Ex vivo imaging of gadolinium contrast agents using MPPC-based Photon-Counting CT

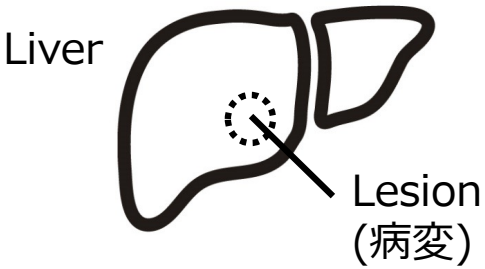
Kanazawa University
Takahiro Tomoda

M. Arimoto, D. Sato, Fitri Lucyana, H. Kawashima, S. Kobayashi, K. Okumura (Kanazawa Univ.)
J. Kataoka, M. Sagisaka (Waseda Univ.)
S. Terazawa, S. Shiota (Proterial Ltd.)

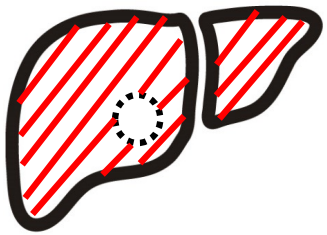
Research background

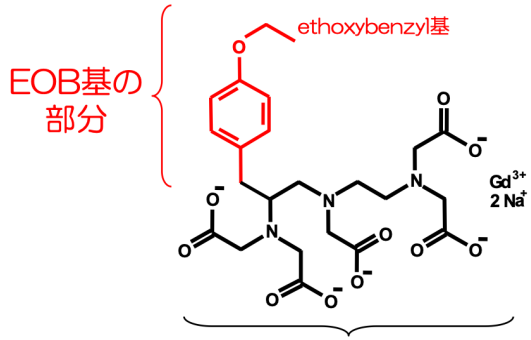
- **Gadolinium contrast agent**
  Contrast enhancement of liver tumors in magnetic resonance imaging (MRI)

Before injection



After injection





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Gadolinium contrast agent is taken up by healthy liver cells.

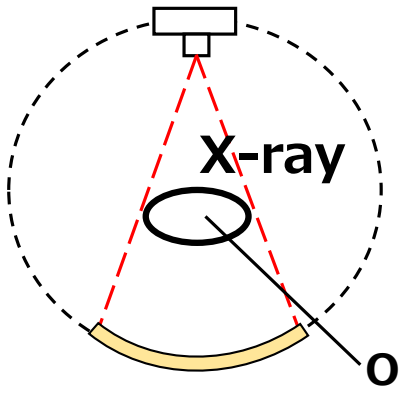
Problem

- Some patients cannot be diagnosed with MRI
  (Patients with body metals, claustrophobic patients, etc.)

Imaging contrast agents for MRI with X-ray CT.

X-ray CT (Computed Tomography)

Technology for nondestructively examining the inside of the object using X-rays



Measure X-ray attenuation information

Reconstruction images

© National Cancer Center Hospital East

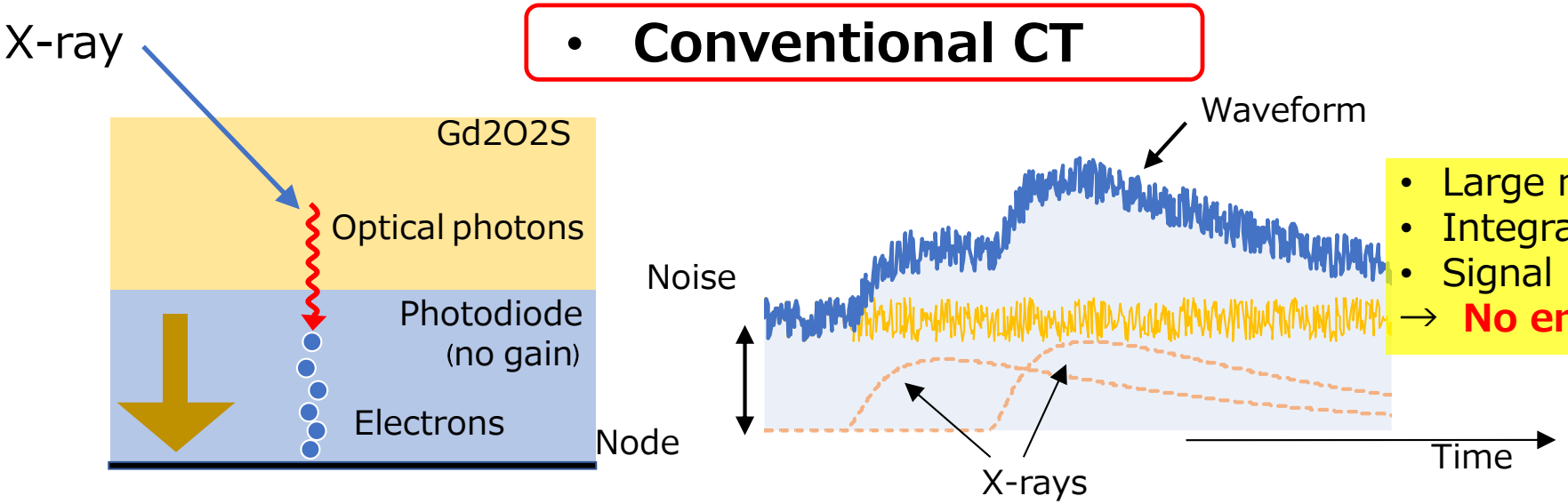
・Problems with conventional CT

Images are monochromatic because X-ray energy information is not available

→Cannot distinguish between the contrast agent and the organ / soft tissue

→X-ray CT image with X-ray energy info

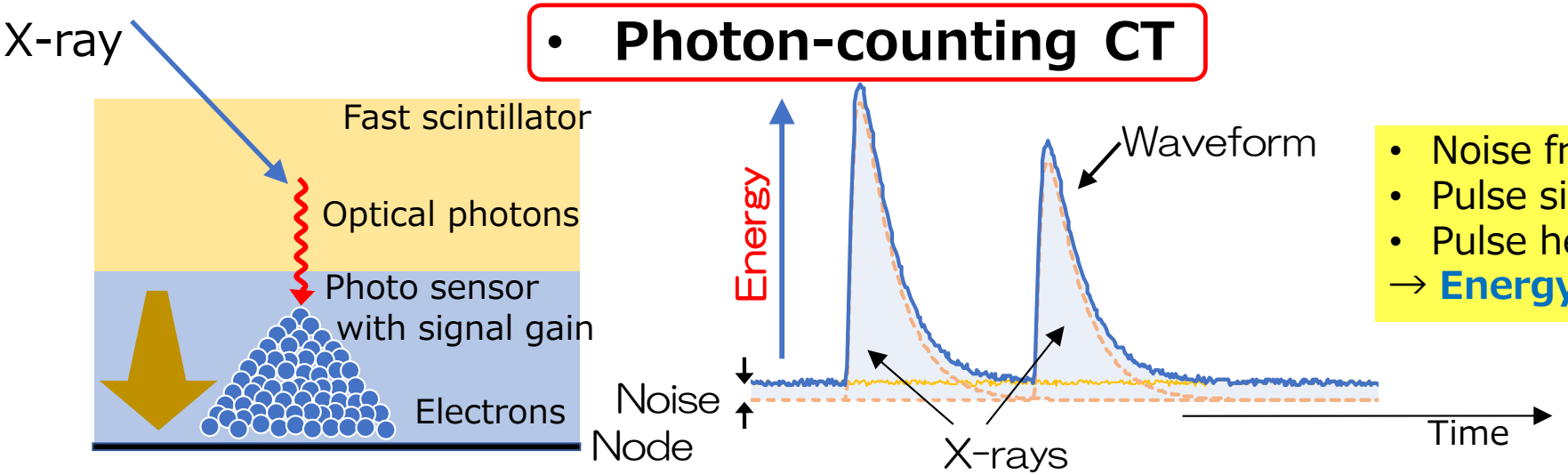
• Conventional CT



- Large noise
- Integrated signal
- Signal integration

→ **No energy info**

• Photon-counting CT



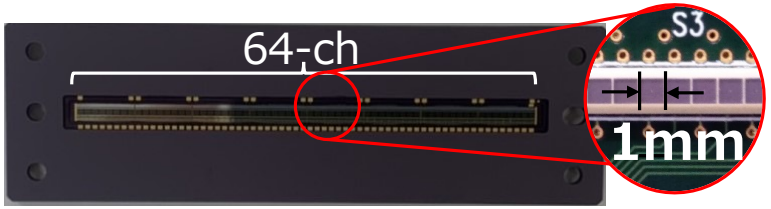
- Noise free
- Pulse signal
- Pulse height

