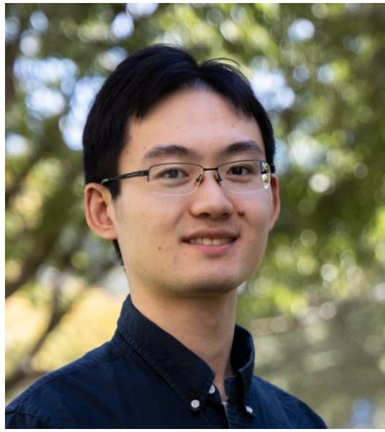
Symposium on AI and Reconstruction for Biomedical Imaging

Image Reconstruction for Positronium Lifetime Tomography



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Department of Biomedical Engineering, UC Davis

March 10, 2026

London, UK

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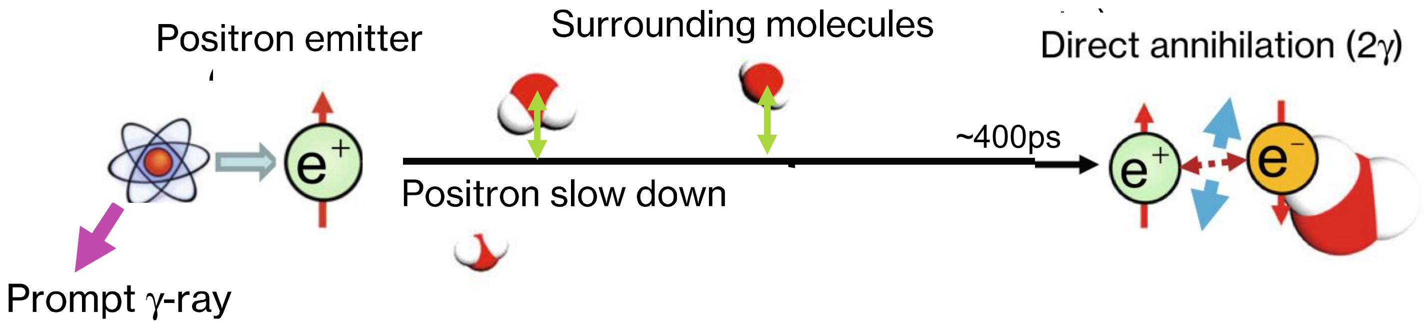
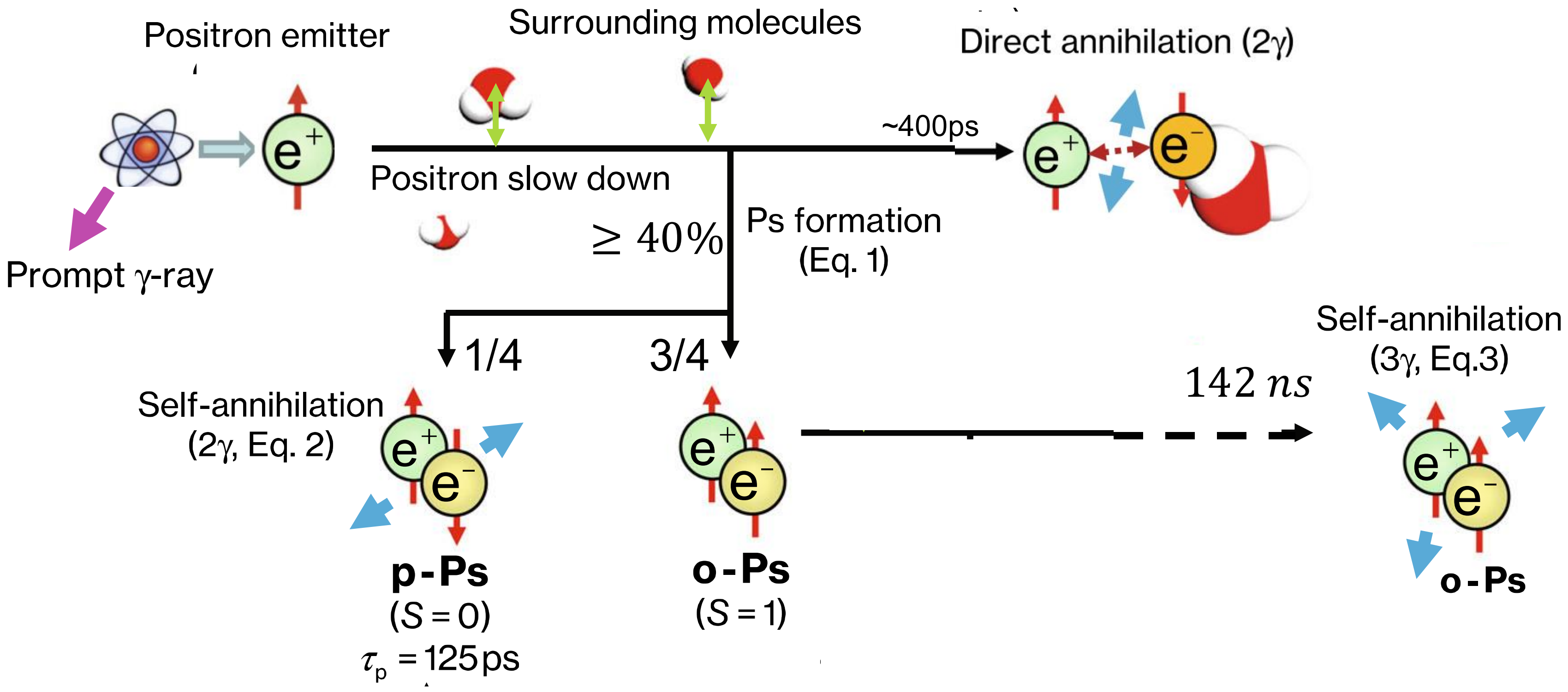
Positronium Lifetime

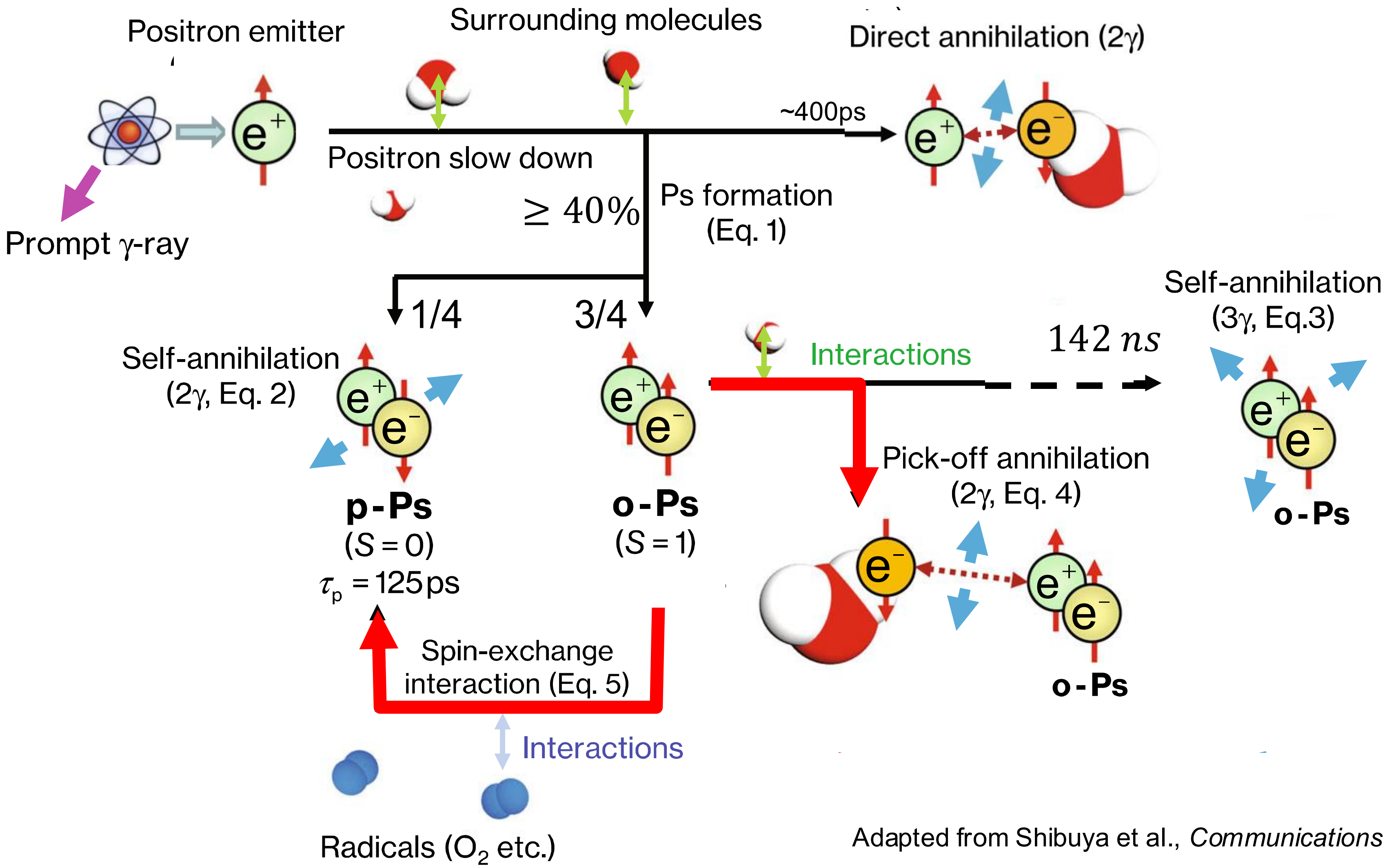


Positronium Lifetime



Adapted from Shibuya et al., *Communications Physics* 3, 173 (2020), CC BY 4.0.

Positronium Lifetime



- The mean lifetime of o-Ps in a human body is expected to range from approximately 1.8 ns in water to approximately 4 ns in skin cells (Moskal et al 2021).

