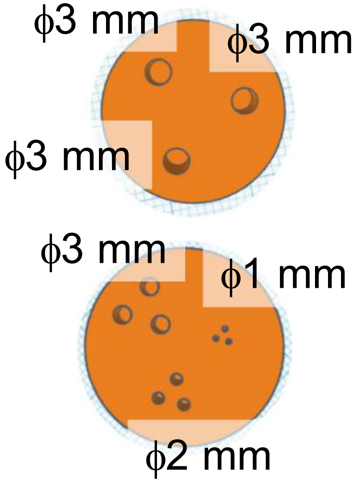
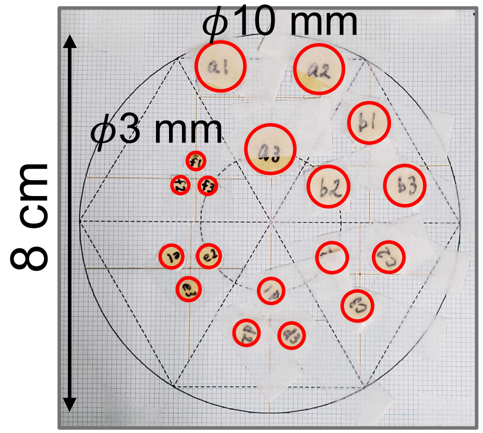
Experimental demonstration

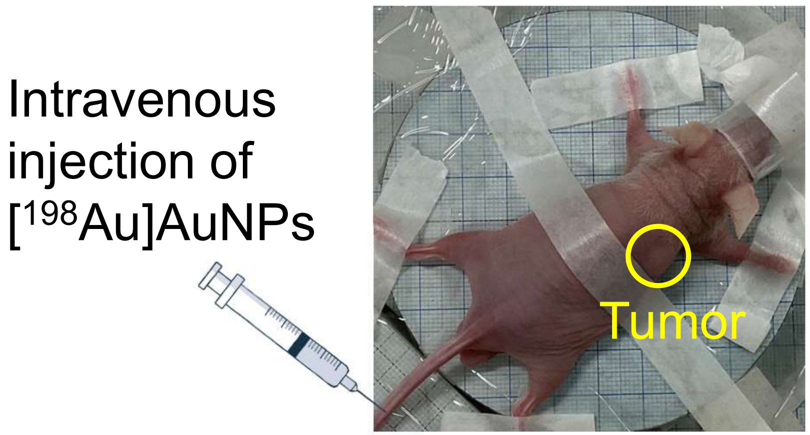
1. Imaging of activated gold (^{198}Au)





- Comparison between Compton camera, Parallel-hole SPECT, HC-SPECT(hourglass hole)
- Performance evaluation of HC-SPECT
- Large-area imaging of Derenzo phantom

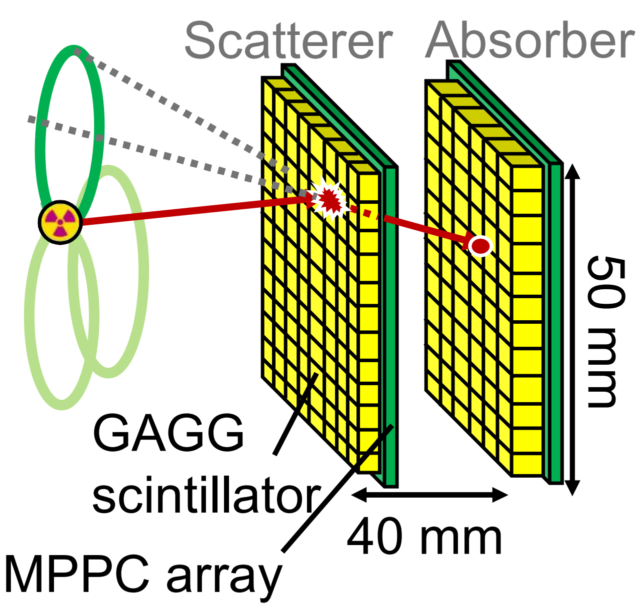
2. In vivo imaging of [^{198}Au]AuNPs



- Imaging of [^{198}Au]AuNPs distribution in tumor-bearing mouse (preliminary results)

Detectors for comparison

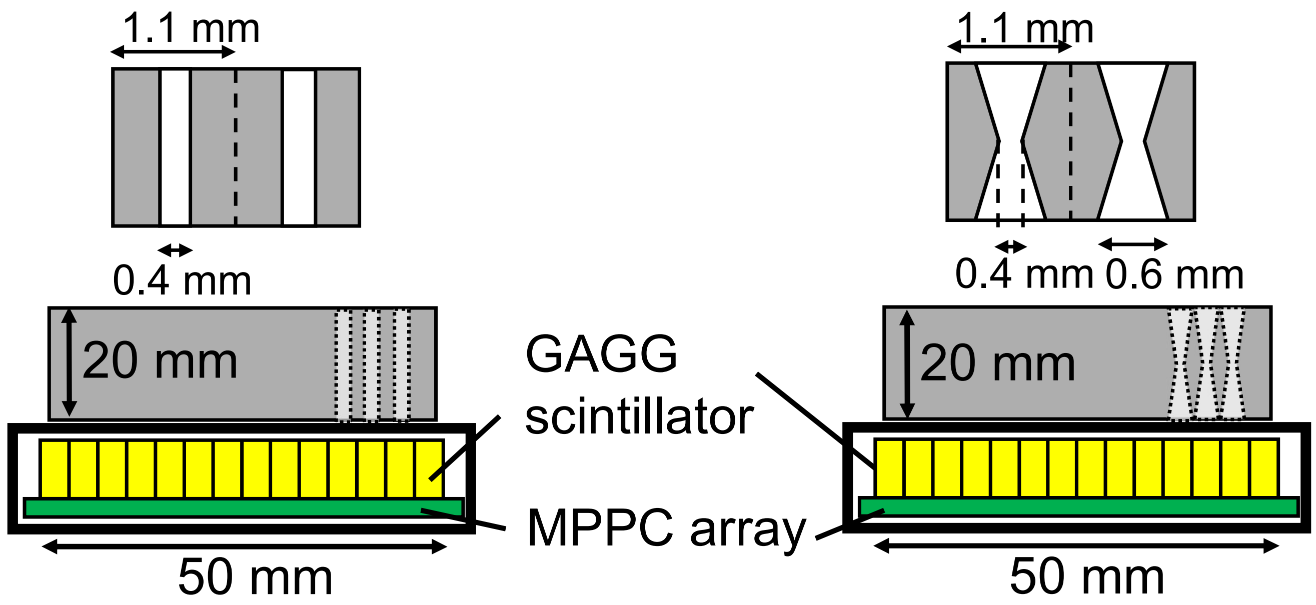
Compton camera



- Pixel pitch: 1×1 mm^2
- 45×45 array
- Scintillator Thickness:
  Scatterer: 3 mm
  Absorber: 5 mm