→ **Energy info**

Photon-Counting CT

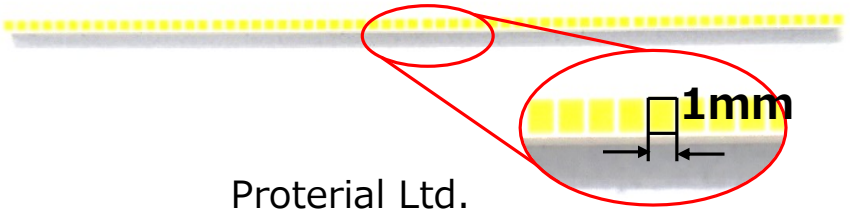
H. Kiji et al., 2020　M. Arimoto et al., 2023

・MPPC (Multi-Pixel Photon Counter)



Hamamatsu Photonics

・YGAG scintillator

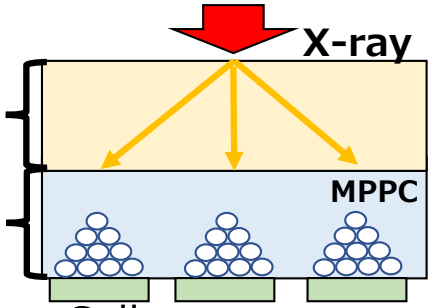


Proterial Ltd.

・Converts X-rays to charge signals

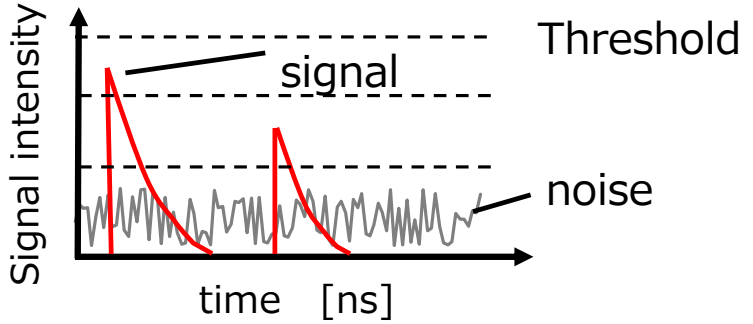
YGAG scintillator
- **Decay time ~ 70 ns**
- **Luminous intensity 5×10^4 photon/MeV**

MPPC
- **Amplification rate ~ 10^6**
- **Time response ~ 1 ns**



Photon → visible light → electron → output

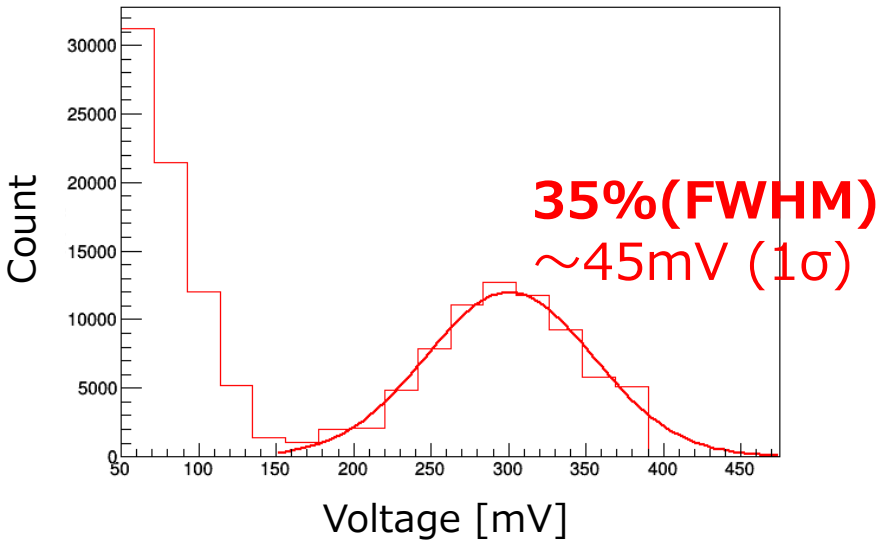
・Height of signal ∝ X-ray energy



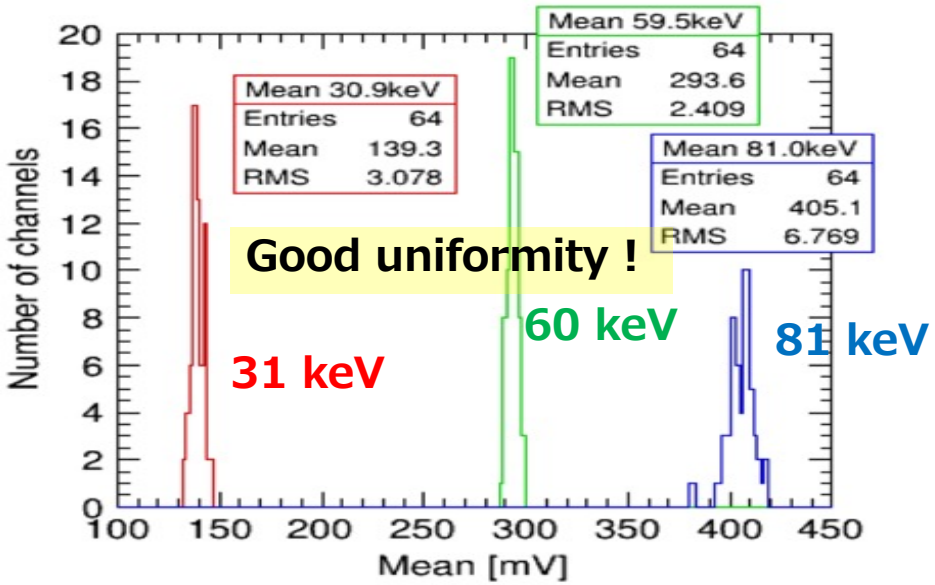
Obtaining X-ray energy info →
- **Substance identification**
- **Concentration estimation**

Performance of X-ray spectroscopy

- Spectrum of ^{241}Am (59.5 keV)



- Distribution of the photo peaks for 64 channels



Detector variation is ~ 1 keV

Target

- In vivo imaging of a mouse injected with iodine contrast agent was succeeded
  (Sato et al., 2023 Sagisaka et al., 2023)
- **This study: Visualize the distribution of Gd contrast agent in a liver of a rat with our photon counting CT system**