O-Ps Lifetime is a Potential Biomarker

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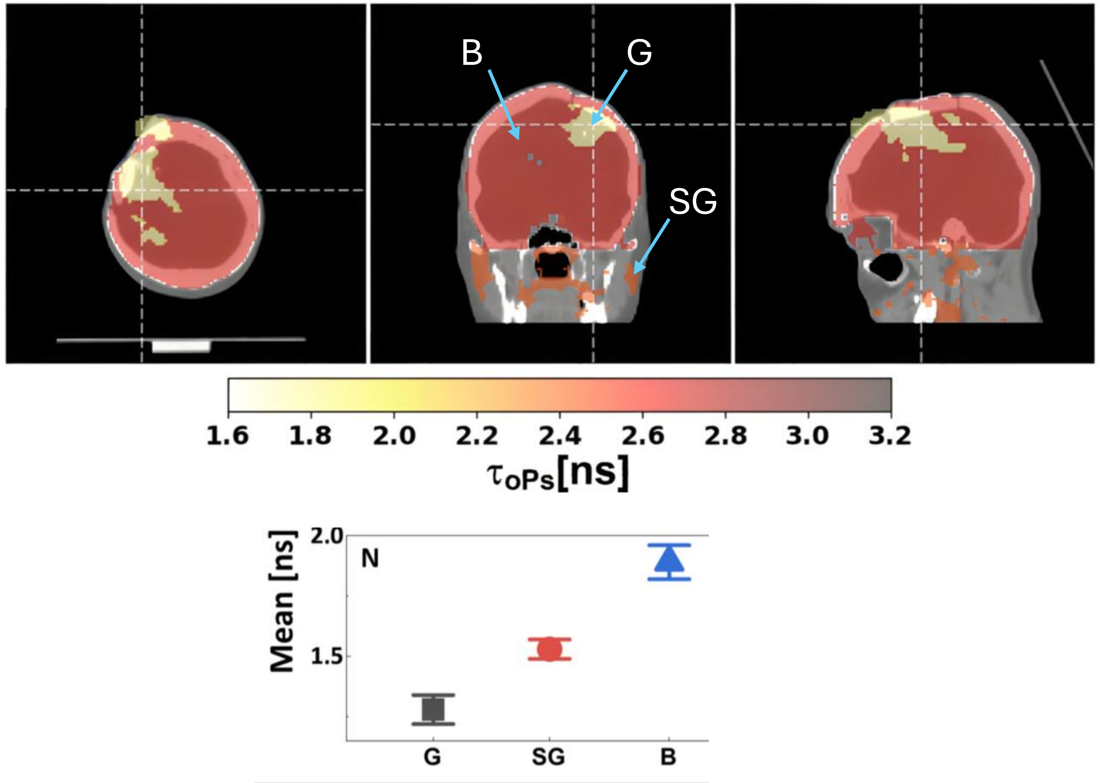
O-Ps lifetime is different in tumor and healthy tissue

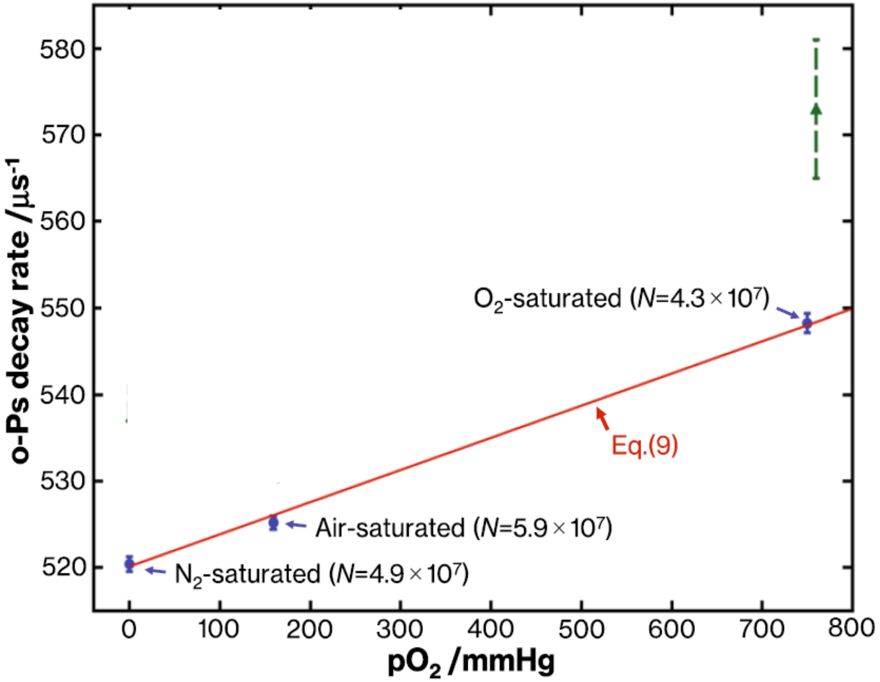
Moskal et al., *Science Adv, 2024*



- O-Ps lifetime in glioblastoma tumor (G) < salivary glands (SG) < healthy brain tissues

O-Ps lifetime is sensitive to concentration of O_2

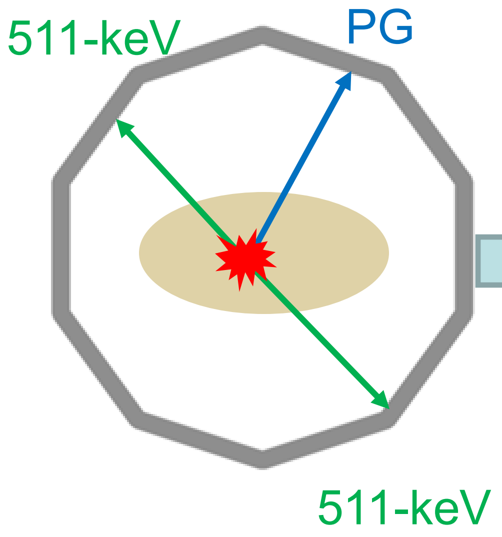
Shibuya et al., *Communications Physics*, 2020



- O-Ps lifetime **decreases** as O_2 concentration **increases**

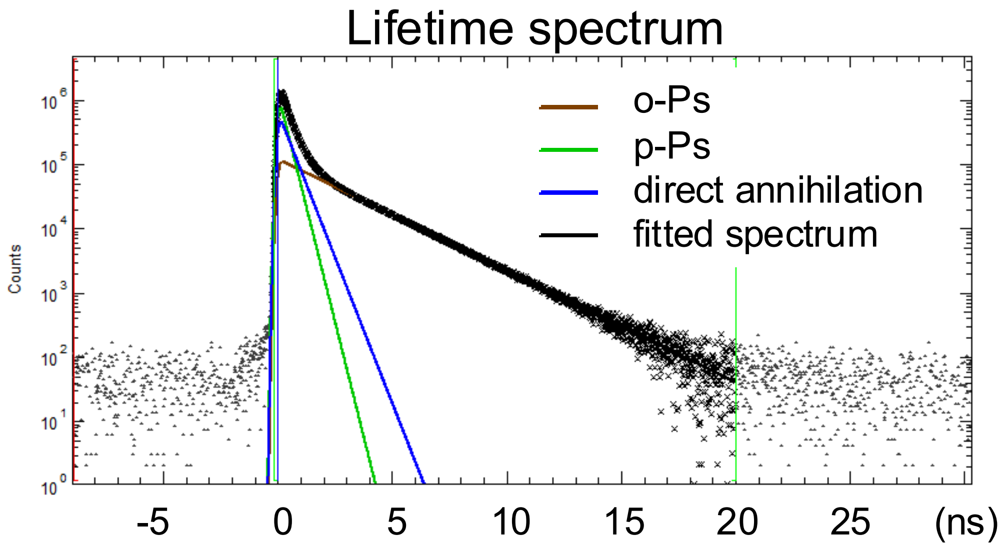
P. Moskal *et al*., "Positronium Imaging: History, Current Status, and Future Perspectives," *IEEE TRPMS*, vol. 9, no. 8, pp. 981-1001, 2025

Lifetime Event Model



Lifetime measurement (after travel-time correction)

$$\tau = \frac{(t_{1st\,511} + t_{2nd\,511})}{2} - t_{PG}$$



List-mode event parameters

- LOR i_k, including TOF information
- Time delay τ_k

Likelihood model of time measurement

$$p(\tau|\boldsymbol{\lambda}, \boldsymbol{A}) = \sum_l g(\tau) * [A_l \lambda_l \exp(-\lambda_l \tau) u(\tau)] + B$$

- λ_l: 1/lifetime of the l^{th} pathway
- A_l: Fraction of the l^{th} pathway
- $g(\tau)$: Detector timing response
- $u(\tau)$: Heaviside function
- B: random background events