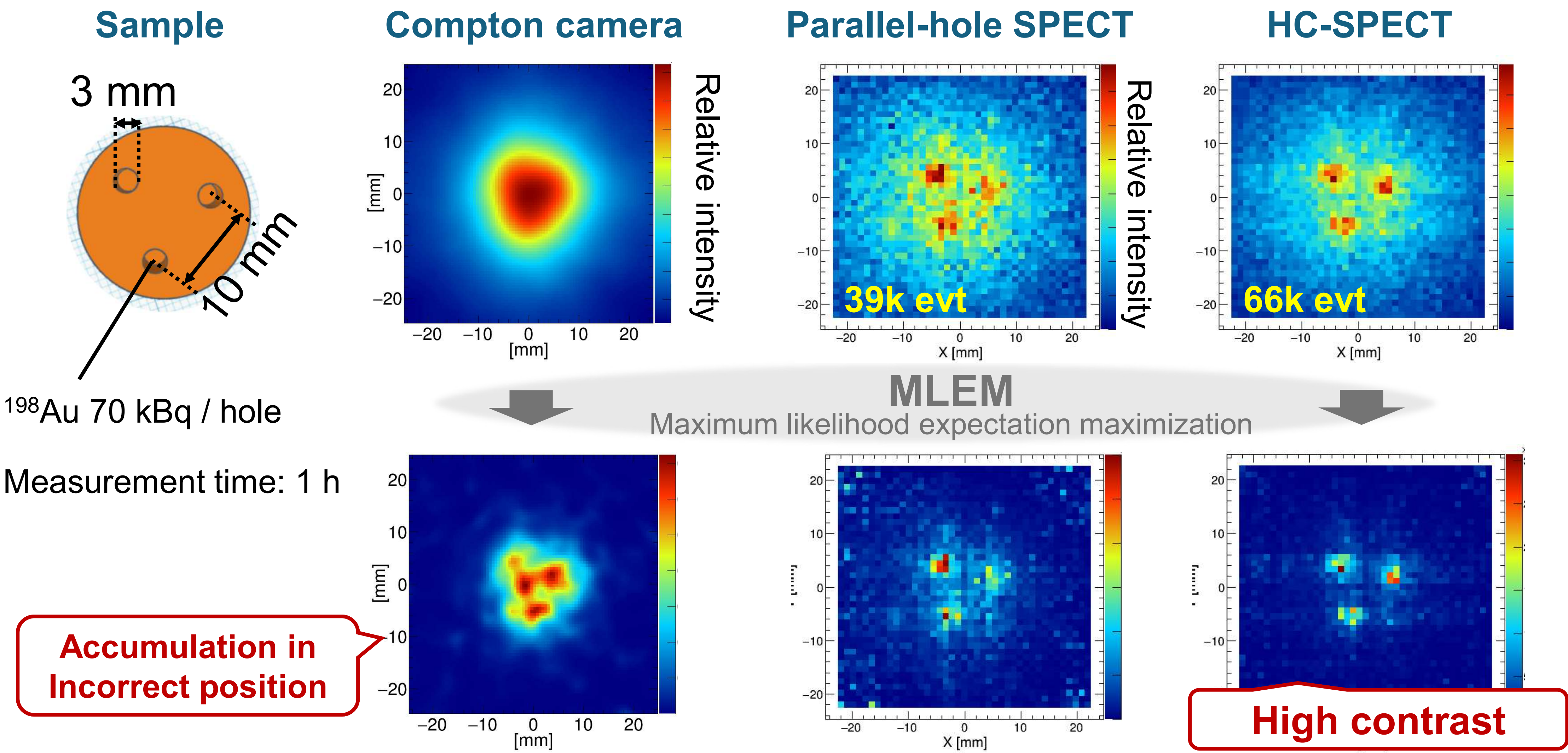
Parallel-hole SPECT

HC-SPECT



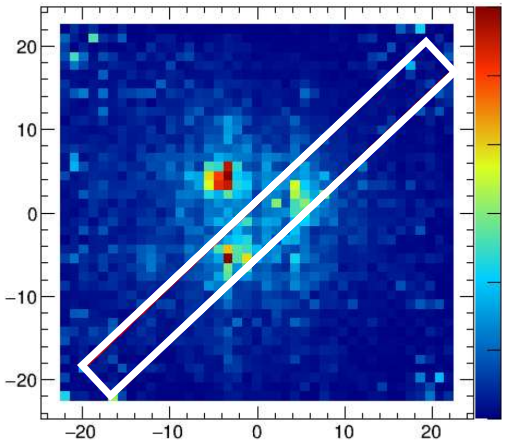
- GAGG / collimator pixel pitch: 1×1 mm^2
- 45×45 array (*1/4 size prototype)
- Scintillator Thickness: 5 mm

