ppc@12.5

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# Dissolved oxygen sensing by positronium for PET

Kengo Shibuya*, H. Saito
Univ. of Tokyo, Japan

F. Nishikido, M. Takahashi, T. Yamaya
NIRS-QST, Japan

東京大学
THE UNIVERSITY OF TOKYO

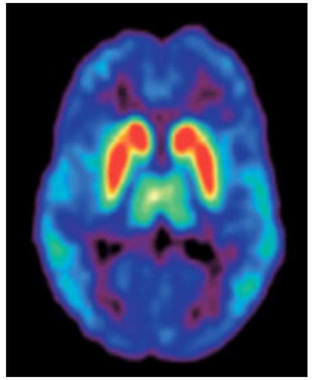
QST 量子科学技術研究開発機構
National Institutes for Quantum and Radiological Science and Technology

# Positron Emitters in PET

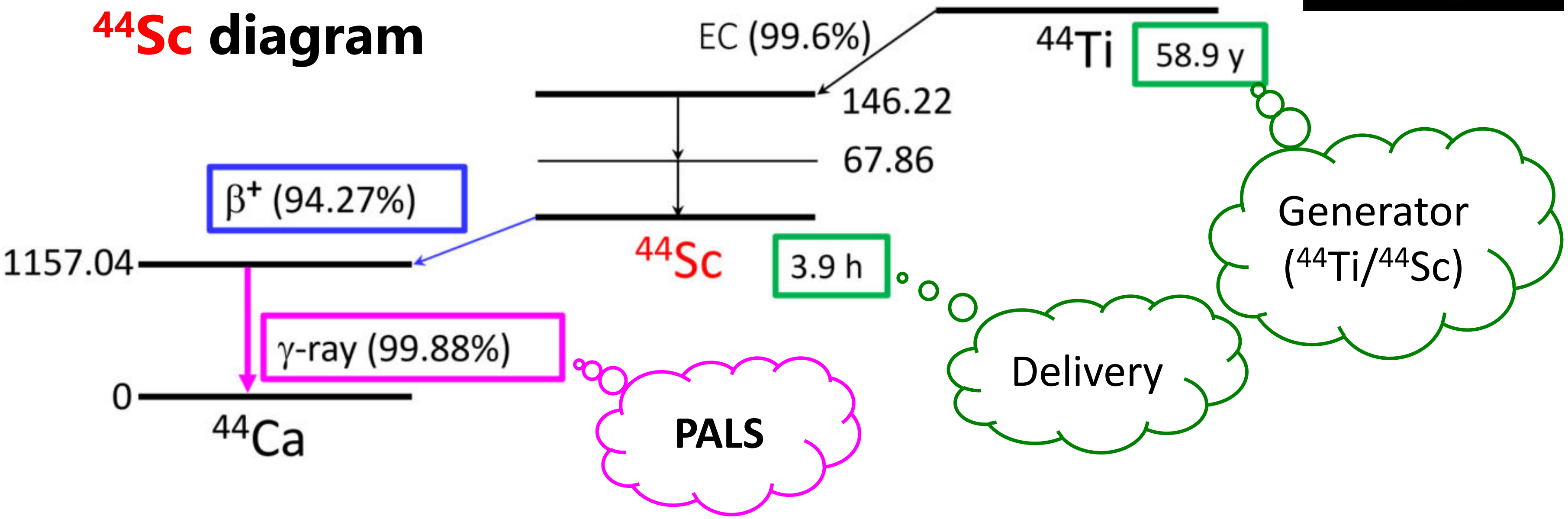
- Conventional PET isotopes: $^{11}C$, $^{13}N$, $^{15}O$, $^{18}F$

- Advanced PET isotopes: $^{44}Sc$, $^{64}Cu$, $^{76}Br$, $^{89}Zr$, $^{90}Y$, $^{124}I$, etc.