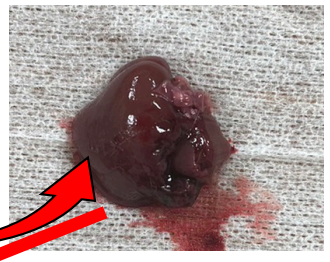
- Rat
  Body weight : 140 g
  Age in weeks: 6 weeks

2.0 ml of Gd contrast agent intravenous injection

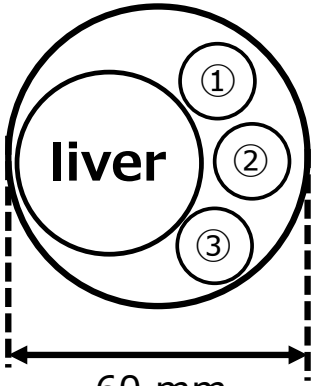
300 mm

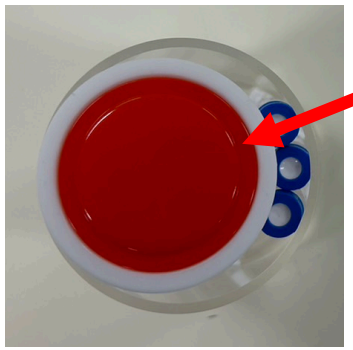
Rat (healthy)

Liver



5 minutes after intravenous injection

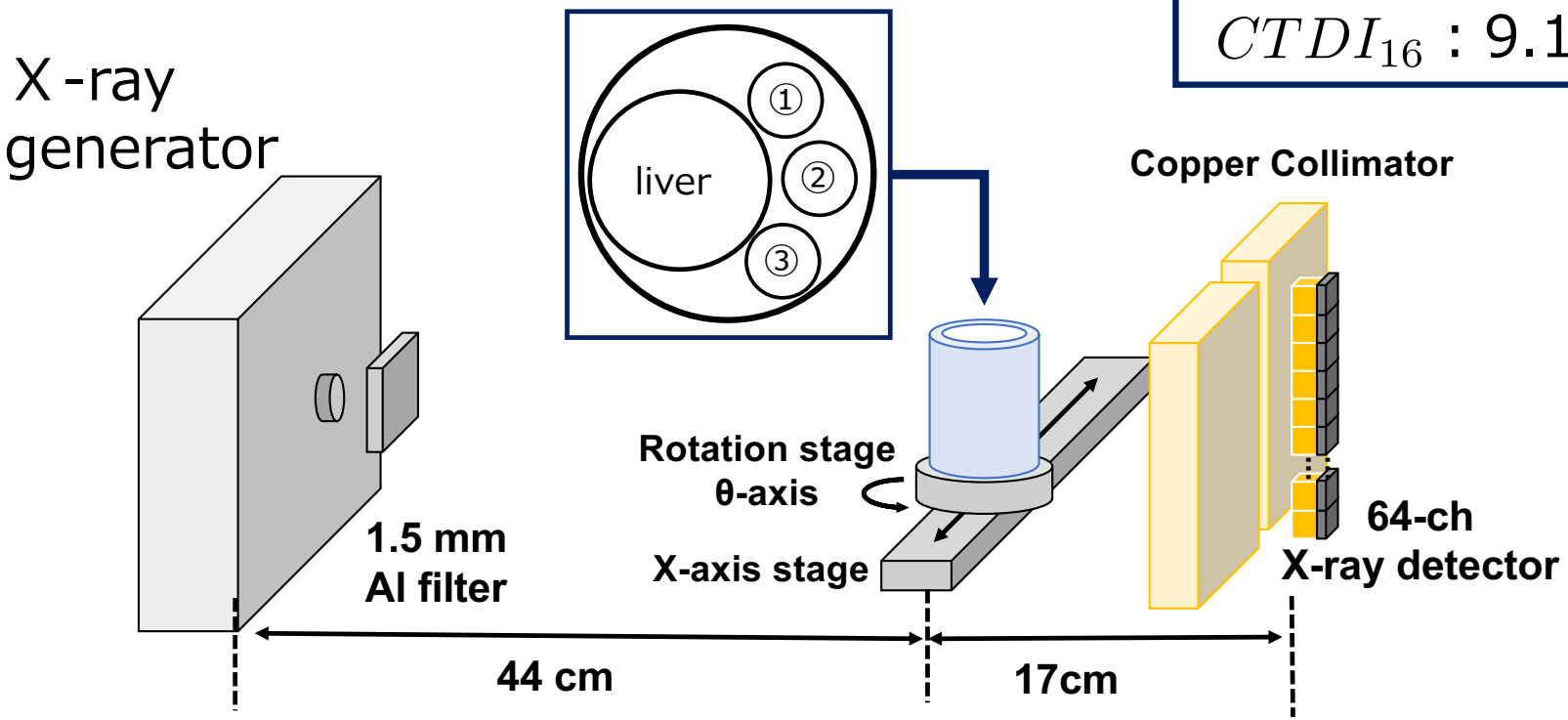




① Water
② Gd contrast agent (10 mg/ml)
③ Gd contrast agent (5 mg/ml)

Experimental environment

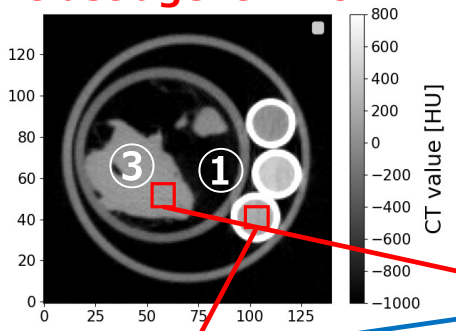
Tube voltage : 100kV
Tube current : 0.5mA
$CTDI_{16}$: 9.1 mGy



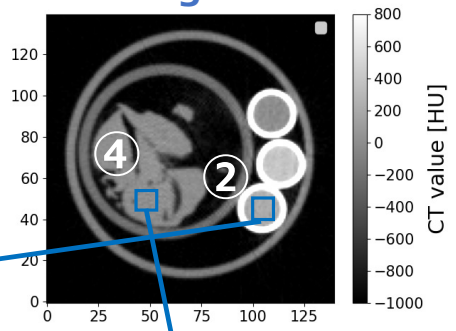
Comparison of CT values

$$CT(HU) = \frac{(\mu_t + \mu_w) - \mu_w}{\mu_w} \times 1000$$ μ_w: Line attenuation of water μ_t : Line attenuation of target

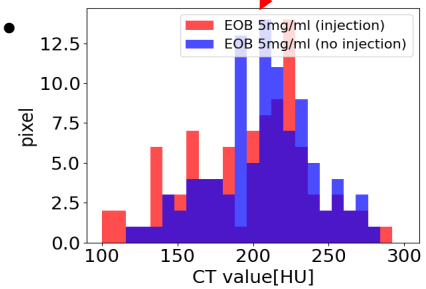
- CT image (35 keV – 45 keV)
  contrast agent : 2.0 ml



- CT image (35 keV – 45 keV)
  contrast agent : 0 ml

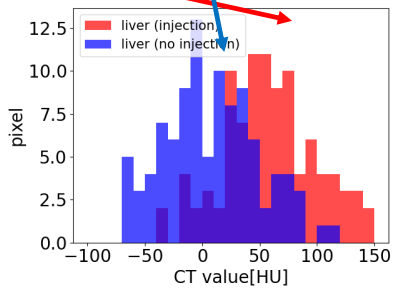


- CT value distribution of contrast agent (5 mg/ml)



Comparison of 1 and 2
KS test
P value : 0.11 > 0.05
(Significance)