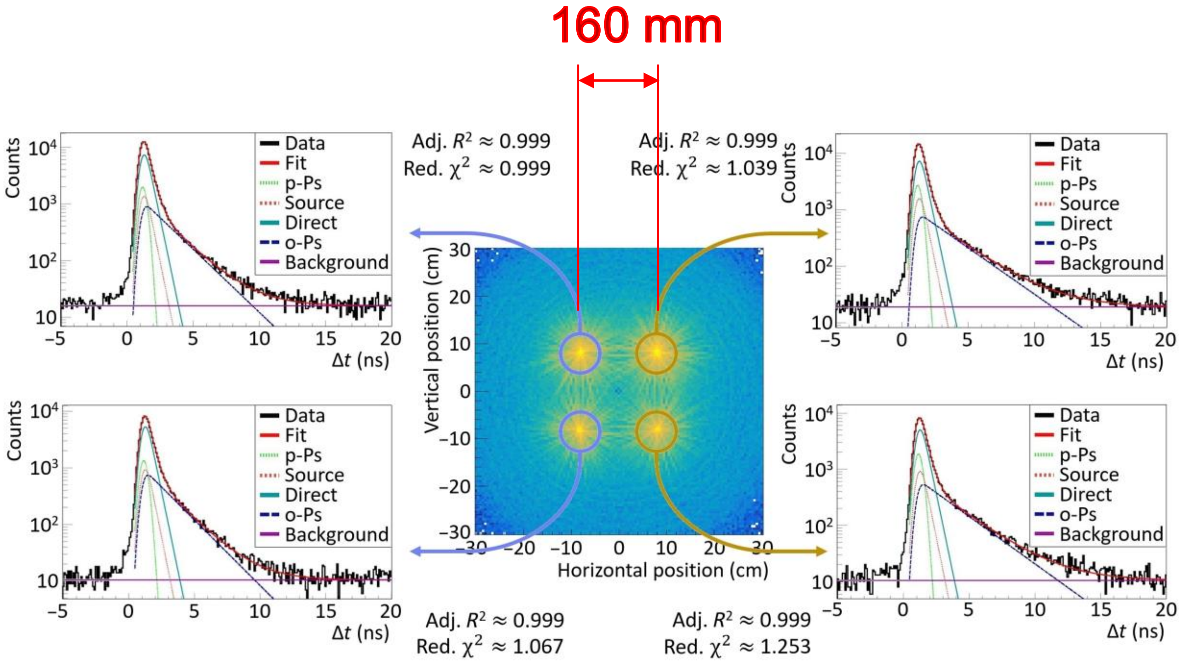
Existing Ps Lifetime Image Reconstruction Method

- **Direct TOF backprojection**

(Moskal et al., *Science Advance*, 2021)

Step 1) Determine the position of each annihilation event using TOF

Step 2) Fit the time delay distribution to get lifetime



$$\text{Fit}(\Delta t) = \sum_{i=1}^{4} I_i \left(\exp\left(-\frac{\Delta t}{\tau_i}\right) * \text{Gaussian}\,(\Delta t, t_0, \sigma) \right) + \text{Background}$$

I_i – Intensity of ith component, τ_i – Mean lifetime of ith component $\sum_{i=1}^{4} I_i = 100\%$

Drawback

- Spatial resolution is limited by the TOF resolution:
  - The predicted spatial resolution (FWHM) of a point source is **30 mm for 500-ps TOF resolution and 50 ps TOF resolution is required** to achieve comparable resolution (~5 mm) as PET images (Moskal et al., *EJNMMI Physics*, 2020)

- Curve fitting for oPs lifetime become more difficult when oPs with different lifetimes are blurred together.

List-mode Maximum Likelihood Method

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- The likelihood function

$$L(\boldsymbol{\lambda}) = \sum_{k=1}^{N} \ln\left(\sum_{j=1}^{J} \frac{H(i_k, j)x_j}{[\boldsymbol{Hx}]_{i_k}} p(\tau_k|\boldsymbol{\lambda}_j, \boldsymbol{A}_j)\right)$$

where $\boldsymbol{H}$ is the system matrix and x_j is the total number of detected annihilations in voxel j estimated using PET reconstruction method (OSEM).

- Monotonically convergent ML algorithm with a closed-form update equation for mono-exponential lifetime model

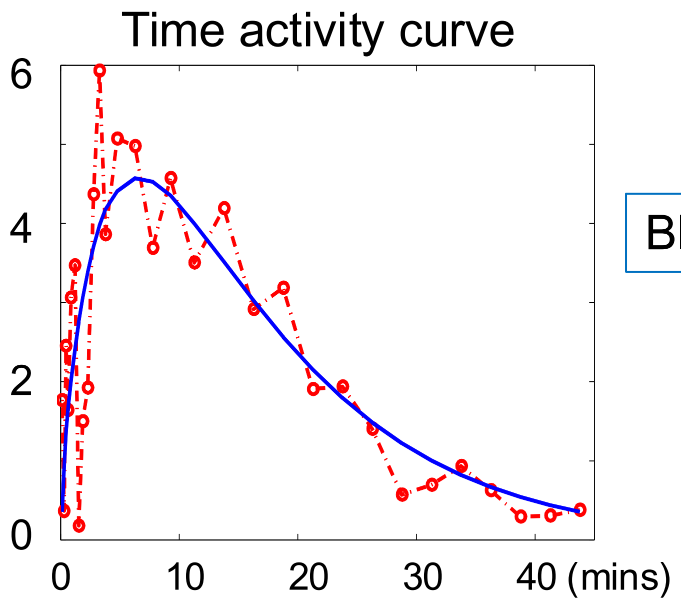
$$\lambda_j^{n+1} = \frac{\sum_{k=1}^{N} H(i_k,j)w_{kj}^n}{\sum_{k=1}^{N} H(i_k,j)w_{kj}^n\tau_k}, \quad \text{where } w_{kj}^n = \frac{x_j\lambda_j^n \exp(-\lambda_j^n\tau_k)}{\sum_{l=1}^{J} H(i_k,l)x_l\lambda_l^n \exp(-\lambda_l^n\tau_k)}.$$

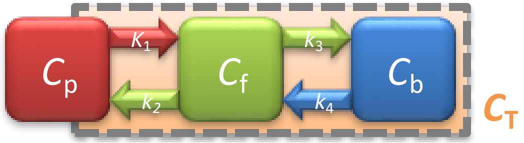
- Drawback:
  - High-computational cost associated with $\sum_{l=1}^{J} H(i_k, l)x_l\lambda_l^n \exp(-\lambda_l^n\tau_k)$

Qi and Huang, Positronium Lifetime Image Reconstruction for TOF PET, IEEE TMI 2022

Parallels between Dynamic PET and o-Ps Lifetime Reconstruction

Dynamic PET



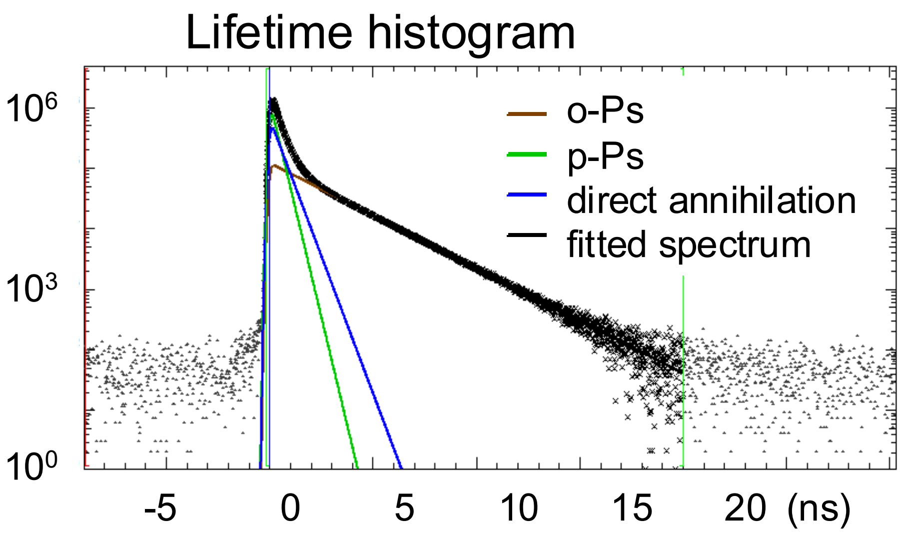


Blood input function

Functions of rate constants ($K_1 \sim k_4$)

$$= c_p(t) * [A_1 \exp(-\alpha_1 t) + A_2 \exp(-\alpha_2 t)]u(t)$$

O-Ps lifetime



$$= g(t) * \left[A_o \exp(-\lambda_o t) + A_p \exp\left(-\lambda_p t\right)\right]u(t)$$

Timing response function

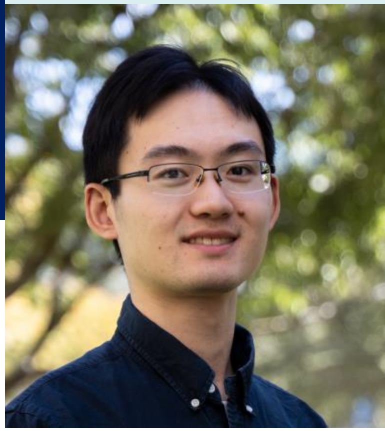
o-Ps fraction

(o-Ps lifetime)$^{-1}$

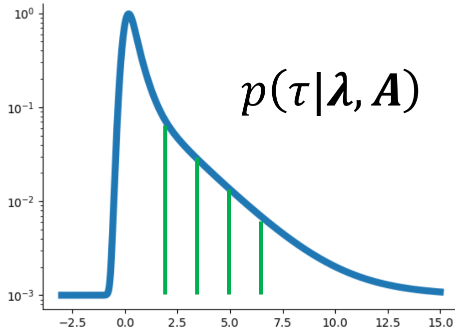
p-Ps fraction

(p-Ps lifetime)$^{-1}$

SPLIT: Statistical Positronium Lifetime Image reconstruction via time-Thresholding



- Define Multiple T_c
- Keep events with time delay < T_c



Subset #1

Subsets of events at each T_c

Subset #N

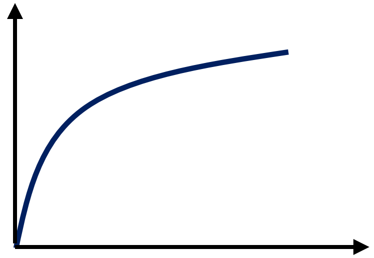
OSEM

Lifetime-cut image #1

Lifetime-cut Images at each T_c

Lifetime-cut image #N

Fit the curve of each voxel $= \int_{-\infty}^{T_c} p(\tau|\boldsymbol{\lambda}_j, \boldsymbol{A}_j)d\tau$ to get $\boldsymbol{\lambda}_j$