Comparison b/w detectors

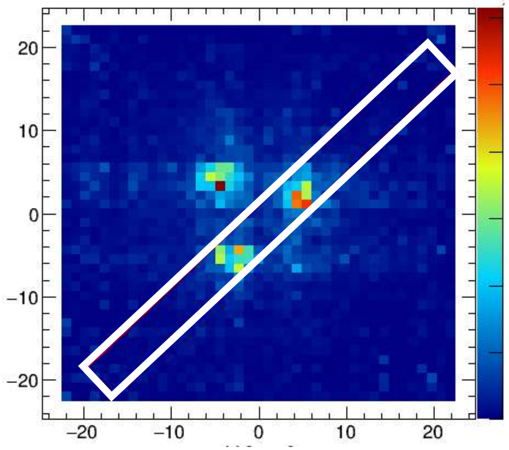


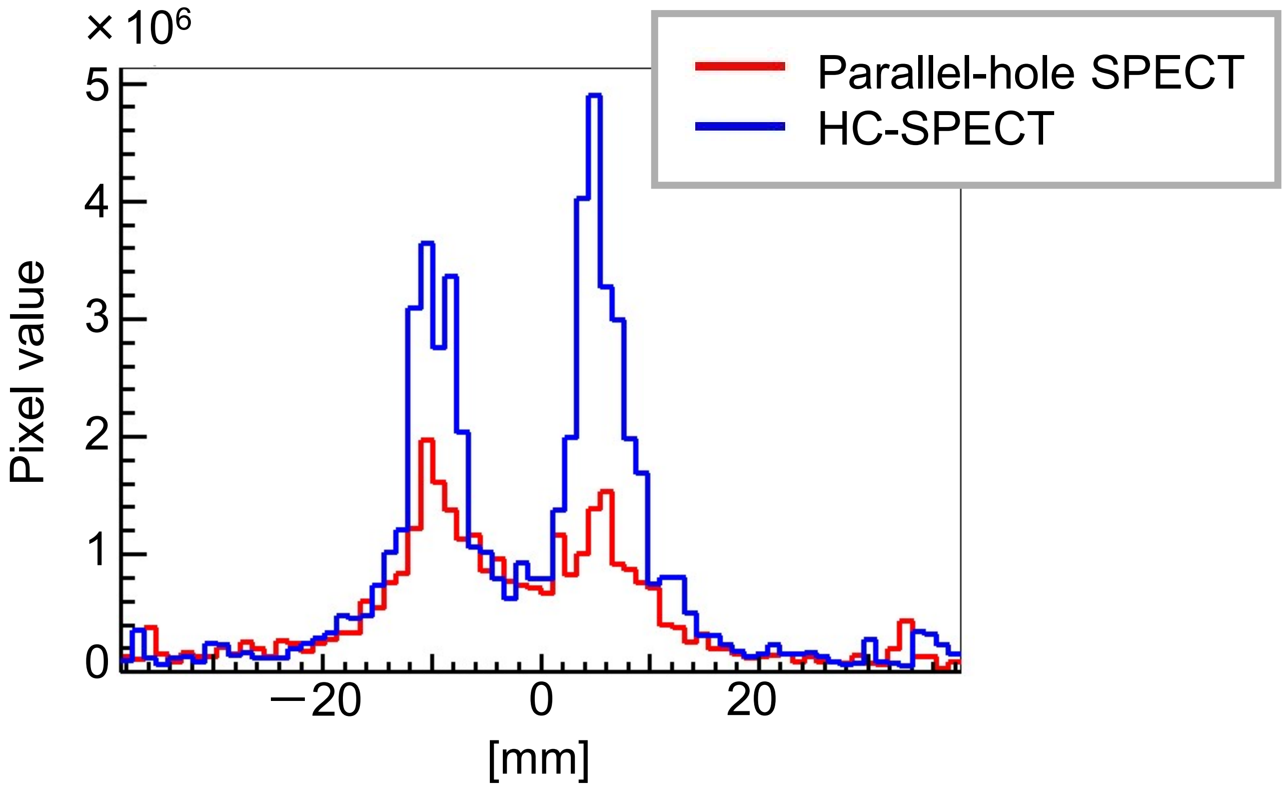
Parallel hole vs. hourglass hole

Parallel-hole SPECT



HC-SPECT

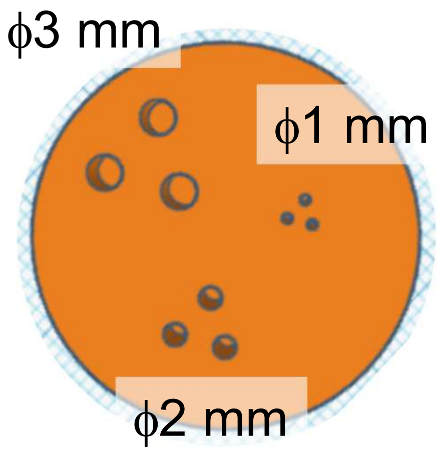




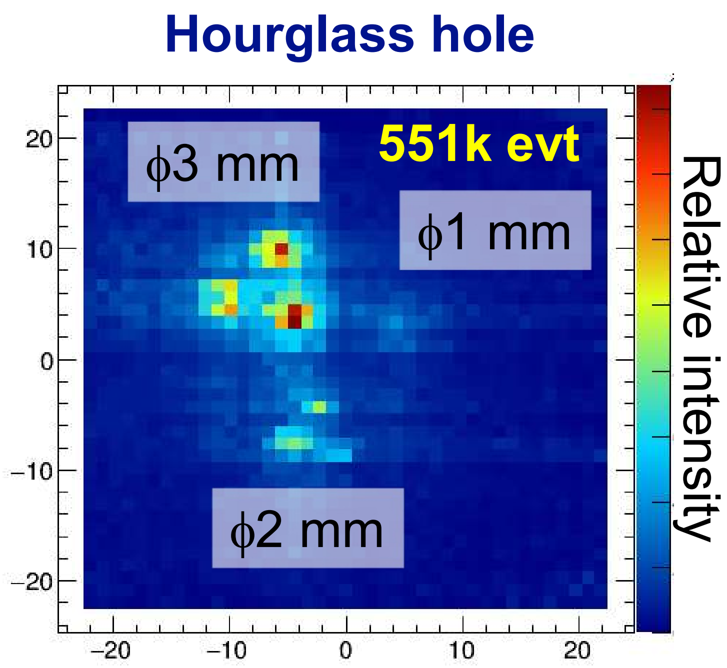
Peak / Valley
Parallel-hole SPECT: 2.6
HC-SPECT: 6.9
× 2.7