- CT value distribution of liver



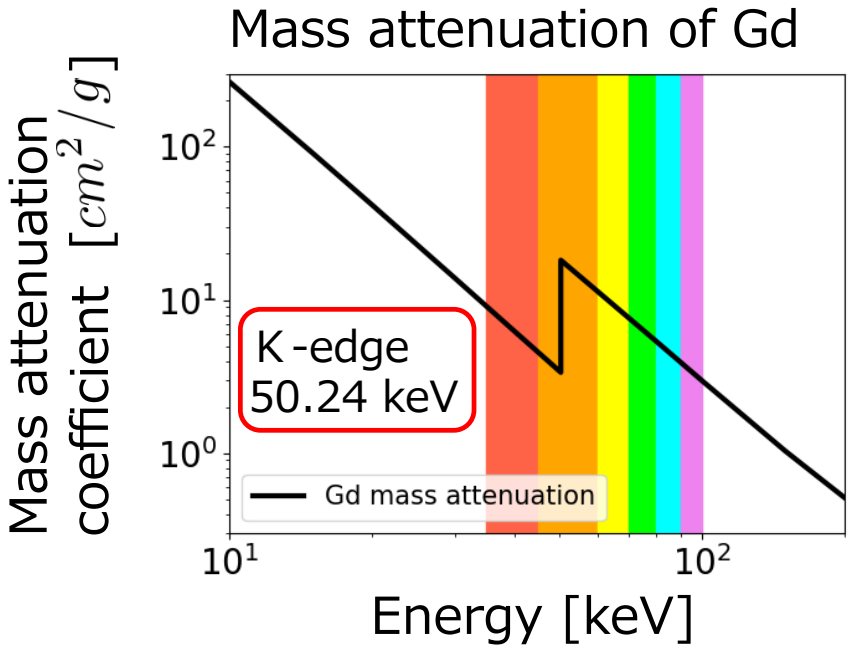
Comparison of 2 and 3
KS test
P value : 3.3×10^{-12}

Comparison of CT values confirmed the accumulation of Gd in the liver.

Concentration Estimation

CT images in multiple energy bands

μ_t' : Mass attenuation of target μ_w': Mass attenuation of water
μ_t : Line attenuation of target μ_w: Line attenuation of water



Pixel value of CT image (CT value)

$$CT(HU) = \frac{(\mu_t+\mu_w)-\mu_w}{\mu_w} \times 1000 \quad ①$$

$$= \rho \cdot \frac{\mu_t'}{\mu_w'} \times 1000 \quad ②$$

$$\mu = \rho \cdot \mu'$$

ρ (g cm^{-3})

Least squares method for CT values in each energy band

$$J = \sum_{E=1}^{6} \left(CT_{measured,E} - \rho \cdot \frac{\mu'_{t,E}}{\mu'_{w,E}} \times 1000\right)^2$$

from NIST

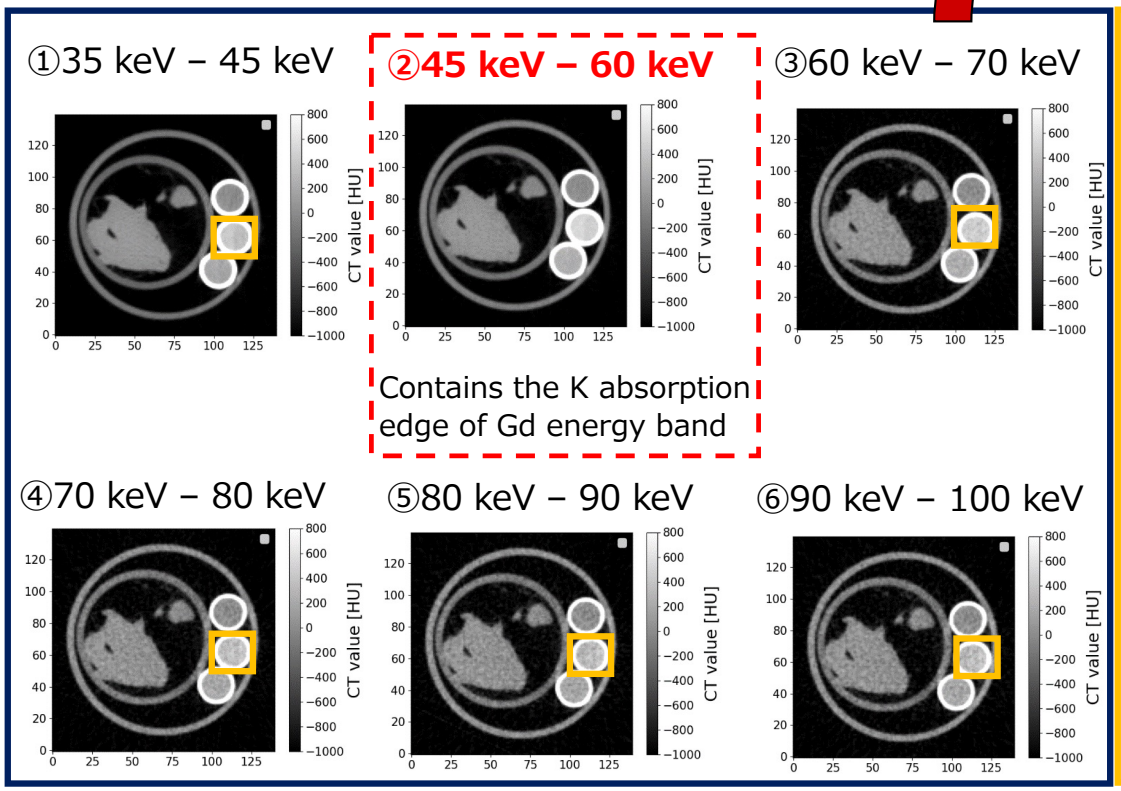
Calculate minimum J value and estimate concentration

Concentration Estimation

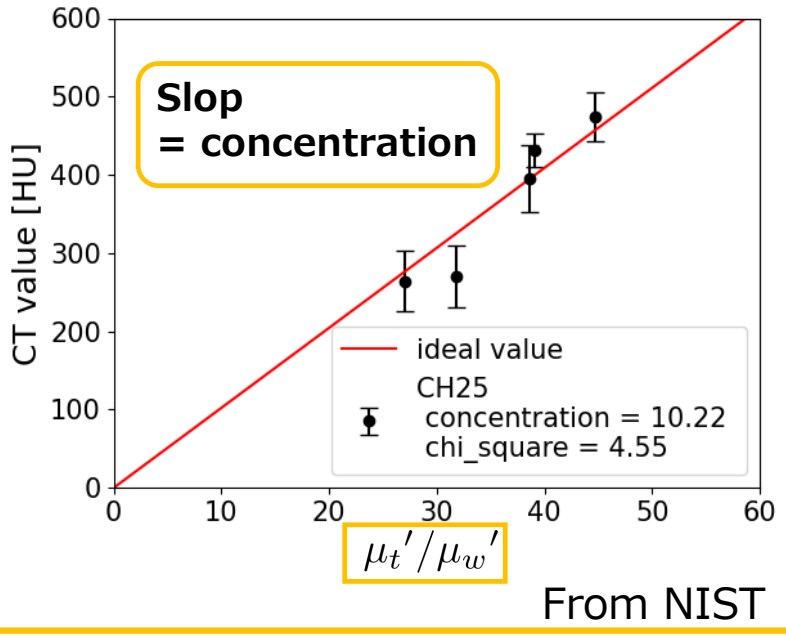
CT image
(contrast agent : 2.0 ml)