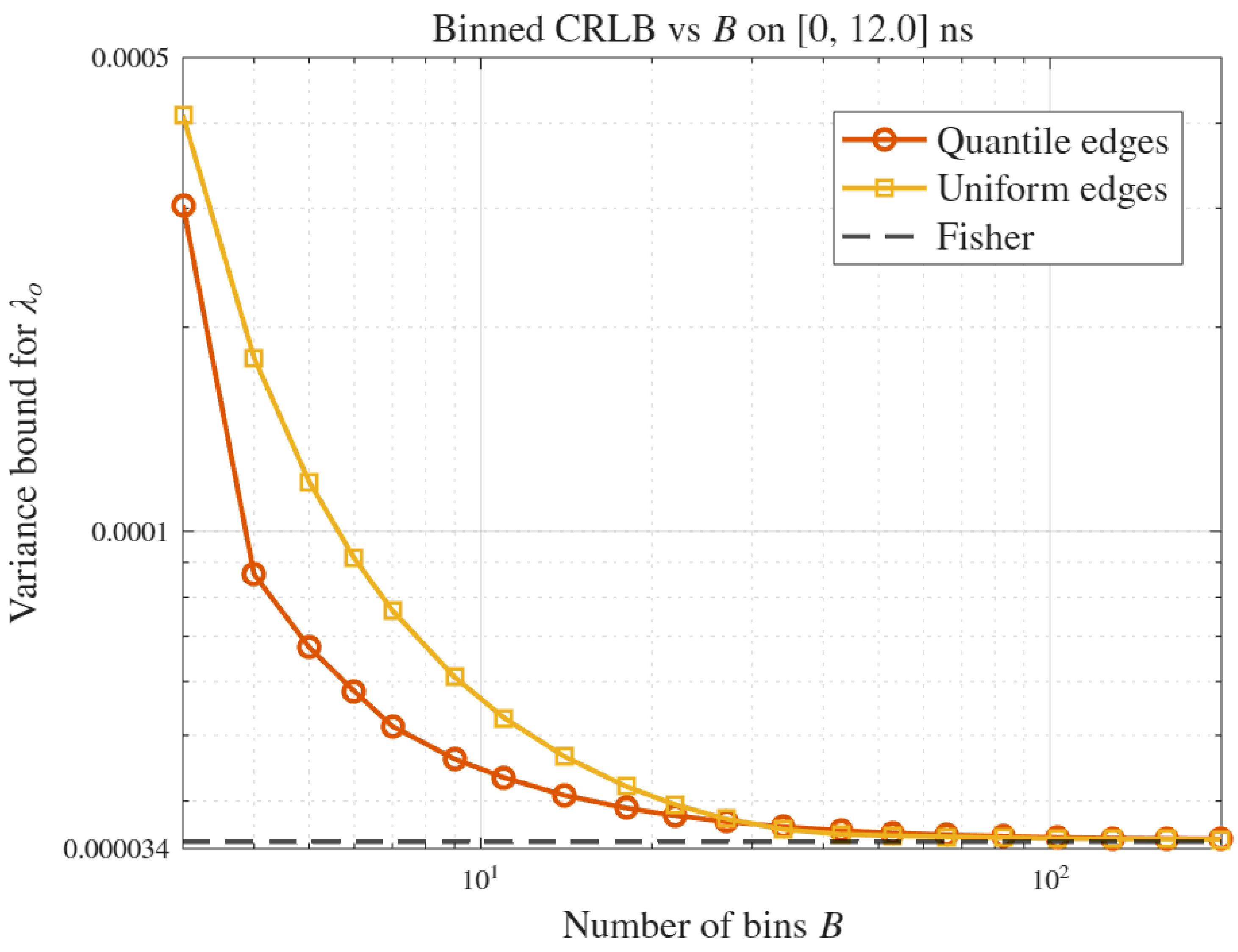
Lifetime image

Positron lifetime events

- **Advantages**
  - Flexible lifetime model
  - Practical for 3D data

Huang, …, Qi, SPLIT: Statistical Positronium Lifetime Image reconstruction via time-Thresholding, *IEEE TMI*, 2024

CRLB of $\hat{\lambda}_o$ vs. Number of Time Bins



Simulation Study

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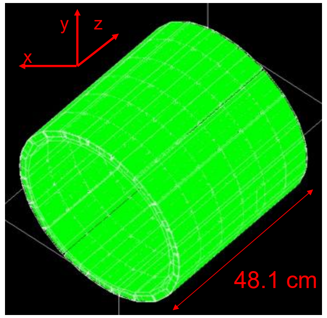
GATE Simulation

Scanner

- NeuroEXPLORER
- Crystal pitch: 1.6 mm (t) x 3.2 mm (a)
- Detector ring: 50 cm (d) x 48 cm (a)
- TOF resolution: 250 ps



Phantom & source

- ^{44}Sc, 20 kBq/cc, 30 min scan
- Activity concentration ratio

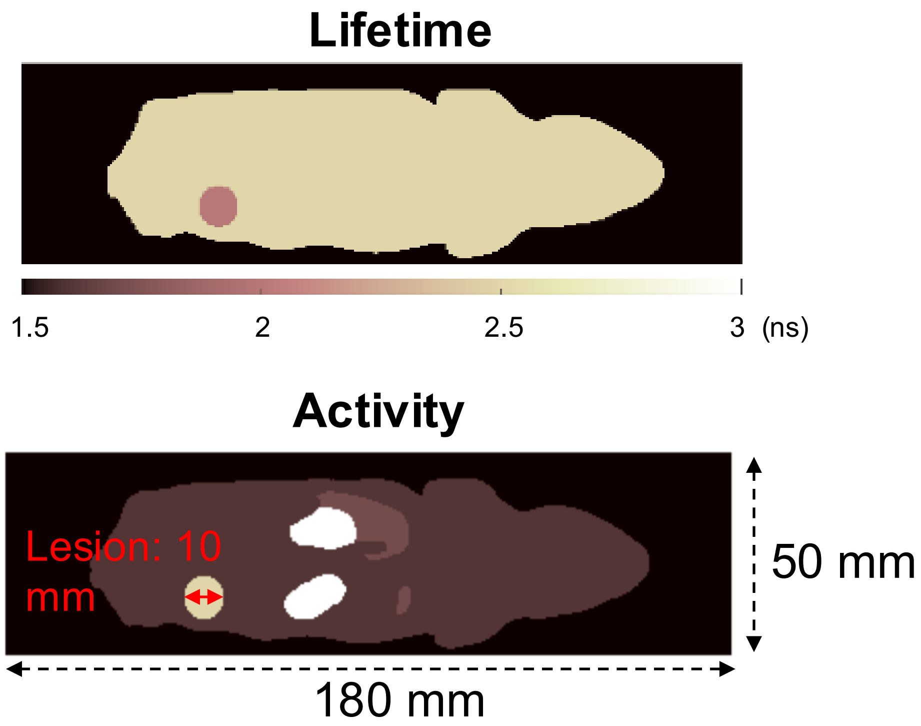
Lesion	Liver	Kidneys	Body background
10	2	15	1

Photon travel time correction

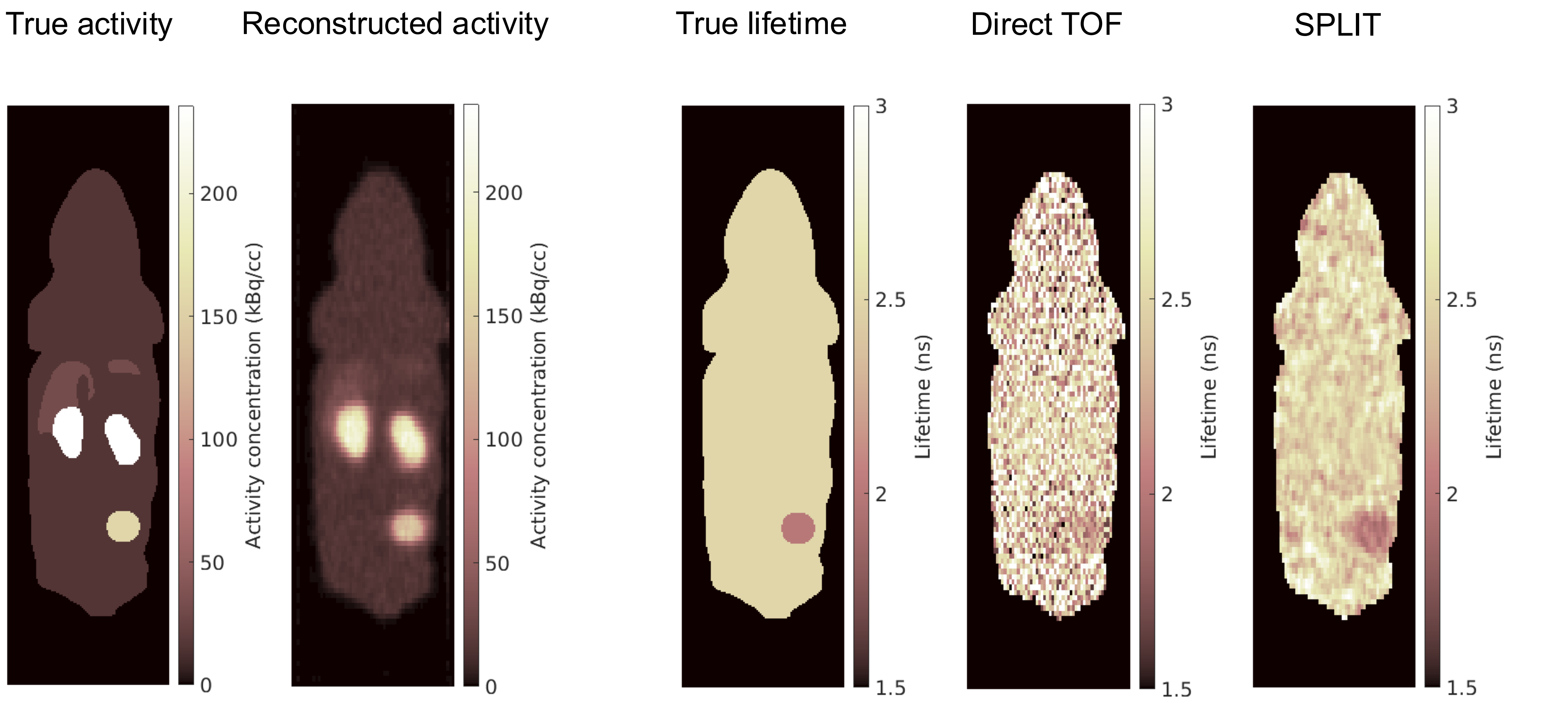
- Compensate for different distances photons travel before being detected