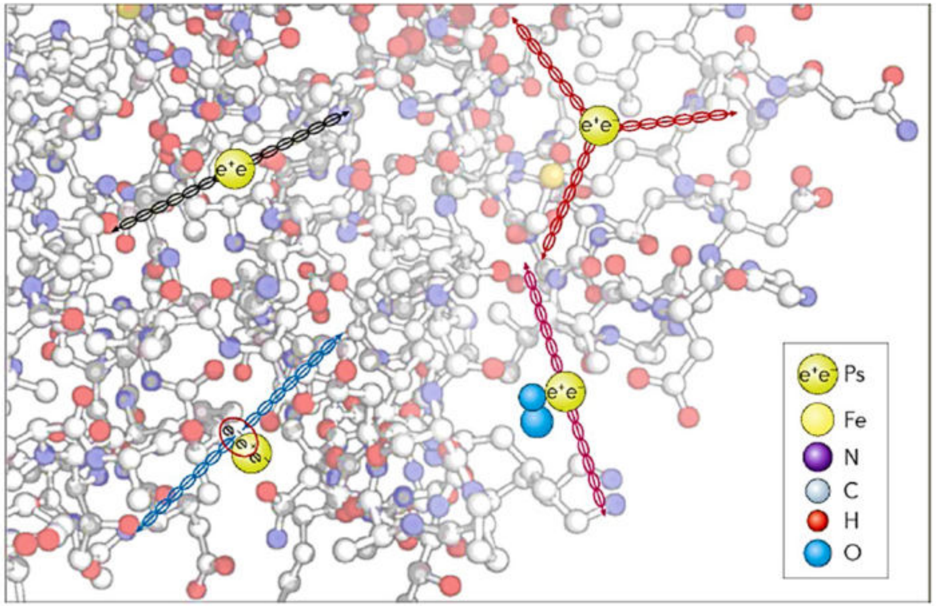
aiming for
  - new tracer
  - multi-modal imaging (PET/MRI, PET/SPECT, ...)
  - radio-theranostics (nuclear imaging + radio-therapy)



**$^{44}Sc$ diagram**



# Positronium Lifetime Imaging (PALS/PET)





[1] P. Moskal *et al*, *Nature Rev. Phys*. **1** (2019) 527.
[2] P. Moskal *et al*, *EJNMMI Phys*. **7** (2020) 44.


Around 30% positron annihilates after forming Ps *in vivo*, and the lifetime depends on

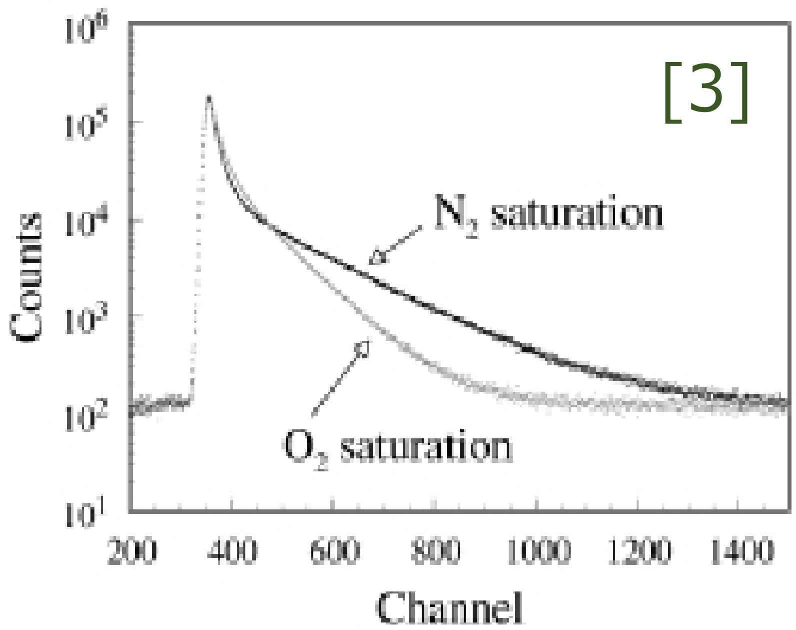
- free volume
- oxygen [This talk.]
- bio-active molecules (radicals)

… possibility as biomarker.

# *o*-Ps Quenching paths

1. Pick-off
2. Electron exchange (unpaired electron)
3. Chemical bonding/trapping ($PsO_2$)
4. ~~Spin conversion (spin-orbit~~)

Liquid experiments must remove $O_2$ gas by bubbling / freeze-pump-thaw.

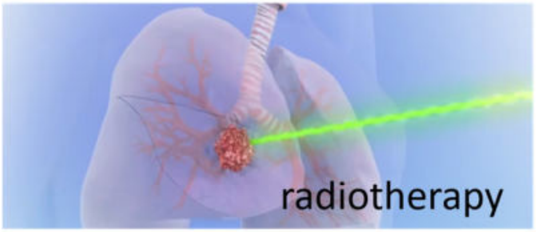



Ps may be used for an $O_2$ sensor.