Plot CT values of **a single pixel** in 5 energy bands

$$\mathrm{CT(HU)} = \rho \cdot \frac{\mu_t{}'}{\mu_w{}'} \times 1000$$

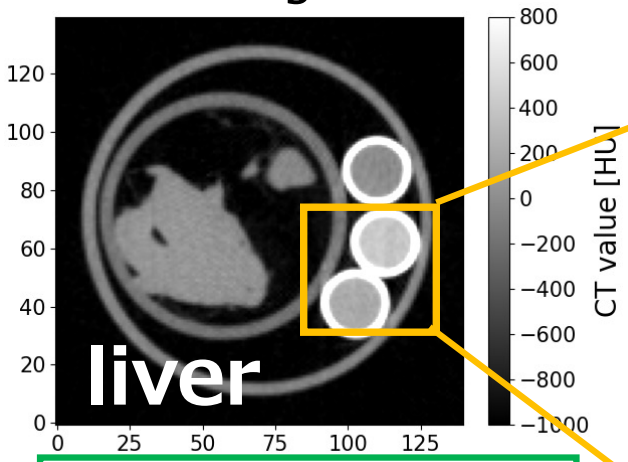


Estimated concentration of one pixel in a region with 10 mg/ml of gadolinium contrast agent



Estimated results of known concentrations

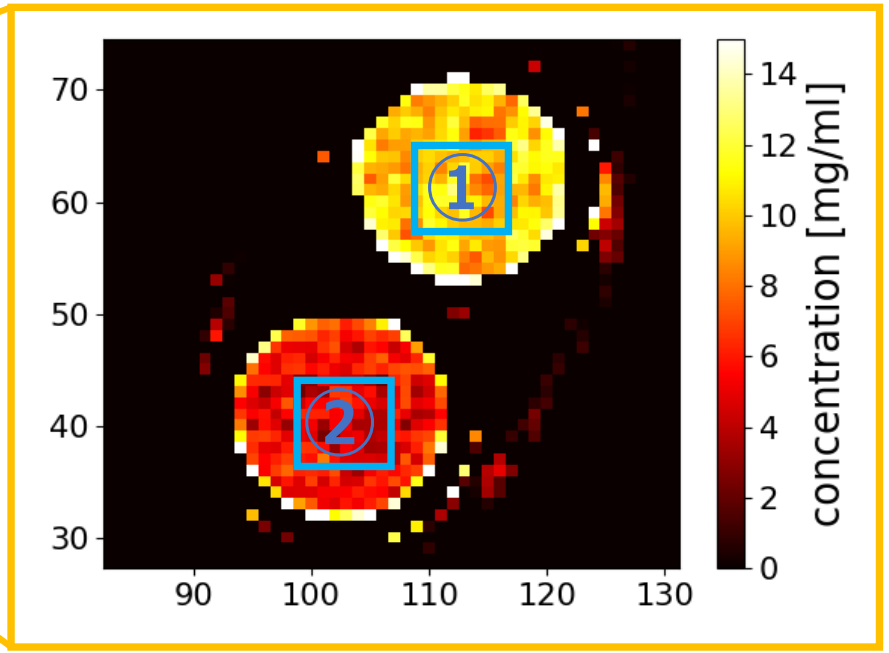
- CT image (35 keV – 100 keV)
  contrast agent : 2.0 ml



$$\mu_t = \rho_{Gd} \cdot \mu'_{Gd} + \mu_w$$

μ_t : Line attenuation of target
μ'_{Gd} : Mass attenuation of Gd
μ_w : Line attenuation of water

- Concentration map of Gd

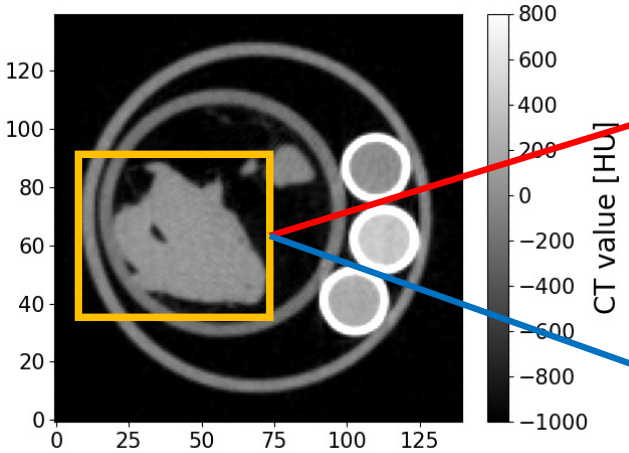


	Ideal [mg/ml]	Estimated values [mg/ml]
①	10	10.10 ± 1.34
②	5	5.13 ± 1.32

Successful ρ estimation of Gd contrast agent

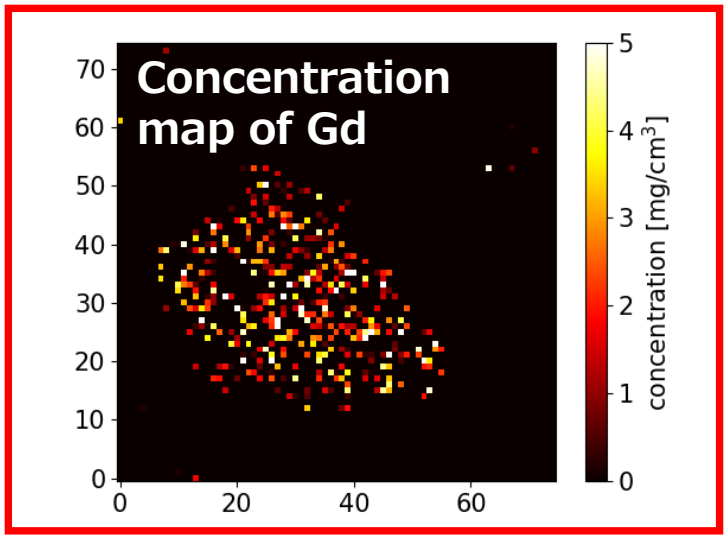
Concentration Estimation in the Liver

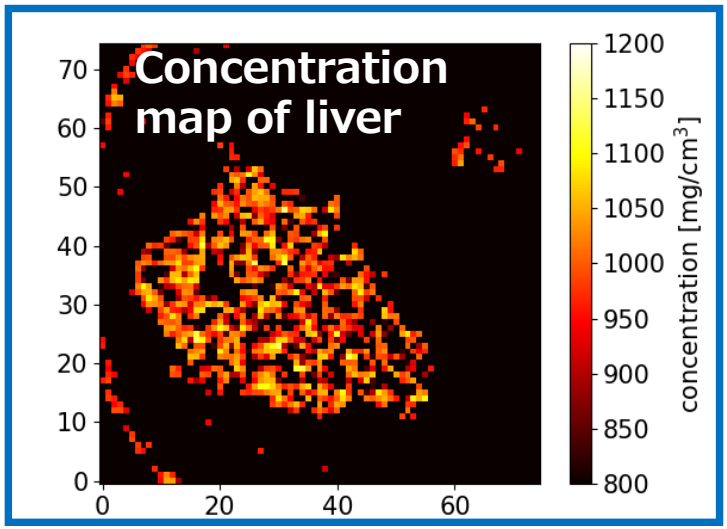
- CT image (35 keV – 100 keV)
  contrast agent : 2.0 ml



ρ_{Gd}

ρ_{liver}





$$\mu_t = (\rho_{Gd} \cdot \mu_{Gd}{}' + \mu_w) + \rho_{liver} \cdot \mu_{liver}{}'$$