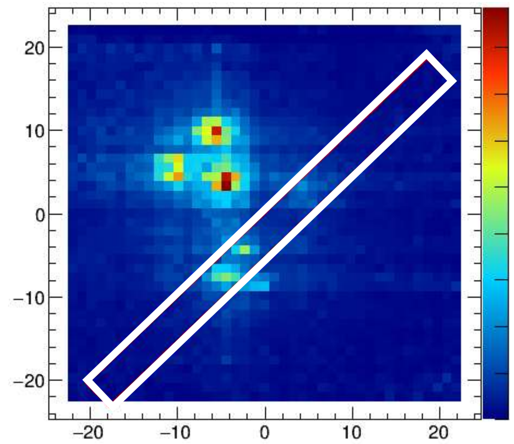
Performance evaluation of HC-SPECT

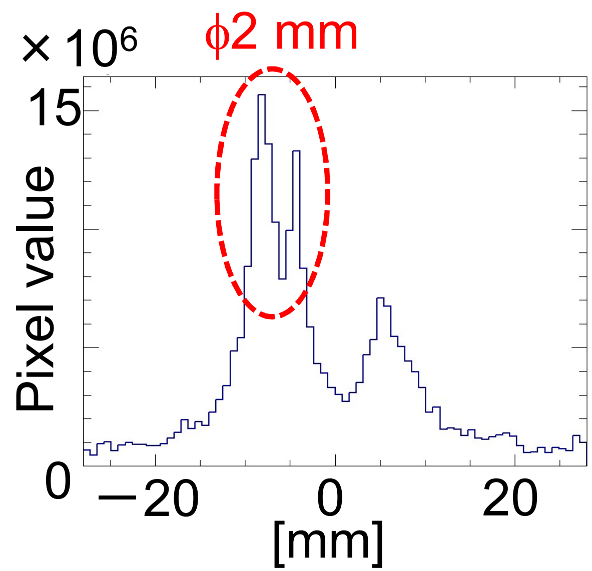
■ **Imaging of Derenzo phantom**



*Distance b/w holes is diameter × 2



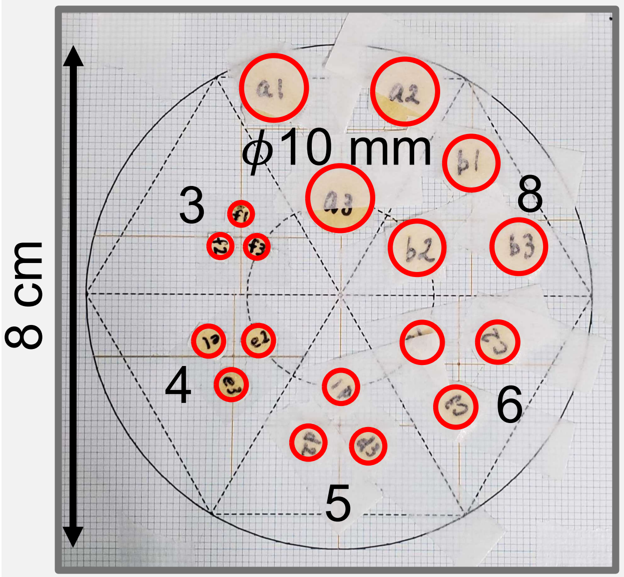




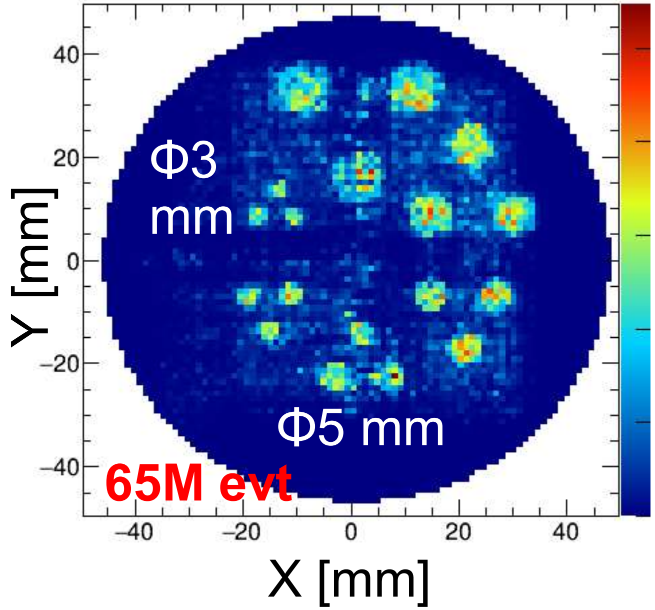
- ^{198}Au 210 kBq (total)
- Measurement time: 10 h
- Energy window: 402-442 keV

Large-area imaging w/ HC-SPECT

Sample: Radioactive gold (^{198}Au) plates ϕ3-10 mm

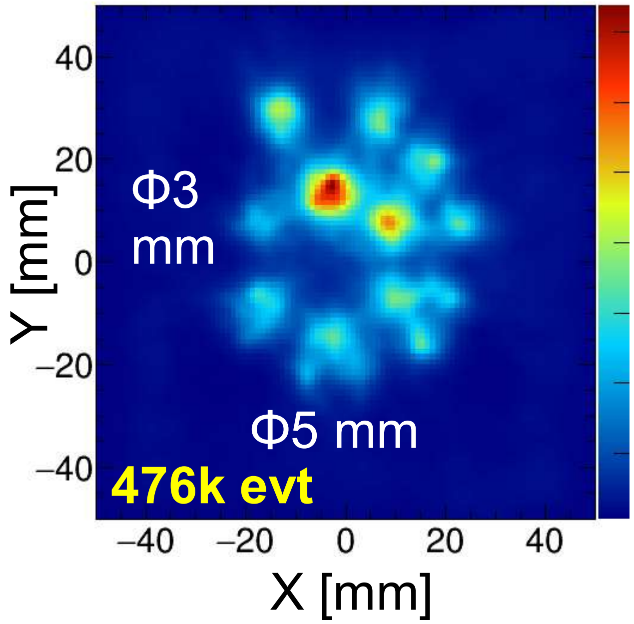


HC-SPECT (Full size: 10 × 10 cm²)



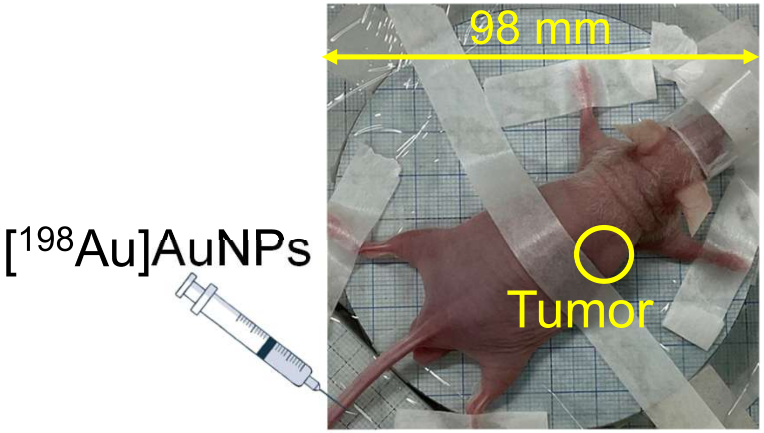
- Activity: 2,190 kBq (total)
- Measurement time: 14 h