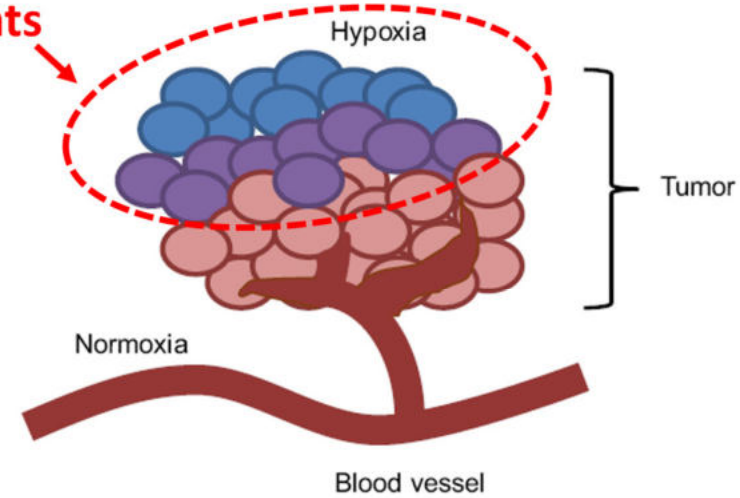

[3] Y. Kino *et al*, *J. Nucl. Radiochem. Sci*. **1**, 63 (2000) 63.

# Motivation: hypoxia sensing

resistant to treatments

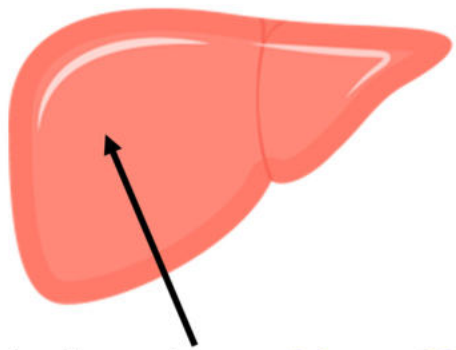




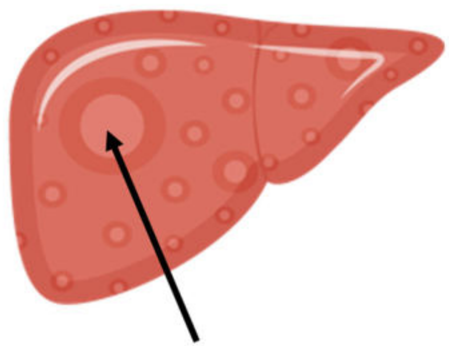



[4] K. Graham, *Int. J. Nanomed.* **13** (2018) 6049.