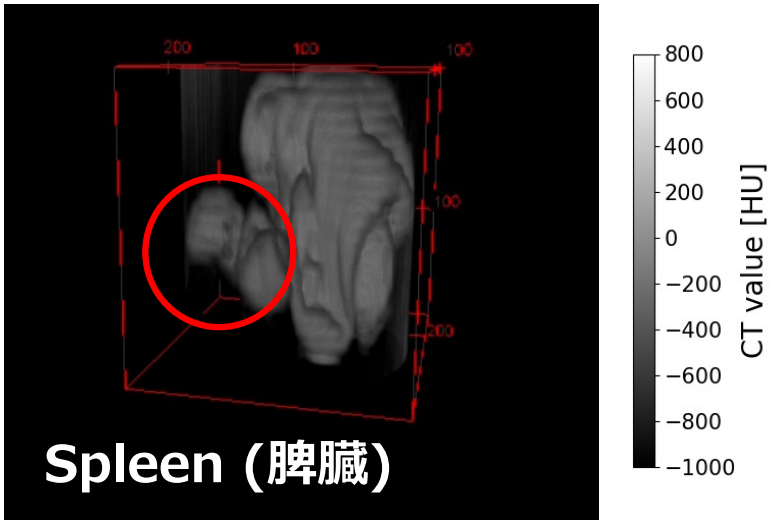
μ_t : line attenuation of target μ'_{Gd} : Mass attenuation of Gd

μ'_w : Mass attenuation of water μ'_{liver} : Mass attenuation of liver (soft tissue)

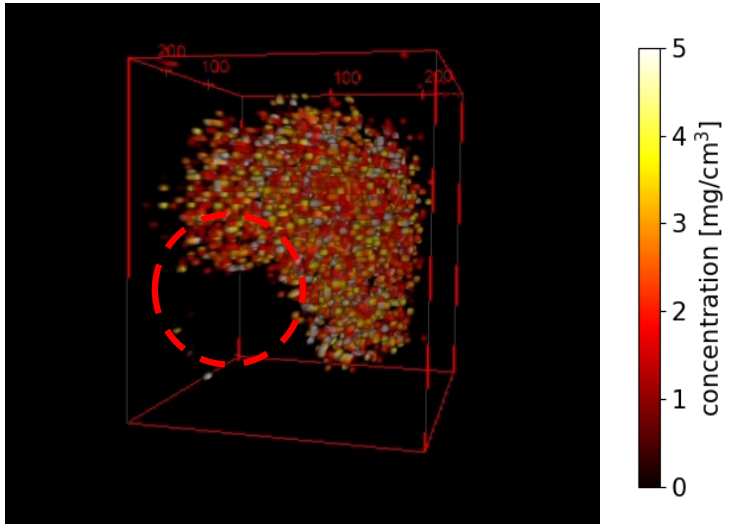
Visualizing Gd accumulation in the liver

3D image

・CT image



・ Gd concentration image



No Gd uptake in spleen

Estimated amount of Gd that accumulates in the liver : **2.95 ± 0.13 mg**
< Injection volume : **78.6 mg**

Successful 3D visualization of Gd accumulated in the liver

Conclusion

- Ex vivo imaging of Gd contrast agents using next-generation X-ray CT

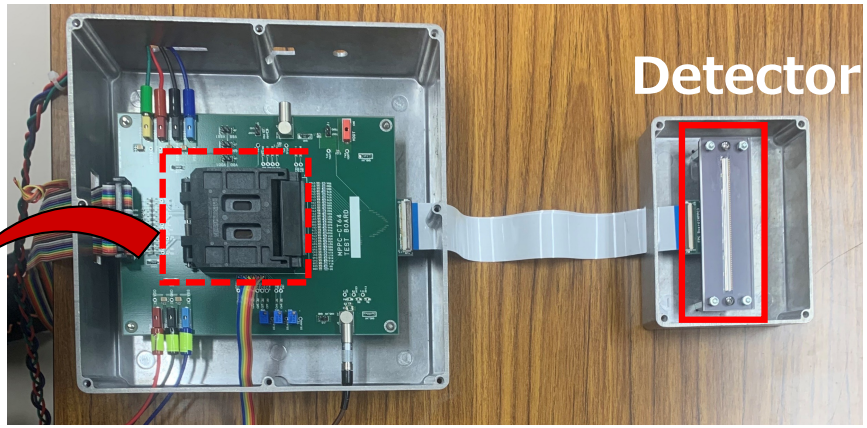
  1. Concentration evaluation of known concentrations
  2. 3D visualization of gadolinium accumulation in the liver

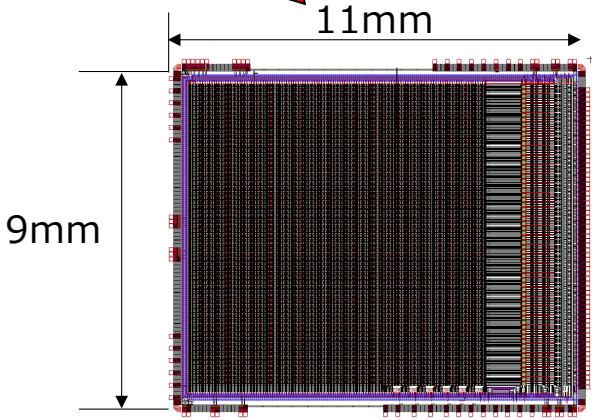
Future work

- Experiments with gadolinium contrast agent in vivo
- Experiments on rats with liver disease or lesions
- More accurate concentration estimation and faster speed
  → Update the detector from 1D array to 2D array