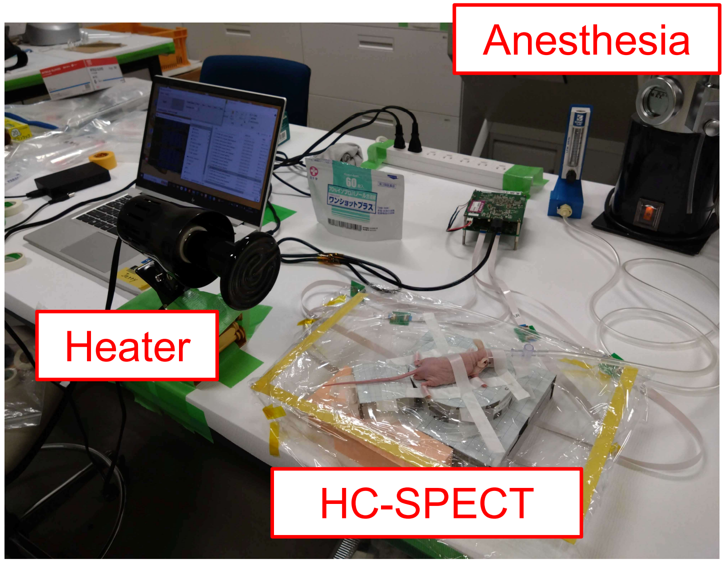
Compton camera



- Activity: 78 kBq (total)
- Measurement time: 16 h

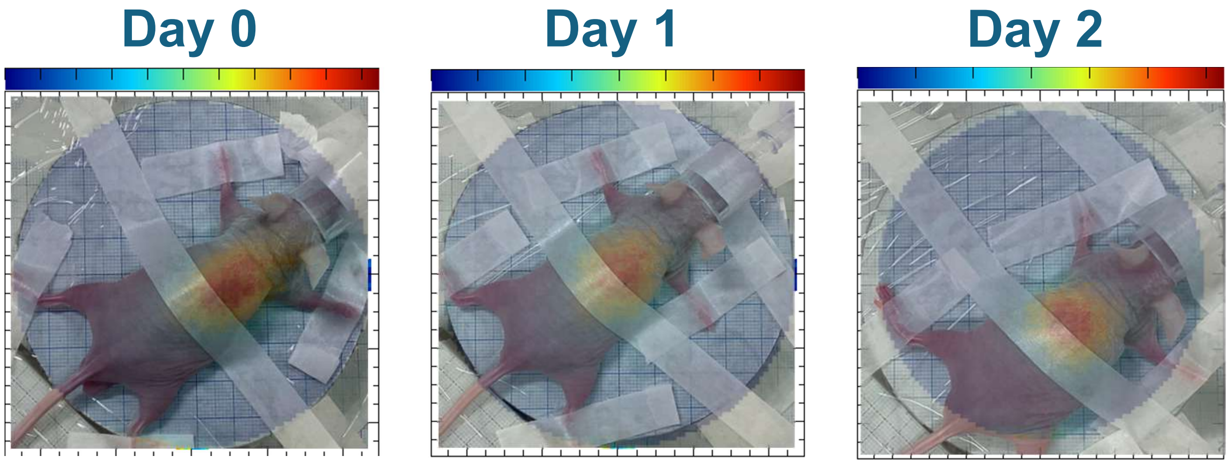
In vivo imaging of [^{198}Au]AuNPs (Preliminary)





- Intravenous injection of [^{198}Au]AuNPs (1.42 MBq)
- Measurement time: ~1 h
- Measured daily up to 2 days after injection

Results



- Gradual accumulation in liver
  (Confirmed by radioactivity of organs)

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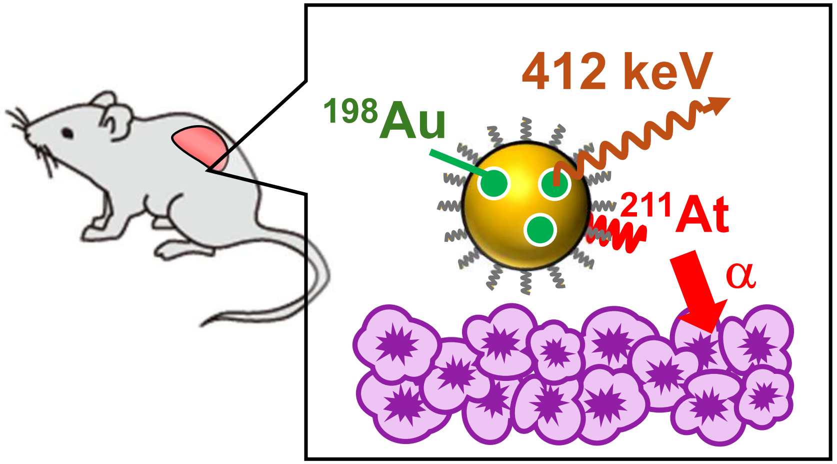
Summary

Summary

- A high-resolution, high-sensitivity imaging device for gamma rays in the **several-hundred keV range** is needed
- We proposed **hourglass hole collimator** to achieve high sensitivity while keeping high resolution
- Hourglass hole collimator showed higher signal-to-noise ratio than parallel hole collimator / higher spatial resolution than Compton camera

Future prospects

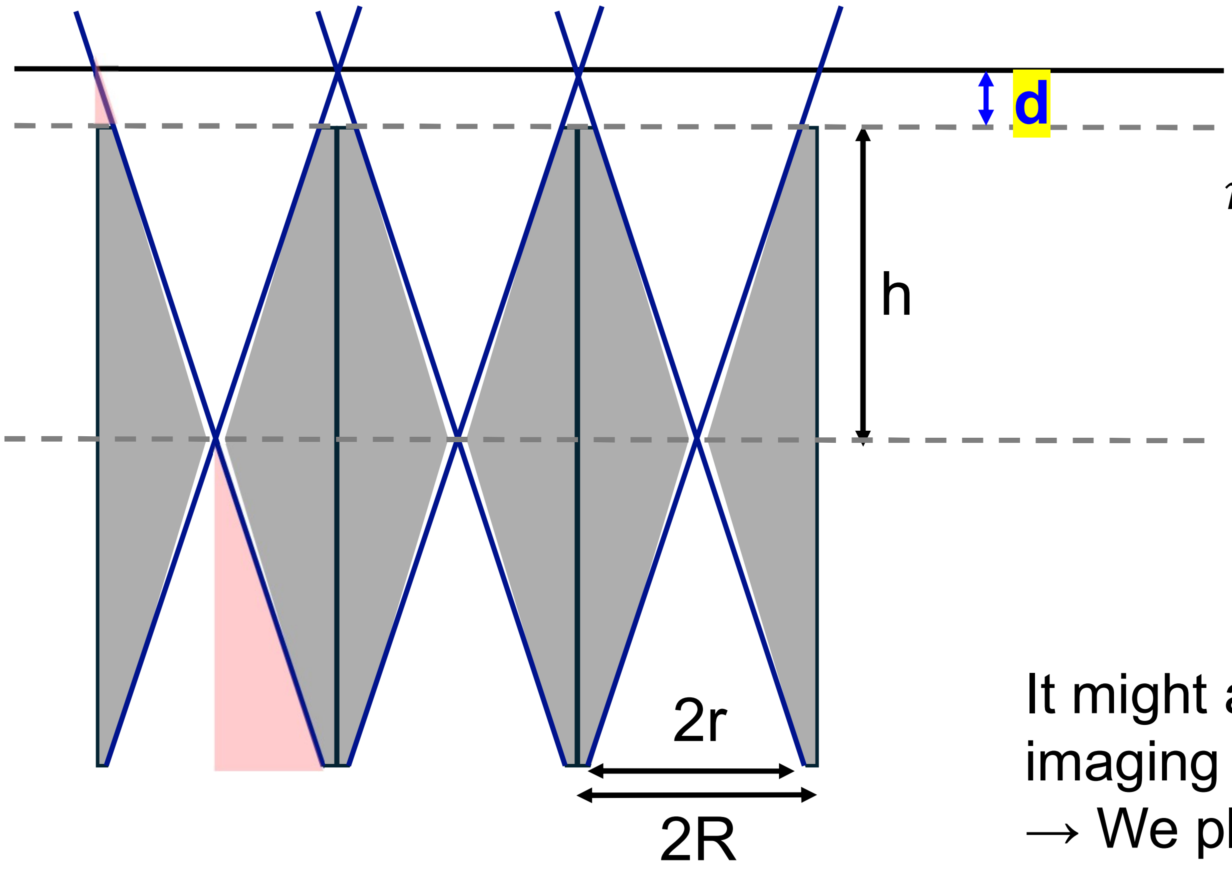
- In-vivo imaging of **^{211}At-[^{198}Au]AuNPs** for high-precision investigation of the dynamics of drug-labeled AuNPs



Thank you for your attention!