Lifetime

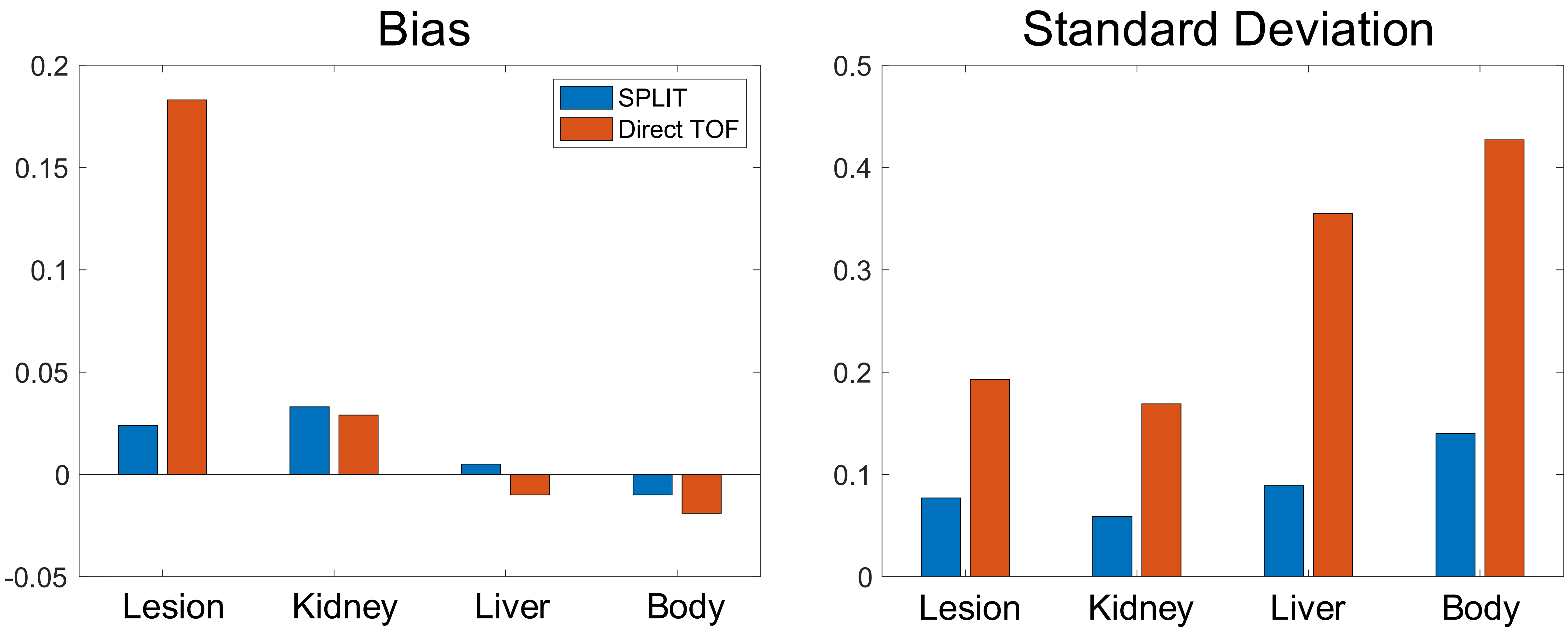
- 30% o-Ps: 2.0 ns for lesion
  2.5 ns for normal tissue
- 10% p-Ps: constant 0.125 ns
- 60% direct annihilation: constant 0.4 ns



Reconstructed Images

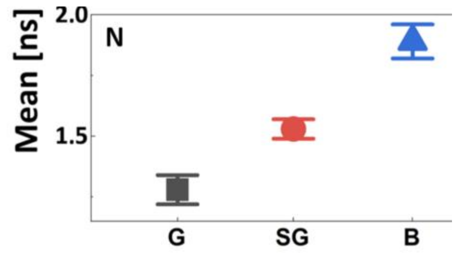


ROI Bias and Standard Deviation



SPLIT has much lower bias in the lesion due to higher resolution and lower noise

Faster Method: SIMPLE (Statistical Image Reconstruction of Positron Lifetime via Time-Weighting)



Moskal et al. (*2024*)

The SIMPLE method reconstructs average lifetime

$$m = E[\tau] = \int_{-\infty}^{\infty} \tau\, p(\tau|\boldsymbol{\lambda}, \boldsymbol{A}) d\tau = \frac{A_o}{\lambda_o} + \frac{A_p}{\lambda_p} + \frac{A_d}{\lambda_d}$$

Positronium lifetime events

Modified OSEM →

Time-weighted image $\boldsymbol{w}$

$$w_j^{(r+1)} = \frac{w_j^{(r)}}{\sum_i H_{ij}} \sum_k \frac{H_{i_k j} \tau_k}{\sum_m H_{i_k m}\, w_m^{(r)}}$$

OSEM →

Activity image $\boldsymbol{x}$

$$x_j^{(r+1)} = \frac{x_j^{(r)}}{\sum_i H_{ij}} \sum_k \frac{H_{i_k j}}{\sum_m H_{i_k m}\, x_m^{(r)}}$$

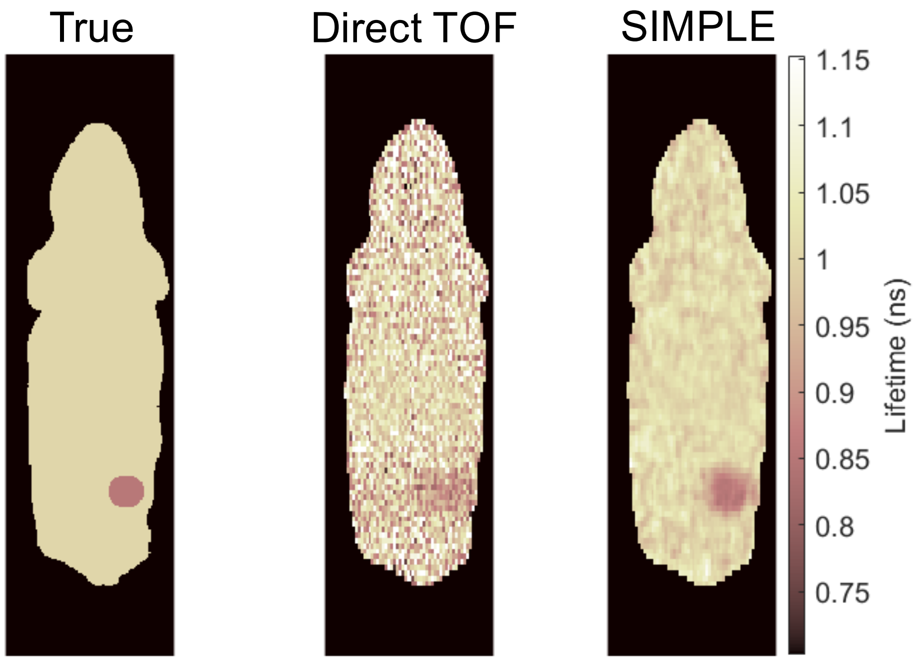
Average lifetime image

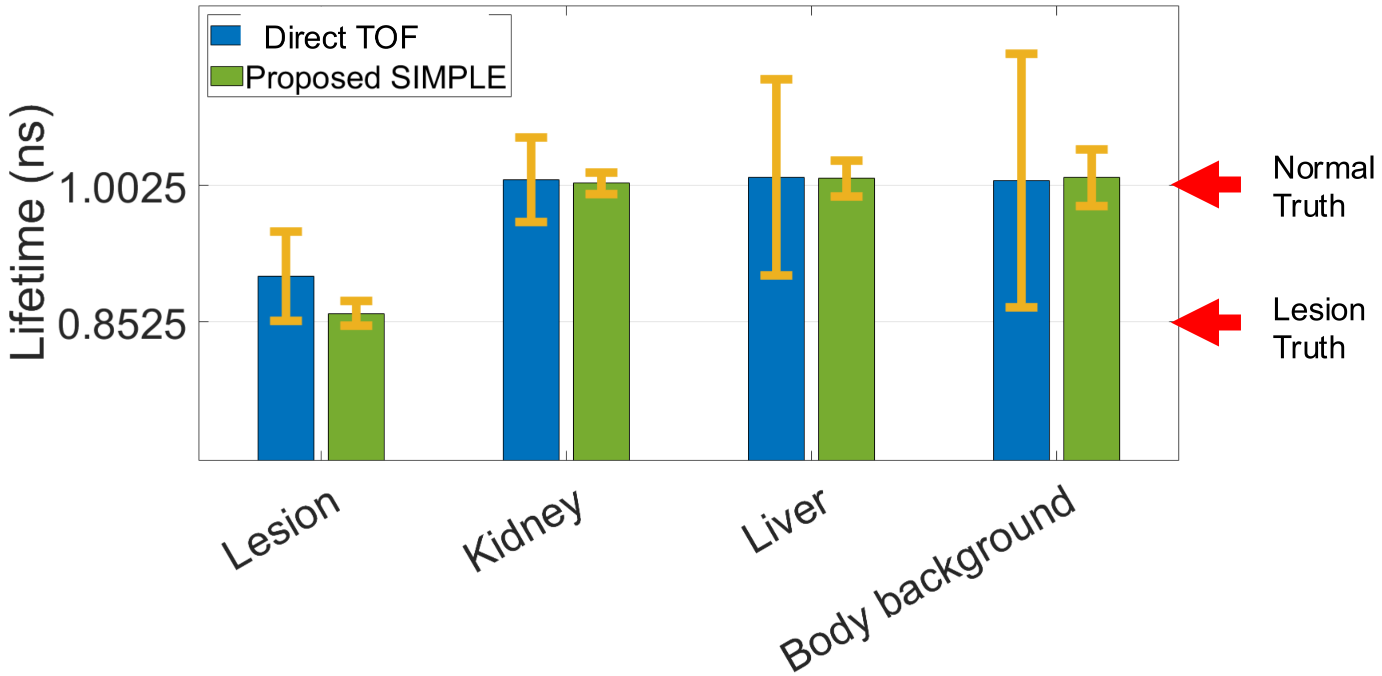
$$\boldsymbol{m} = \frac{\boldsymbol{w}}{\boldsymbol{x}}$$

- Computation cost equivalent to reconstructing two PET images

Huang, …, Qi. Fast High-resolution Lifetime Image Reconstruction for Positron Lifetime Tomography. *Communications Physics*, 2025.