Appendix

Signal processing circuit

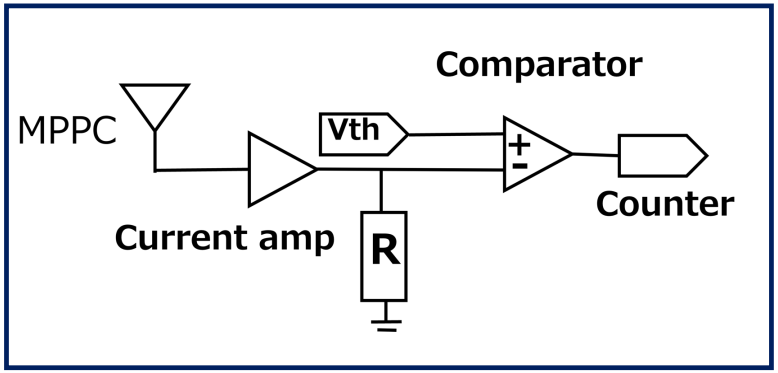




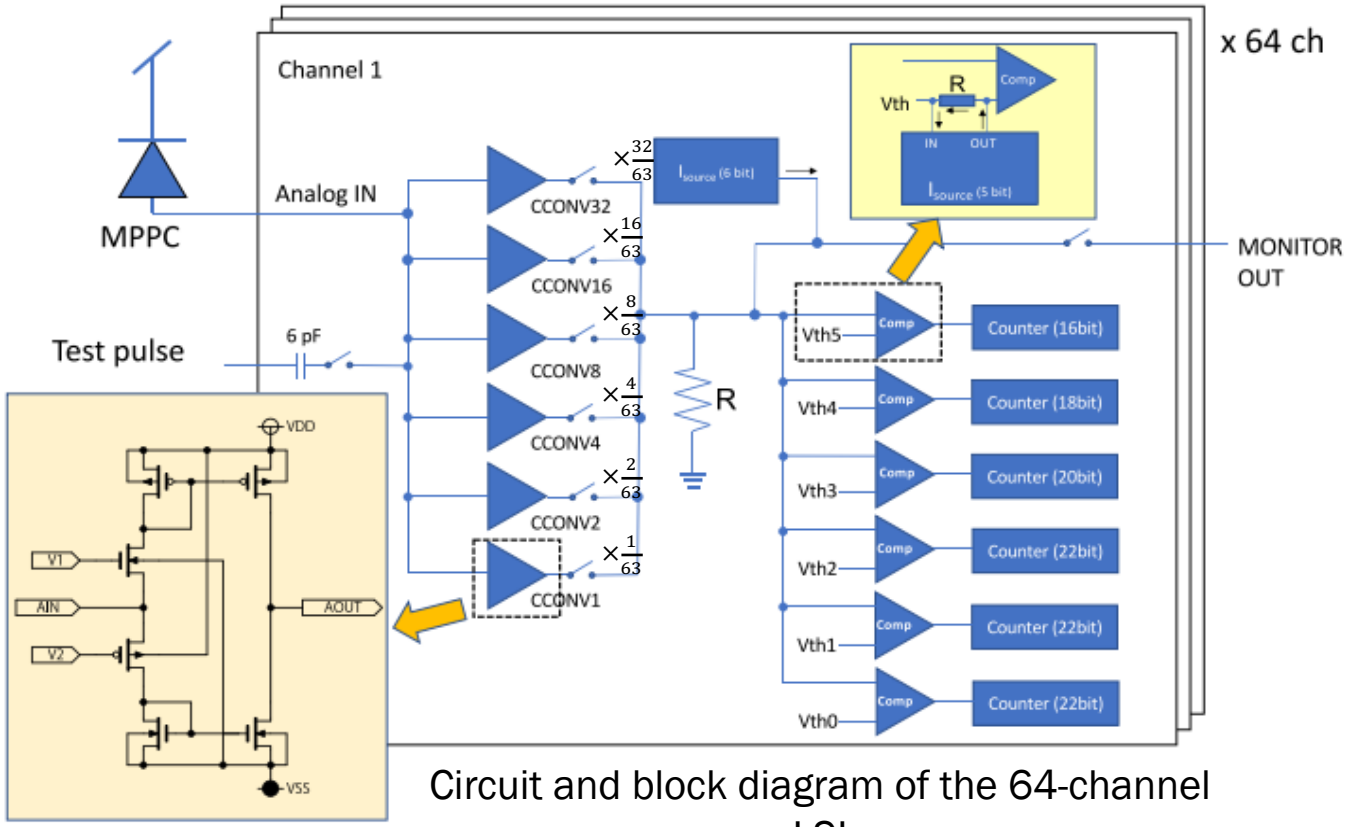
LSI (Arimoto et.al. 2023)

Internal circuit of LSI

x 64



LSI



Circuit and block diagram of the 64-channel LSI

- Overcoming the challenges of conventional CT

When substance discrimination becomes possible.

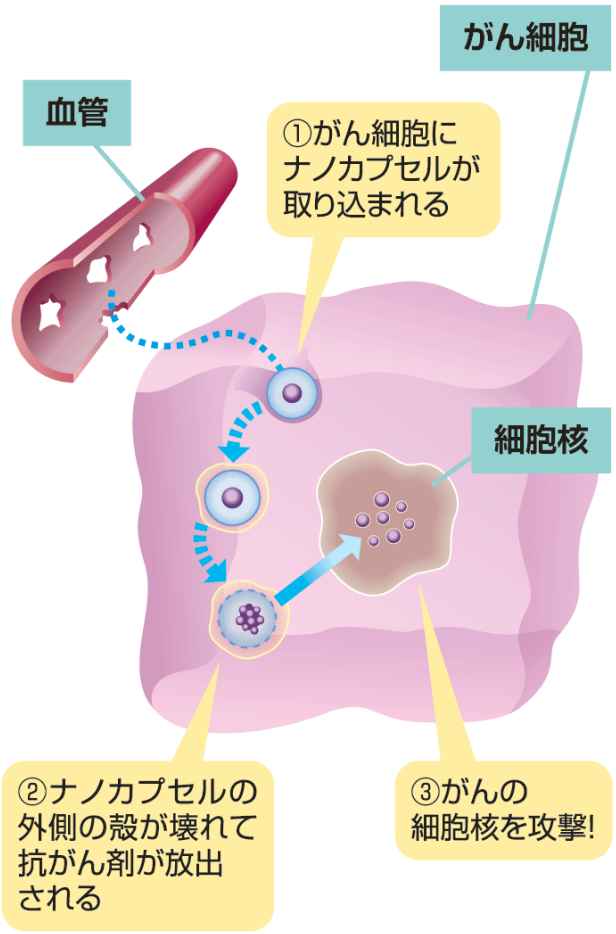
Drug Visualization

→Visualization of drug delivery to target organs

→ Optimize drug dosage based on drug reach and efficacy

CT-based approach to next-generation dosing systems will be available.

https://imidas.jp/jijikaitai/f-40-125-15-09-g591



ドラッグデリバリーシステム

Estimation of the concentration of two materials

Estimate ρ

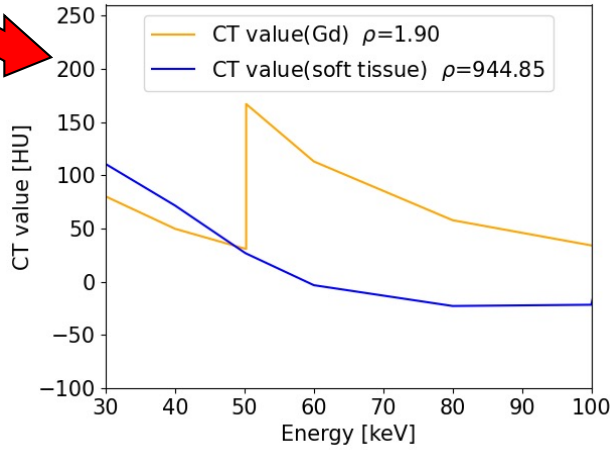
・CT value

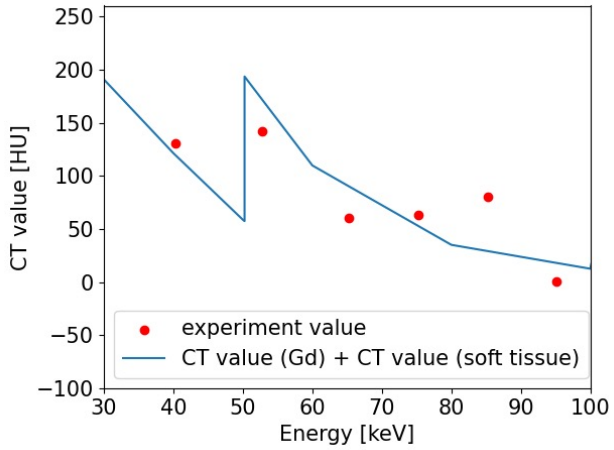
$$CT(HU) = \frac{(\rho_{Gd}\cdot\mu_{Gd}{}' + \mu_w) - \mu_w}{\mu_w} \times 1000 + \frac{\rho_{liver}\cdot\mu_{liver}{}' - \mu_w}{\mu_w} \times 1000$$