Appendix

Overlapping



$$r\!:h = (R-r)\!:d \Rightarrow d = \frac{h(R-r)}{r}$$

$$2h = 20\ \text{mm} \qquad h = 10\ \text{mm}$$
$$2r = 0.6\ \text{mm} \qquad r = 0.3\ \text{mm}$$
$$2R = 1.1\ \text{mm} \qquad R = 0.55\ \text{mm}$$

$$\boldsymbol{d = 8.33\ \text{mm}}$$

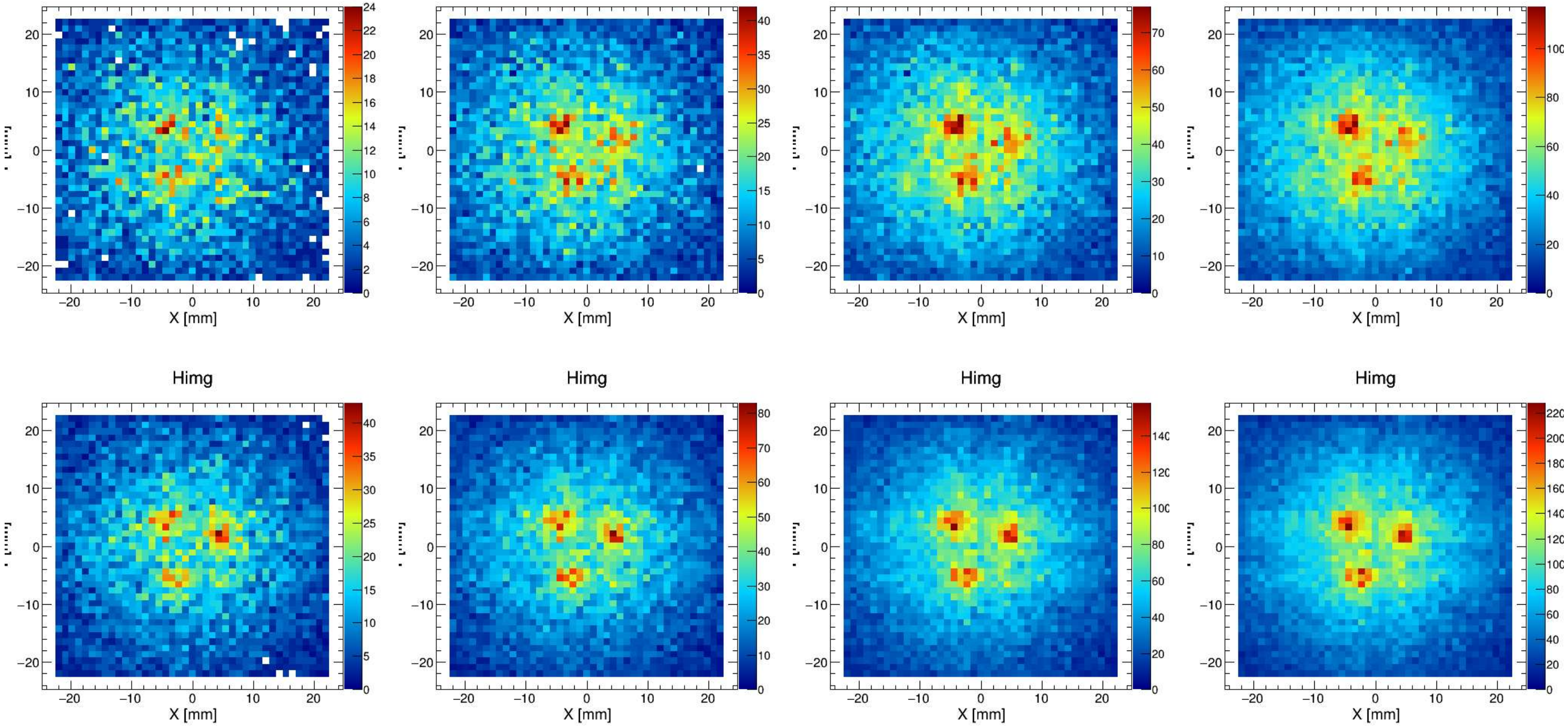
It might affect spatial resolution when imaging an actual mouse…?
→ We plan optimization
(more than 10 mm would be certain?)

Measurement time

15 min | **30 min** | **60 min** | **90 min**

Parallel hole (evt: 18 Hz)

Hourglass hole (evt: 11 Hz)



- 15 min may be sufficient to obtain a rough visualization of the sources using an hourglass-hole collimator.

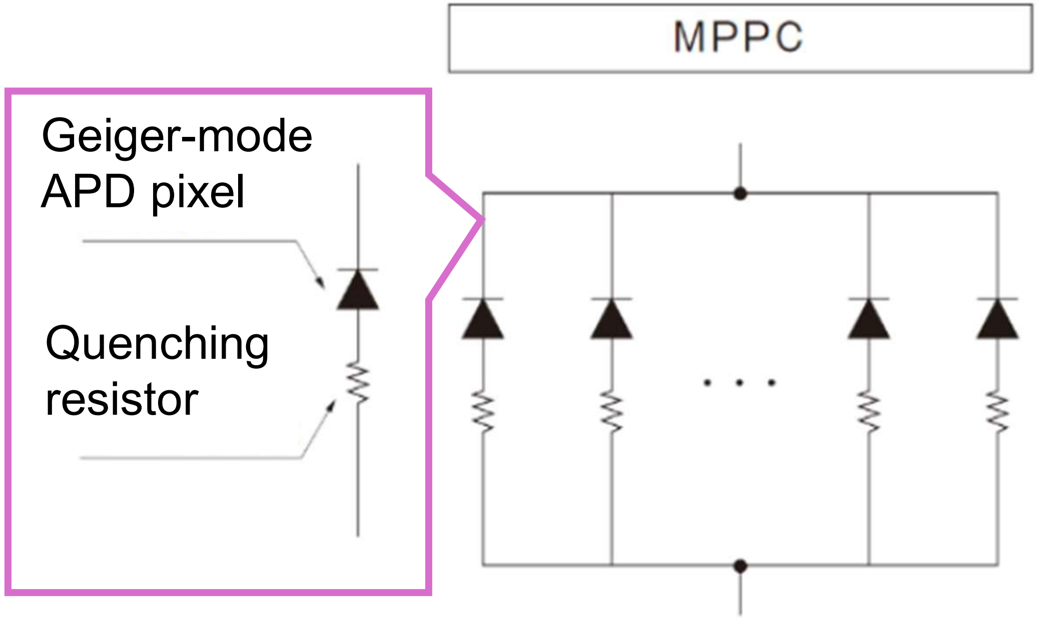
GAGG scintillator

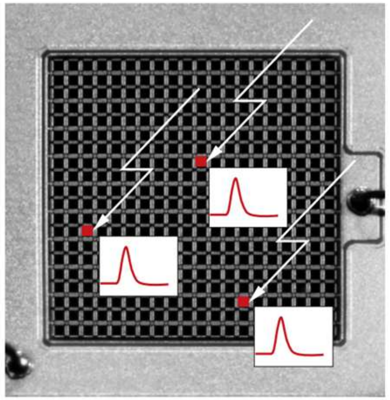
- ✓ Large light output
- ✓ Fast decay time
- ✓ Non-hygroscopic