Reconstruction Results





Lifetimes in lesion, kidney, liver and body background

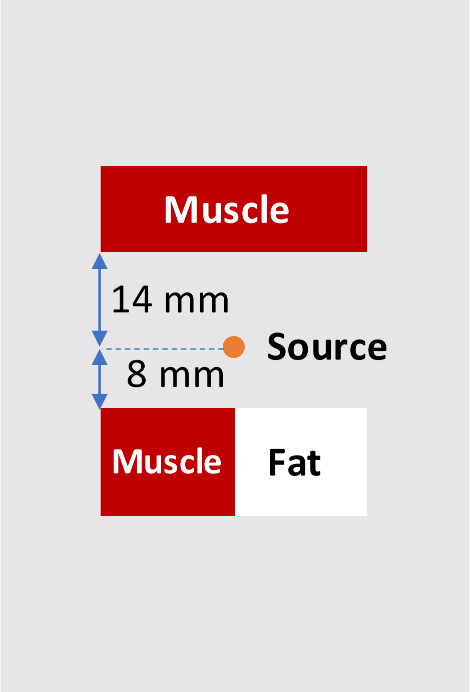
- SIMPLE results in much lower bias in the lesion due to higher resolution and lower variance than direct TOF

Ex vivo Bovine Tissue Data

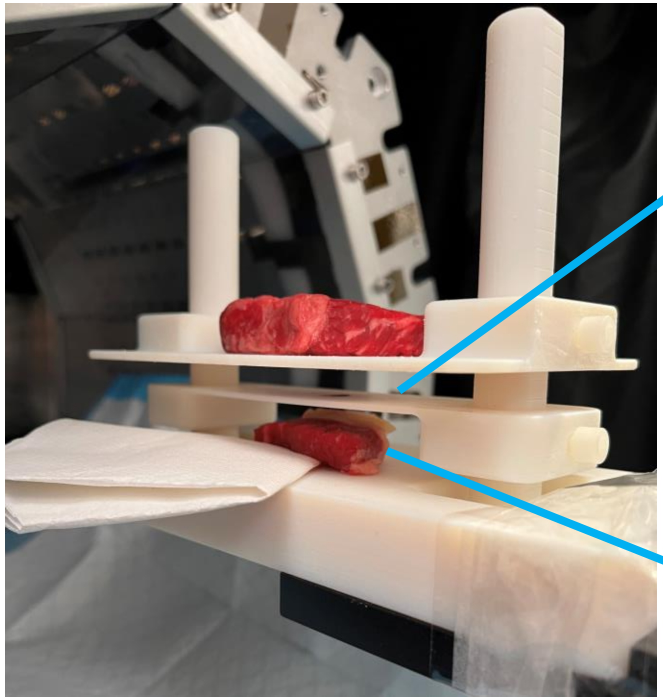


Dr. Amir Goldan Xinjie Zeng Zipai Wang
Cornell Univ.

- Irradiating tissue surface with positrons
- Prism-PET prototype scanner:
  - 25.5 mm axial FOV
- 3.7 MBq ^{22}Na source
- 4 M triple coincidences in 13 hours

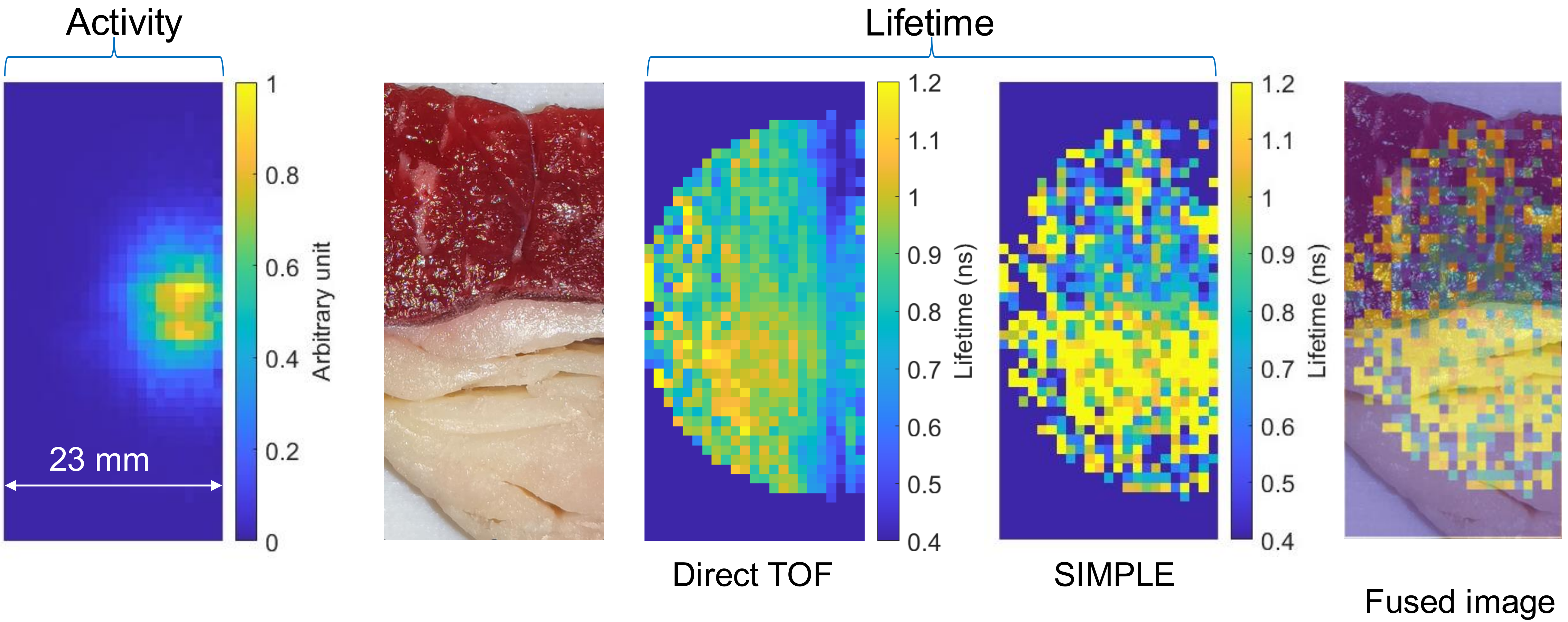


Geometry



The setup

Reconstructed Lifetime Images



- The lifetime image reconstructed by the SIMPLE method shows clear contrast between fat and muscle

Huang et al, Fast High-resolution Lifetime Image Reconstruction for Positron Lifetime Tomography. *Communications Physics.*

Extension to SIMPLE-Moment

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o-Ps lifetime can be recovered by using higher-order moments of lifetime

The n^{th} moment of the time measurement

$$m^n = E[\tau^n] = \int_{-\infty}^{\infty} \tau^n \, p(\tau | A_l, \lambda_l, l \in \{o,p,d\}) d\tau$$

Density of time measurements

$$p(\tau | A_l, \lambda_l, l \in \{o,p,d\}) = g(\tau) * \sum_{l \in \{o,p,d\}} A_l \lambda_l \exp(-\lambda_l \tau) \, u(\tau)$$

$$\Rightarrow \quad m^n = \sum_{s=0}^{n} \binom{n}{s} \mu_{n-s} G_s$$

- $\mu_k = E_{g(\tau)}[\tau^k]$ is the k^{th} moment of normal distribution $g(\tau)$ -- known
- $G_k = \sum_{l \in \{o,p,d\}} k! \frac{A_l}{\lambda_l^k}$ is k^{th} moment of exponential distribution -- contains unknowns

Huang and Qi, High-resolution positronium lifetime tomography by the method of moments, PMB, 2024

Moment Image Reconstruction

We extended the SIMPLE method to reconstruct higher-order moment lifetime images

Positronium lifetime events

Modified OSEM →

n^{th} moment-weighted image

$$w_j^{(r+1)} = \frac{w_j^{(r)}}{\sum_i H_{ij}} \sum_k \frac{H_{i_k j} \tau_k^n}{\sum_m H_{i_k m} w_m^{(r)}}$$

OSEM →

Activity image $\boldsymbol{x}$

$$x_j^{(r+1)} = \frac{x_j^{(r)}}{\sum_i H_{ij}} \sum_k \frac{H_{i_k j}}{\sum_m H_{i_k m} x_m^{(r)}}$$

n^{th} moment lifetime image $\boldsymbol{m}^n = \frac{\boldsymbol{w}}{\boldsymbol{x}}$

From Moments to o-Ps Lifetime

Reconstruct 1st and 2nd moment images m^1, m^2 ⇒

$$\begin{cases} G_1 = m^1 - \mu_1 \\ G_2 = (m^2 - \mu_2 - 2\mu_1 G_1) \end{cases}$$

⇒

$$\begin{cases} \lambda_o = \frac{-b+\sqrt{b^2-4ac}}{2a} \\ A_o = \frac{G_1 - \lambda_d^{-1}}{\lambda_o^{-1} + \frac{1}{3}\lambda_p^{-1} - \frac{4}{3}\lambda_d^{-1}} \end{cases}$$