Gadolinium Contrast Agent (Aqueous solution)

liver

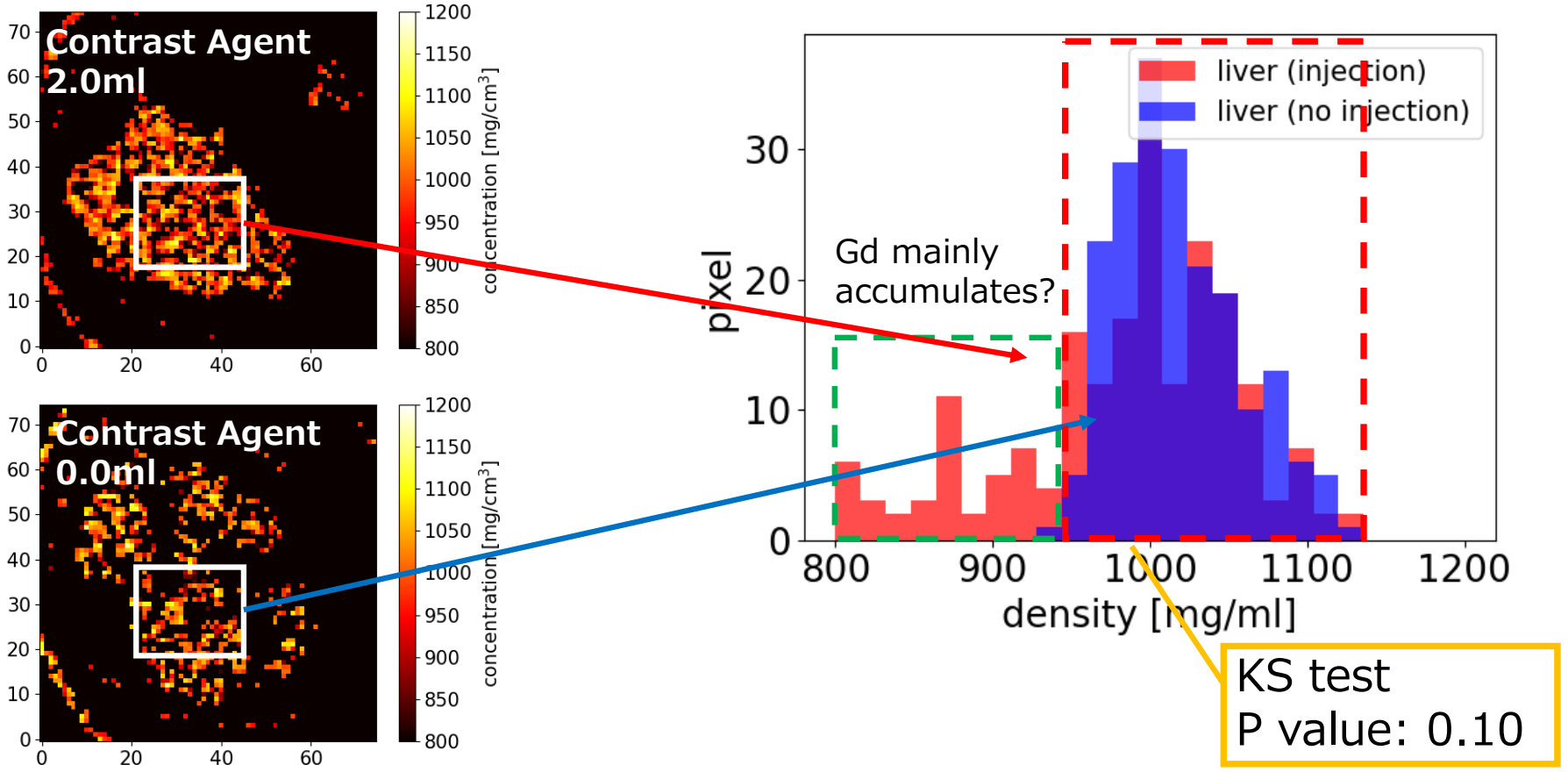
$$= 1000 \cdot \rho_{Gd} \cdot \frac{\mu_{Gd}{}'}{\mu_w} + 1000 \cdot \rho_{liver} \cdot \frac{\mu_{liver}{}'}{\mu_w} - 1000$$





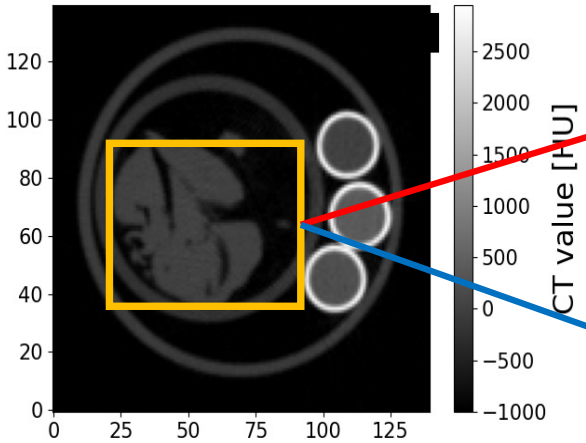
Estimated liver density evaluation

Density map of liver



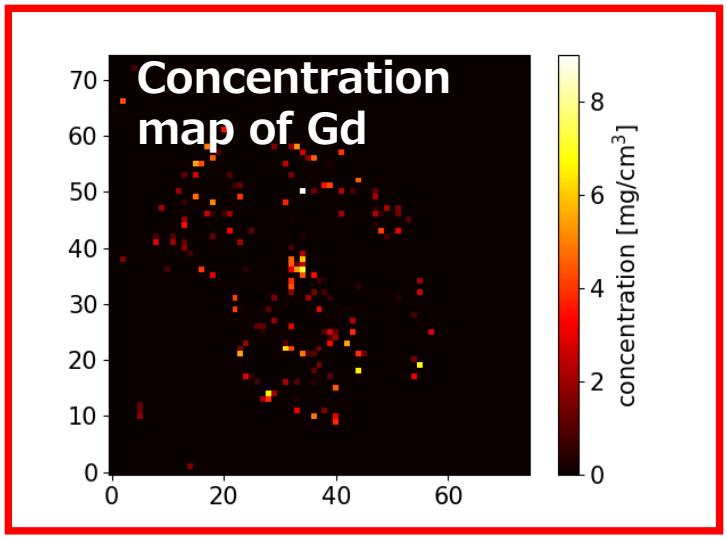
Concentration Estimation in the Liver

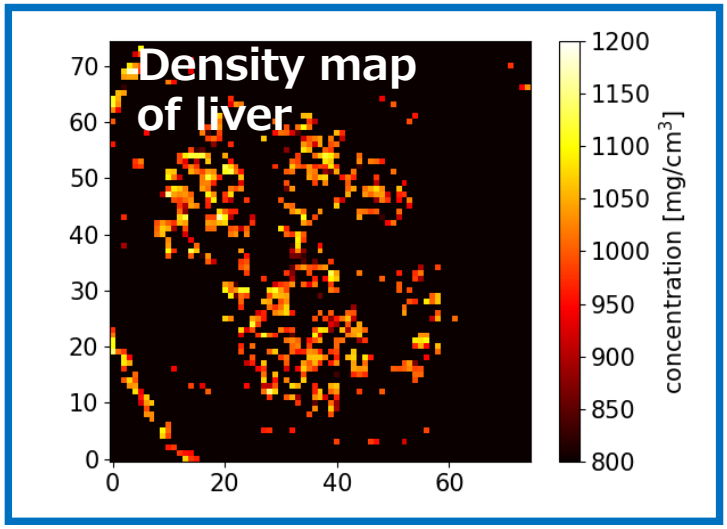
- CT image (35 keV – 100 keV)
  contrast agent : 0.0 ml



ρ_{Gd}

ρ_{liver}





$$\mu_t = (\rho_{Gd} \cdot \mu_{Gd}{}' + \mu_w) + \rho_{liver} \cdot \mu_{liver}{}'$$

μ_t : line attenuation of target μ'_{Gd} : Mass attenuation of Gd

μ'_w : Mass attenuation of water μ'_{liver} : Mass attenuation of liver (soft tissue)