Scintillator	**Density [g/cm^3]**	**Decay time [ns]**	**Light output [photon/MeV]**	**Energy resolution [%]**
Ce:GAGG	6.63	88	**60,000**	6.3
Pr:LuAG	6.7	20	22,000	4.2
BGO	7.13	300	8,000	12
Ce:LSO	7.4	40	26,000	9
Tl:NaI	3.67	230	45,000	5.6
Tl:CsI	4.53	1,050	56,000	5.7

*Cs-662, 5 mm cubic crystal

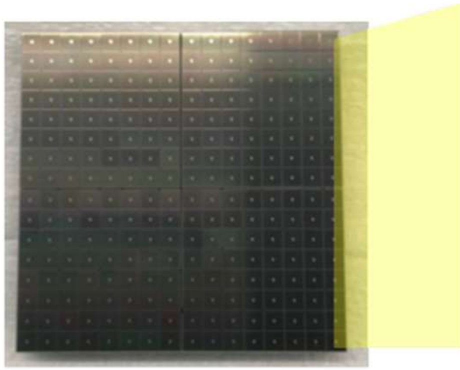
Multi-pixel photon counter（MPPC）



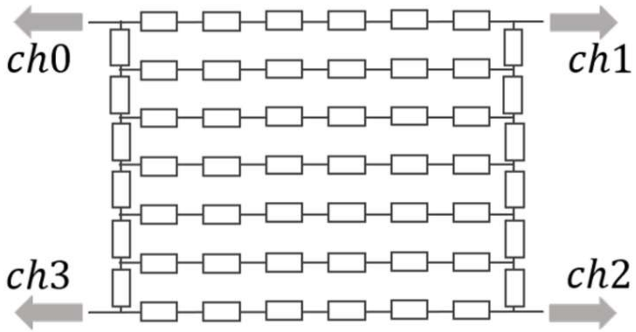


- Each APD detect **whether a photon came or not**
- Output:
  number of the photons
- Multiple photons in
  a APD -> worse linearity

- 50 μm pitch MPPC
  16 × 16 array
  （Pixel number: 3,531）



A resistor-divider circuit
determine the interaction position
through centroid calculation

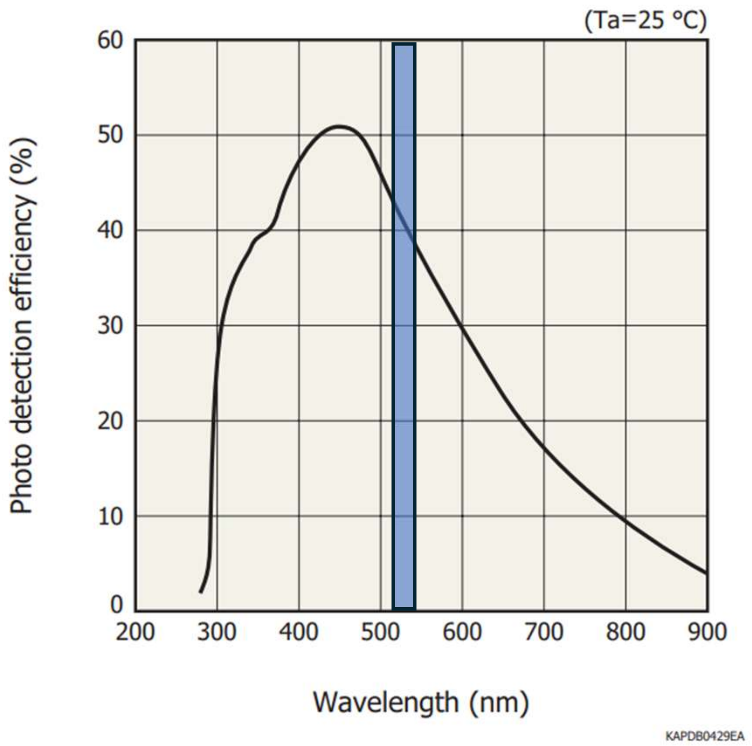


Intake of ^{198}Hg?

- In 2003, a study conducted by the Ministry of Health, Labour and Welfare of Japan reported that the total **daily mercury intake from food** for Japanese people was **8.1 µg/day**.
- Question:
  If 200 MBq of ^{198}Au is administered to the human body, how much mercury (Hg) would be produced?
  200 MBq = $\frac{\ln 2}{\tau} N \Rightarrow N = 6.73 \times 10^{13}$ = 1.1×10^{-10} mol
  1.1×10^{-10} mol × 198 = 2.2×10^{-8} g = $\mathbf{2.2 \times 10^{-2}}$ **µg**（22 ng）
- The amount of mercury generated is <u>negligible</u>.

Photon detection efficiency of MPPC

Photon detection efficiency vs. wavelength (typical example)



Photon detection efficiency does not include crosstalk and afterpulses.

- GAGG: 520-540 nm
  Detection efficiency: ~40%

Detection efficiency & spatial resolution (@412 keV)

Detector	Detection efficiency	Spatial resolution [mm]
Hybrid Compton camera	1×10^{-3}	4.7
Parallel-hole SPECT	2×10^{-4}	Same as HC-SPECT
HC-SPECT	4×10^{-4}	1.4

【Detection efficiency】

$$\frac{\text{Number of events used for image reconstruction}}{\text{Number of photons incident to the detector}}$$