# $pO_2$ in Liver



Healthy liver tissue: **41 mmHg**

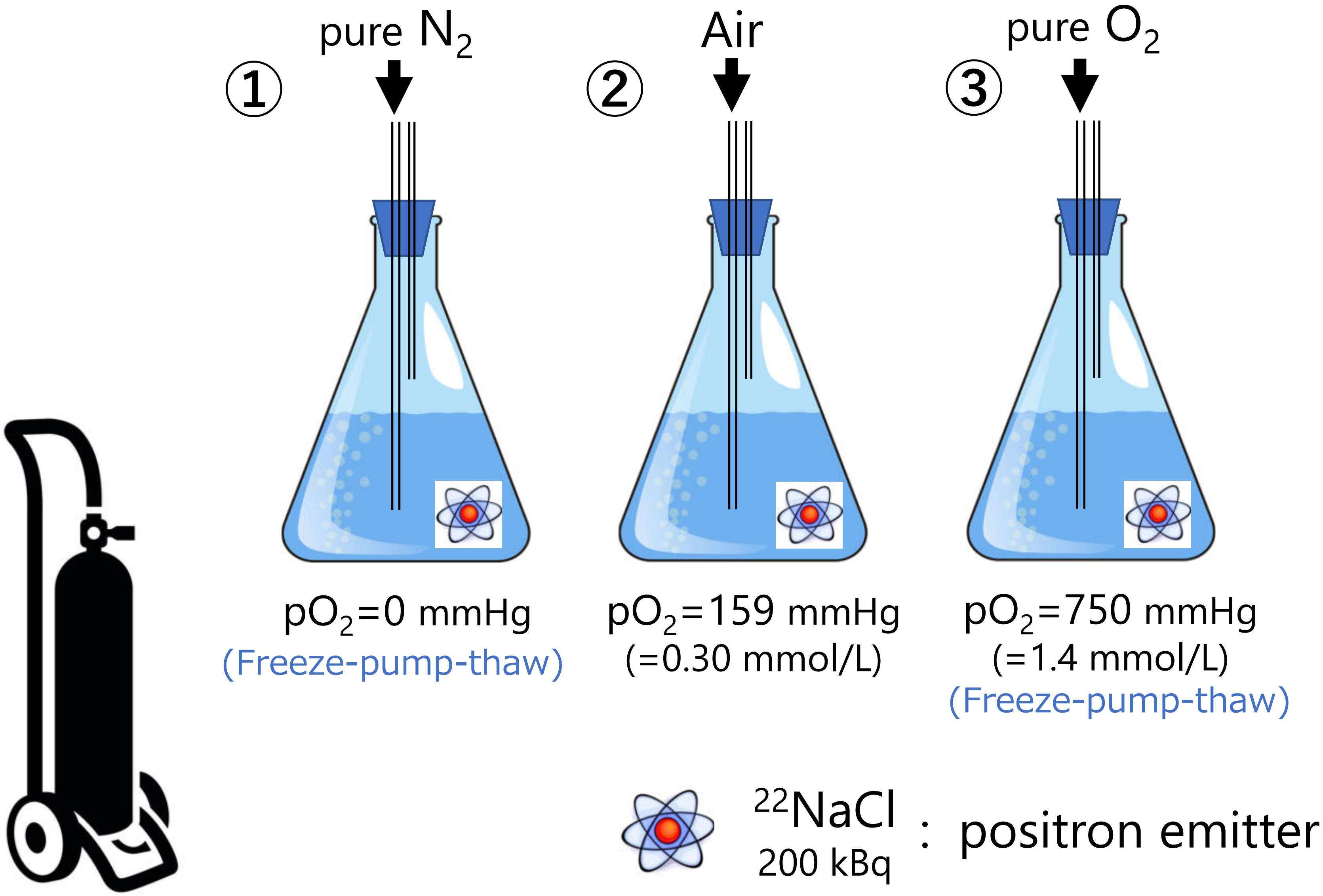


Liver tumor: **6 mmHg**

[5] A. Carreau, *J Cell Mol Med.* **15 (2011)** 1239. [6] P. Vaupel, *Antioxid Redox Signal* **9** (2007) 1221.