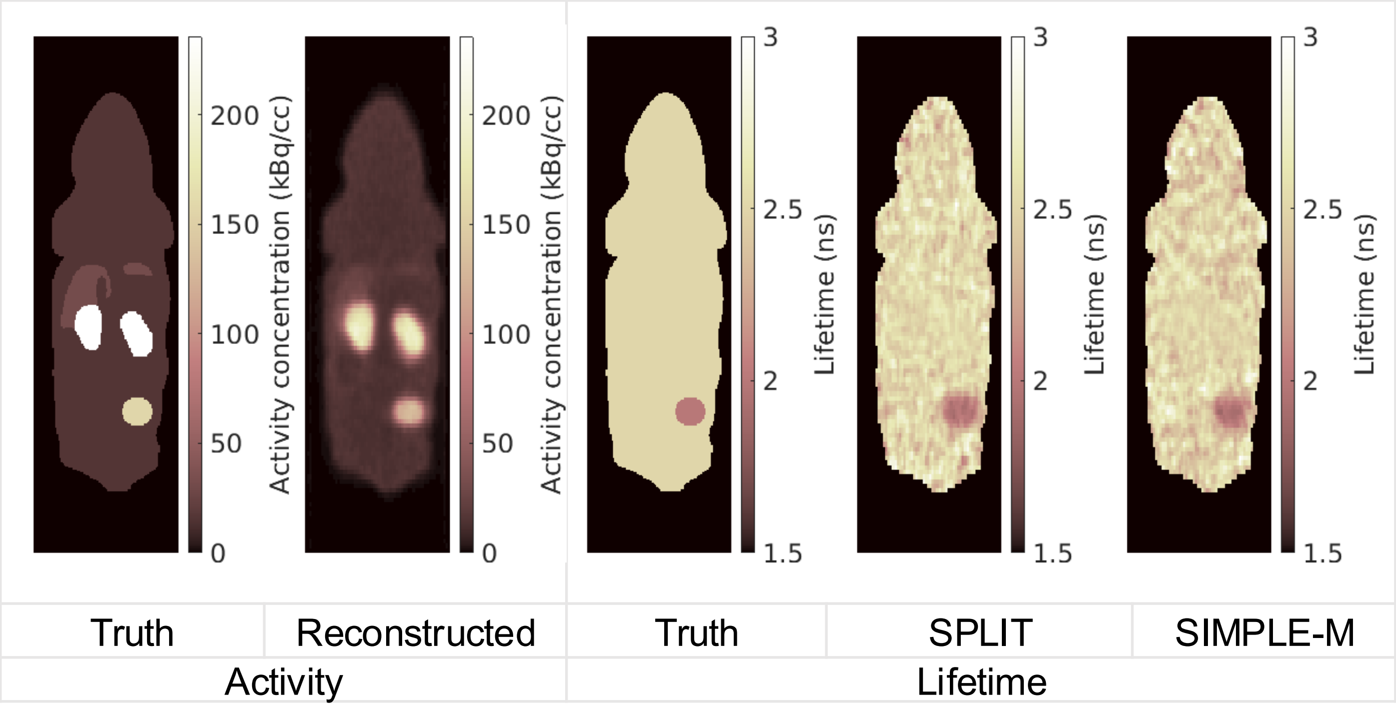
where

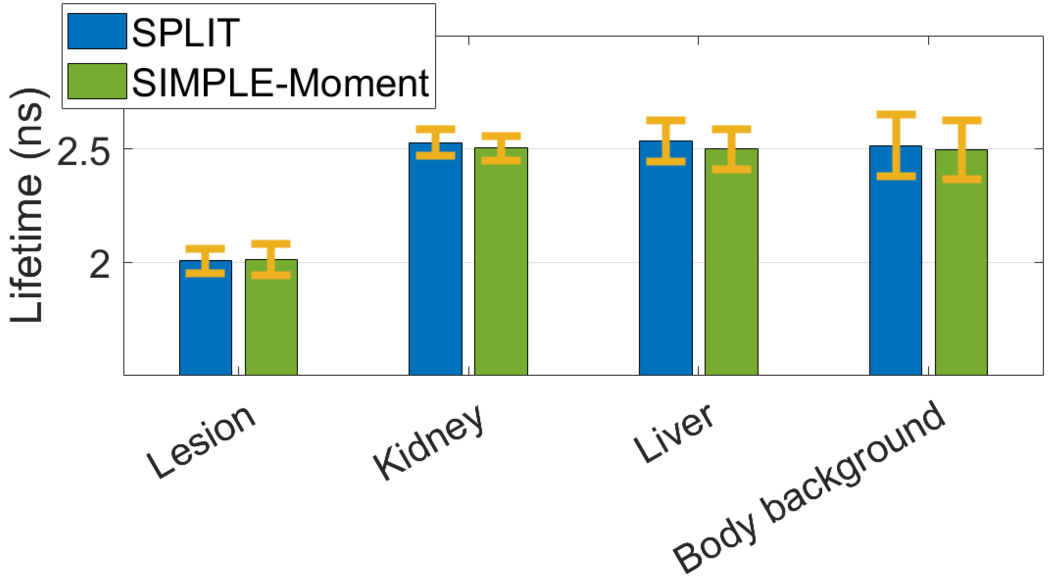
$$\begin{cases} a = G_0\lambda_d - G_1\lambda_d^2 - G_0\lambda_p + G_2\lambda_p\lambda_d^2 + 4G_1\lambda_p^2 - 4G_2\lambda_p^2\lambda_d \\ b = -3G_0\lambda_p^2 + 3G_2\lambda_p^2\lambda_d^2 \\ c = 3G_0\lambda_p^2\lambda_d - 3G_1\lambda_p^2\lambda_d^2 \end{cases}$$

- Assuming
  (1) p-Ps and direction annihilation lifetimes (i.e., λ_p and λ_d) are known
  (2) $A_o : A_p = 3:1$

Huang and Qi, High-resolution positronium lifetime tomography by the method of moments, PMB, 2024