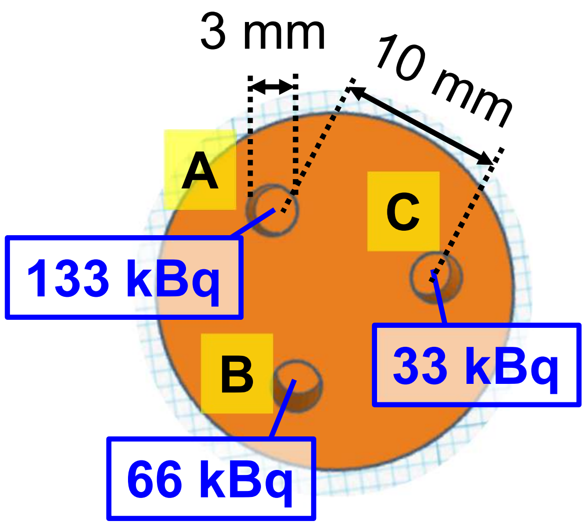
【Spatial resolution】

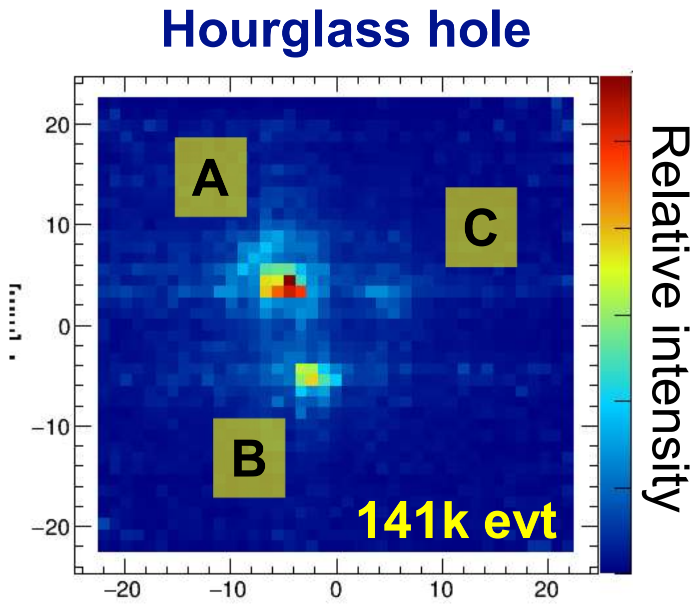
Compton camera: Angular resolution (ARM) = 9° (FWHM). Source–detector distance assumed to be 3 cm.

HC-SPECT: Detector resolution estimated from the FWHM of the accumulated activity profile when imaging a φ3 mm source.

Performance evaluation of HC-SPECT

■ Phantom with different concentrations

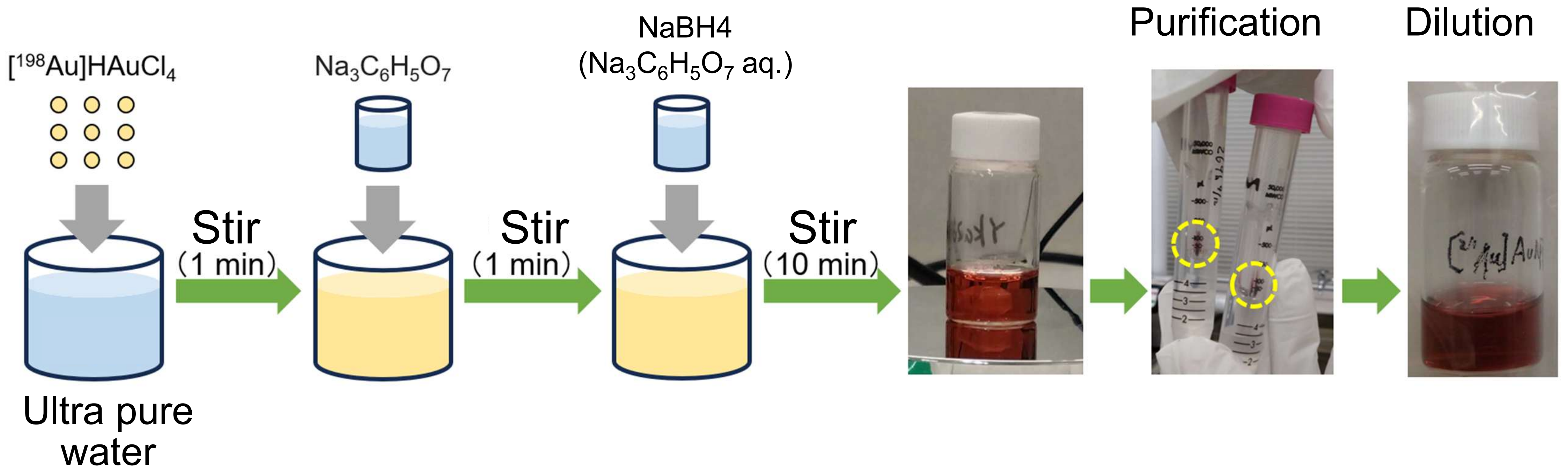




- Concentration ratio
  A:B:C=4:2:1
- ^{198}Au 232 kBq (total)
- Measurement time: 2.4 h

Concentration ratio
A/B = 1.88±0.09
B/C = 2.52±0.22
Sample adsorption onto the pipette?

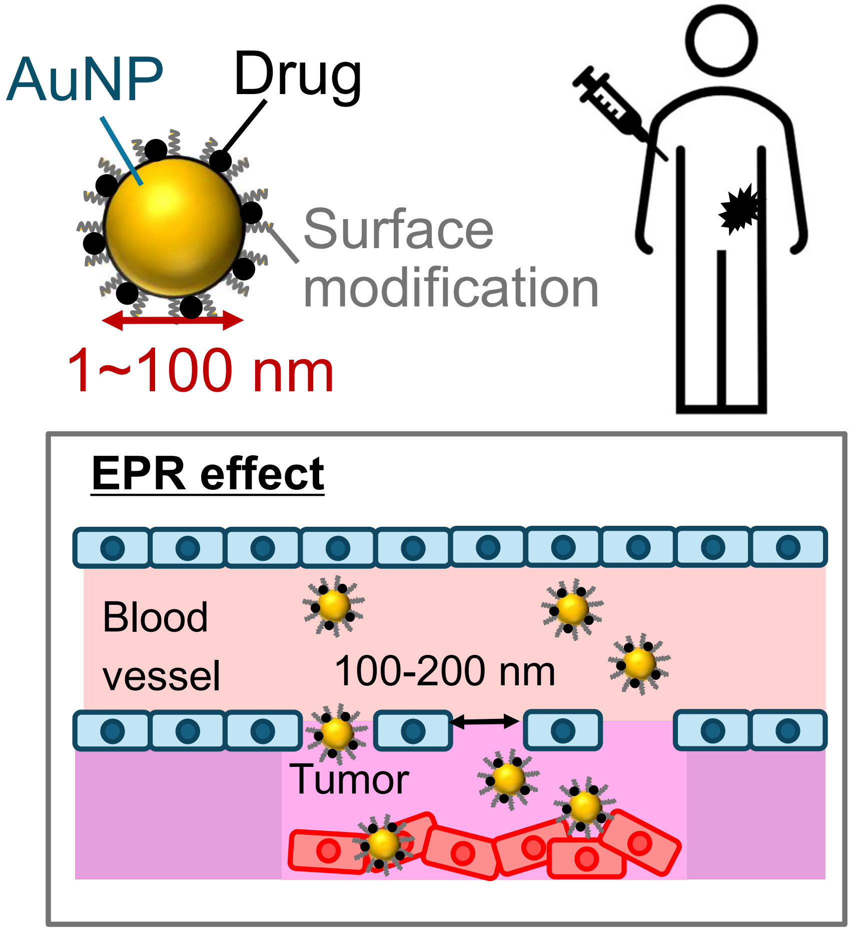
How to make AuNPs?



EPR effect

- **Gold nanoparticles (AuNPs)**
  ...Promising **drug carrier**

  ✓ Accumulation in tumors through the **enhanced permeability and retention (EPR) effect**
  ✓ High biocompatibility
  ✓ Easy surface modification



Distribution varies with size, shape, etc.
→ **Visualization of AuNPs** is important