Lifetime Images

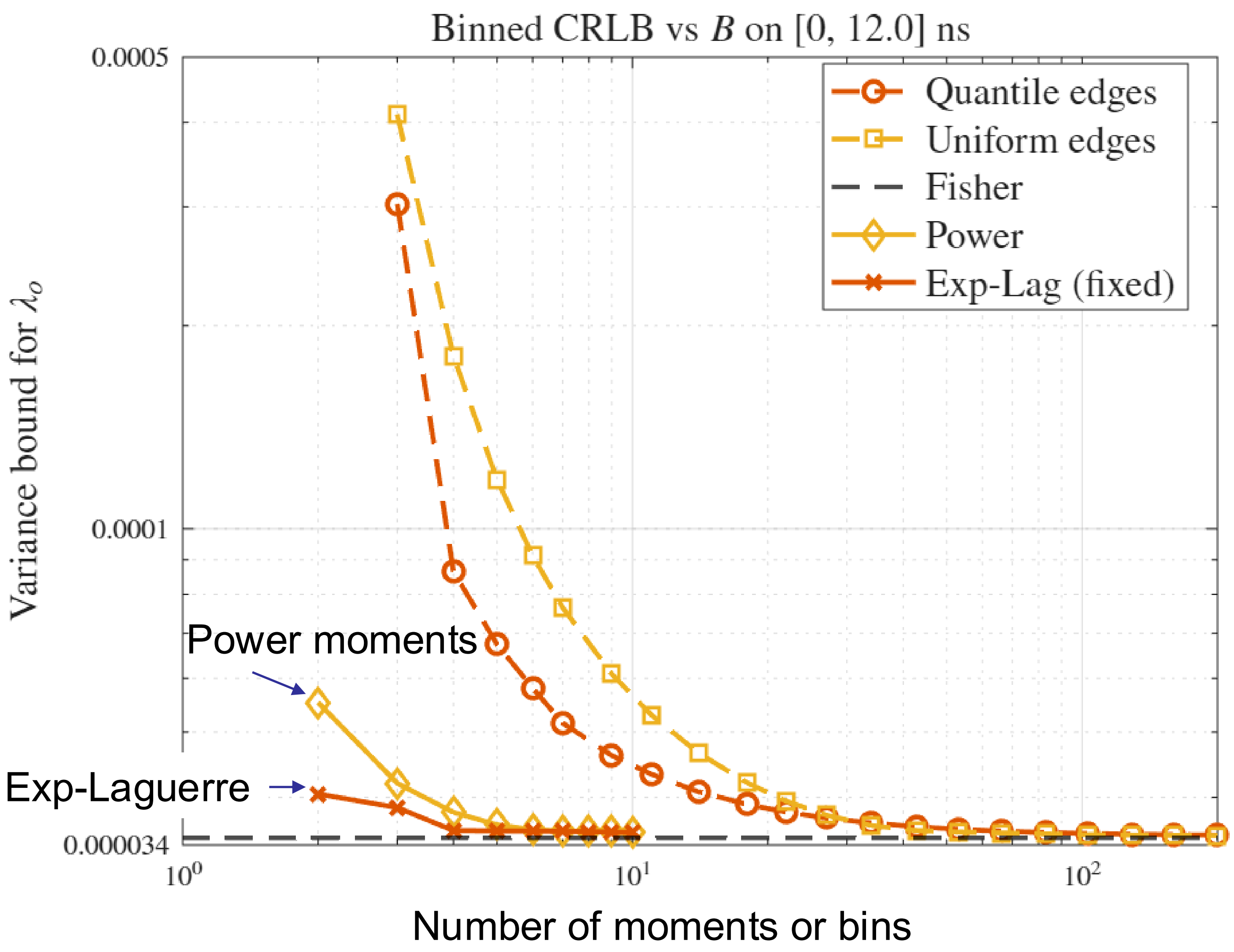




Average lifetime values in ROIs

- Comparable performance as SPLIT

CRLB of $\hat{\lambda}_o$ vs. Order of Moments

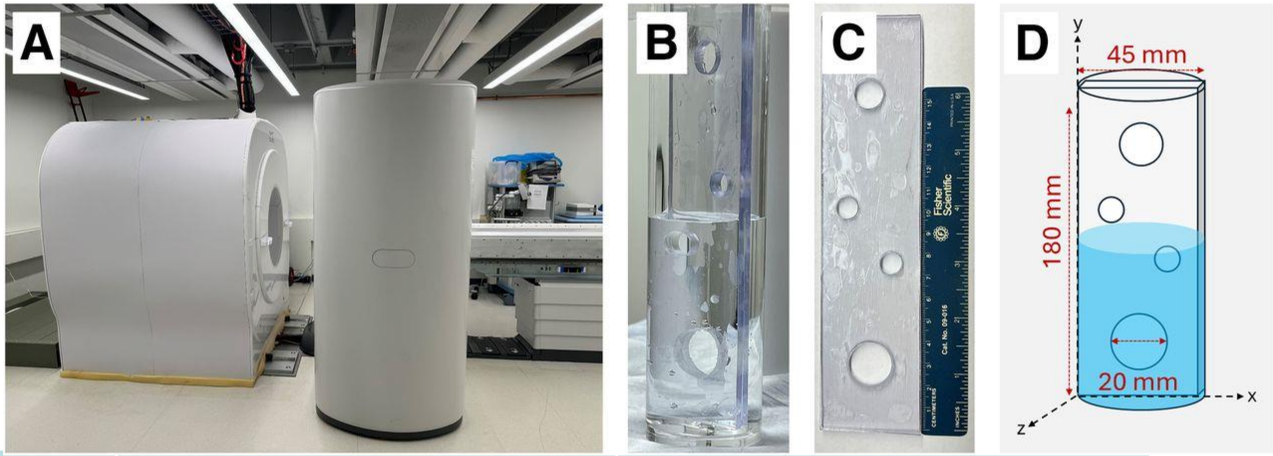


- Variance can be further reduced by using
  - >2nd order moments
  - exponentially weighted Laguerre moments
  - but closed form solution is no longer available.

Feasibility of PLI in Clinical Setting

PennPET Explorer

- 1.4-m axial FOV
- TOF resolution: 250 ps
- Spatial resolution: 3.8mm(t)x4.2mm(a)



Positronium lifetime imaging

- Three isotopes: ^{82}Rb, ^{68}Ga, and ^{44}Sc

	^{82}Rb	^{68}Ga	^{44}Sc
Half-life	1.25 mins	68 mins	4.04 hours
Prompt gamma energy (keV)	777	1077	1157
Fraction of $\beta^+ + \gamma$	13.0%	1.2%	94.3%

- A phantom with polycarbonate slab in solution to create lifetime contrast

Energy Spectrum and Lifetime Spectrum

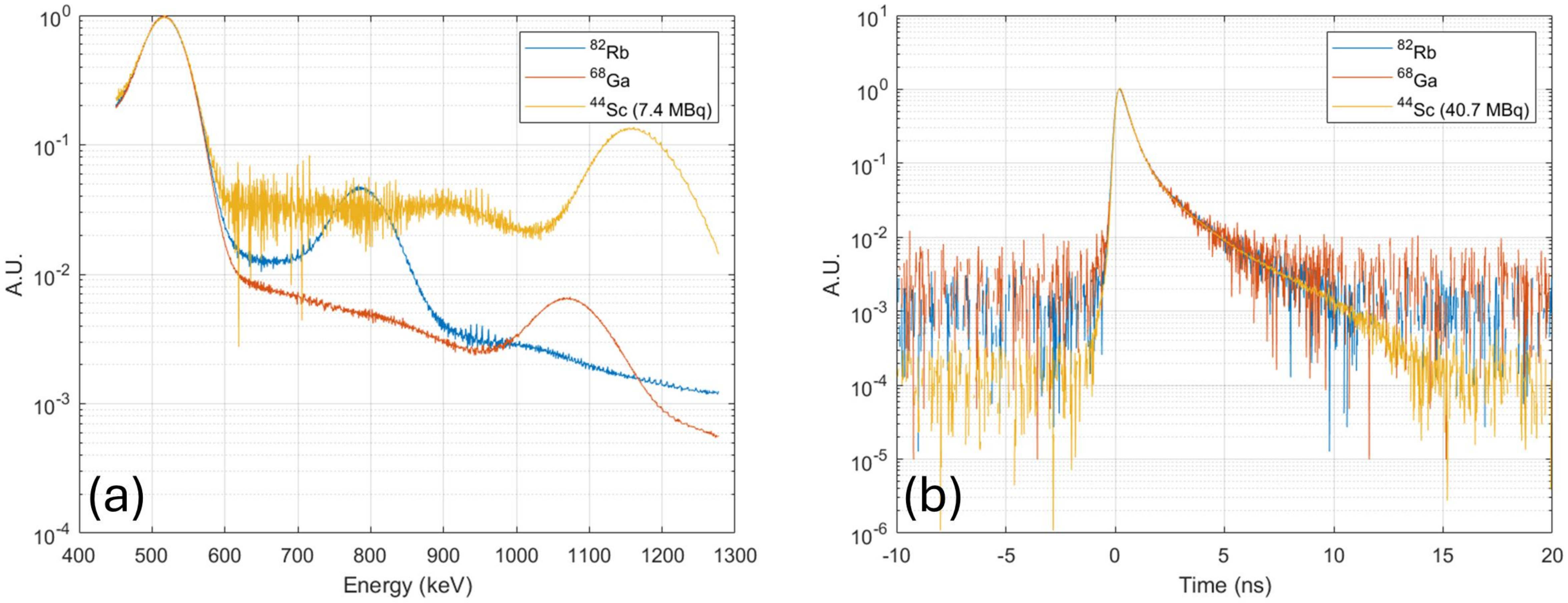
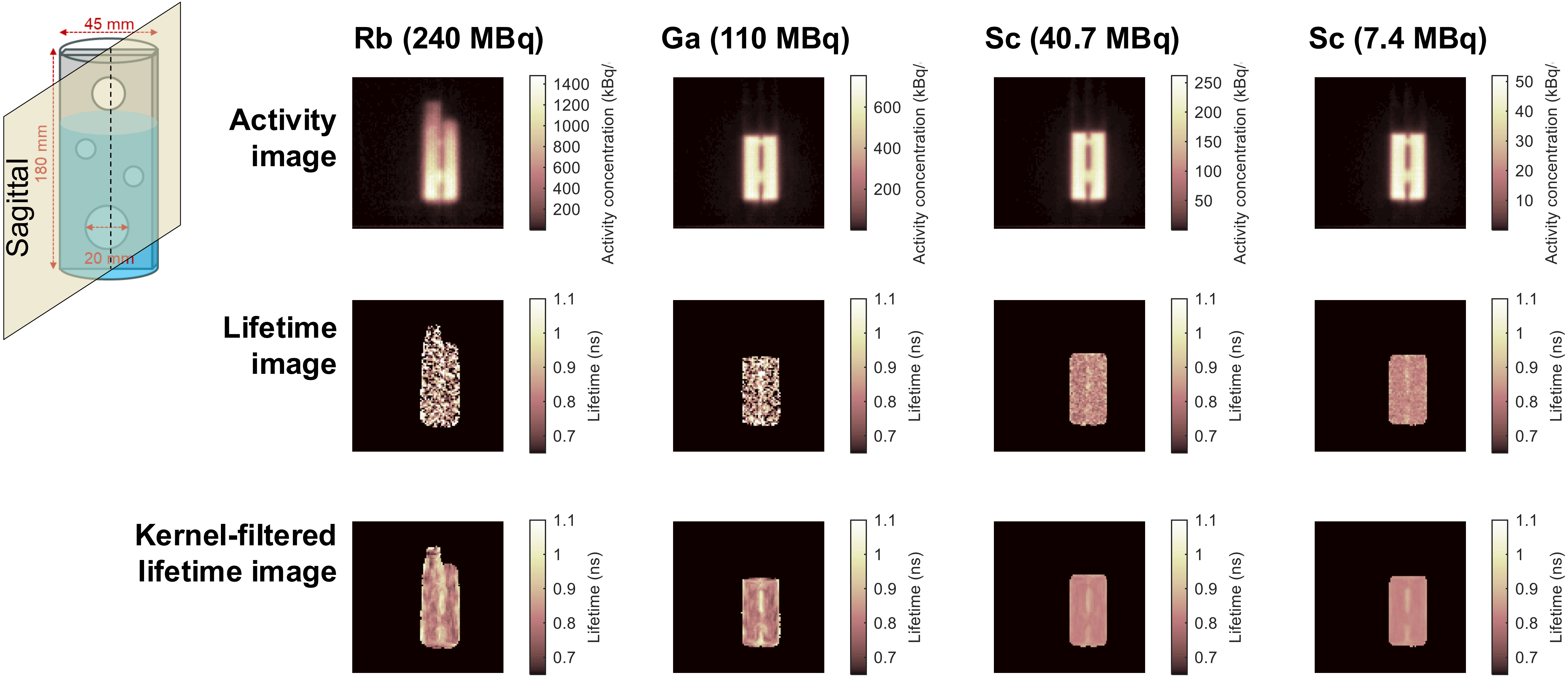


Photo peaks of 511-keV photons and prompt gammas are clearly identified.

Reconstruction Results



Measured PLT spatial resolution

- 3.7±1.8 mm radial
- 3.9±0.4 mm axial

Huang, …, Qi. High-Resolution Positronium Lifetime Tomography at Clinical Activity Levels on the PennPET Explorer. Journal of Nuclear Medicine 2025, jnumed.125.270130.

Summary

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- We have developed high-resolution image reconstruction methods for positronium lifetime tomography (PLT).
- We have demonstrated high-resolution PLT using ^{82}Rb, ^{68}Ga, and ^{44}Sc at activity levels relevant to human imaging.
- **Simultaneous PET/PLT** has the potential of assessing disease-specific tracer uptake and tissue microenvironment in one scan.
- AI can be employed to reduce image noise and to develop fast and efficient reconstruction methods.

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Gerard Ariño-Estrada
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PEMI Team

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http://qilab.bme.ucdavis.edu