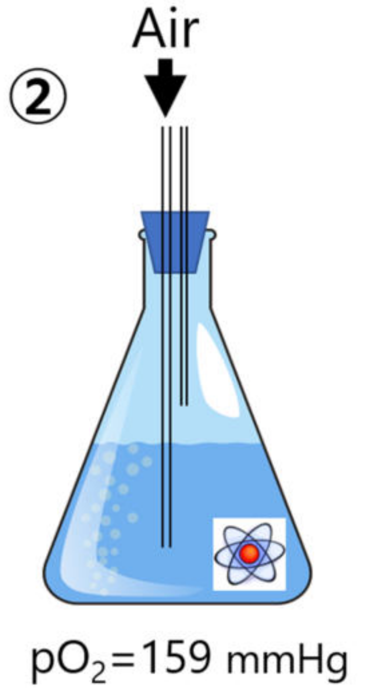
# Measurements and Results

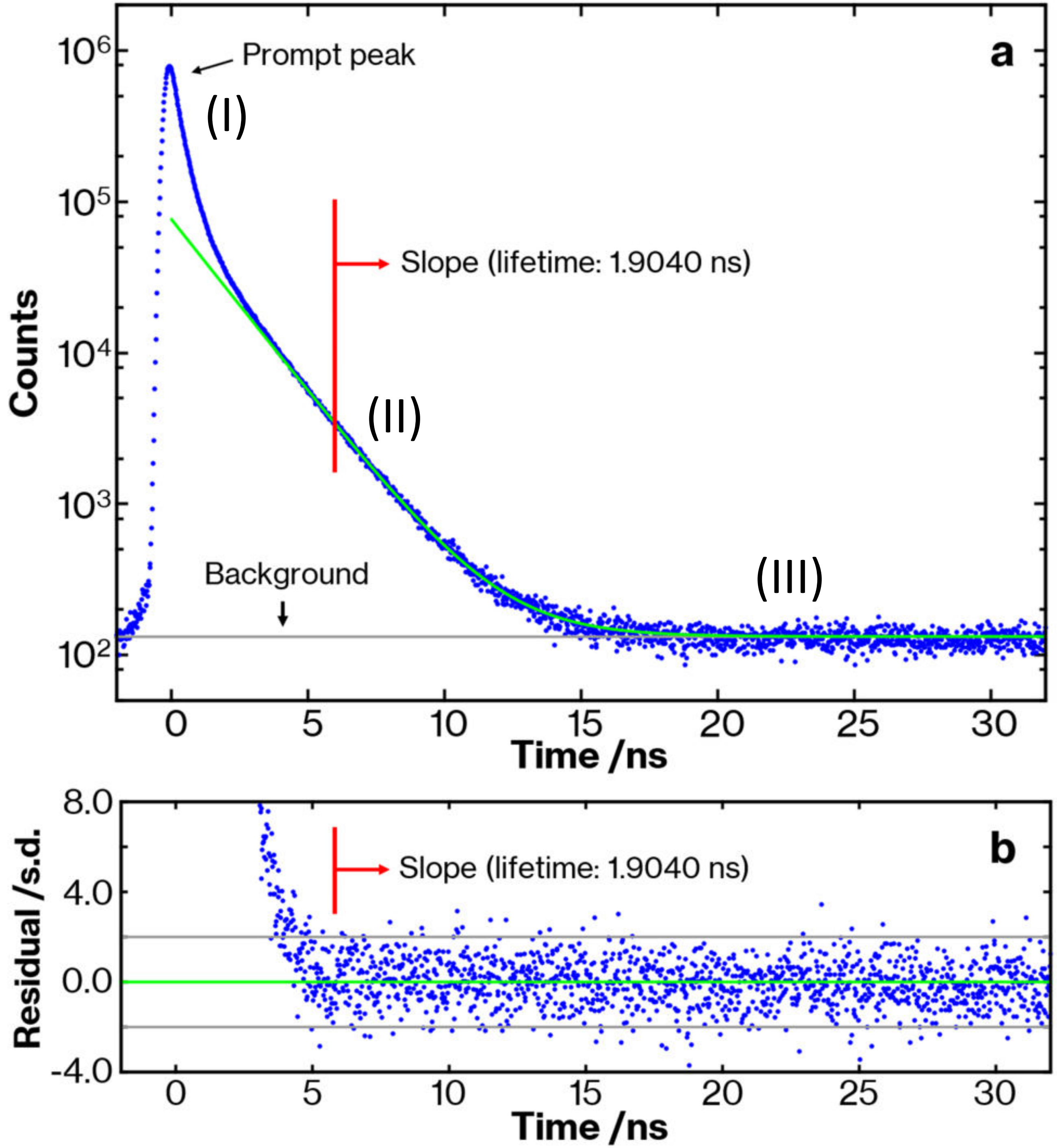
# Samples



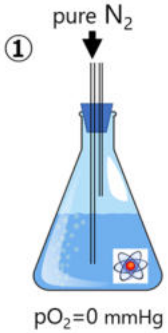
① pure $N_2$
② Air
③ pure $O_2$
$pO_2$=0 mmHg
(Freeze-pump-thaw)
$pO_2$=159 mmHg
(=0.30 mmol/L)
$pO_2$=750 mmHg
(=1.4 mmol/L)
(Freeze-pump-thaw)
$^{22}$NaCl 200 kBq : positron emitter

# Data (Air-saturated)



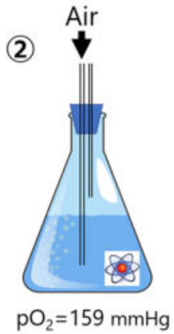



# Results



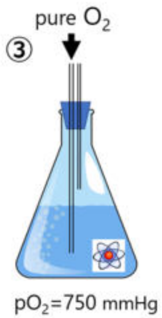

$$\tau_{N_2} = 1.9215(32)\ \text{ns}$$

$$\Rightarrow \lambda_{\text{o-Ps}} + \lambda_{H_2O} + 705.1(7)\,\kappa_{N_2} = \frac{1}{\tau_{N_2}} = 548.3(1.1)\ \mu s^{-1}$$




$$\tau_{Air} = 1.9040(29)\ \text{ns}$$

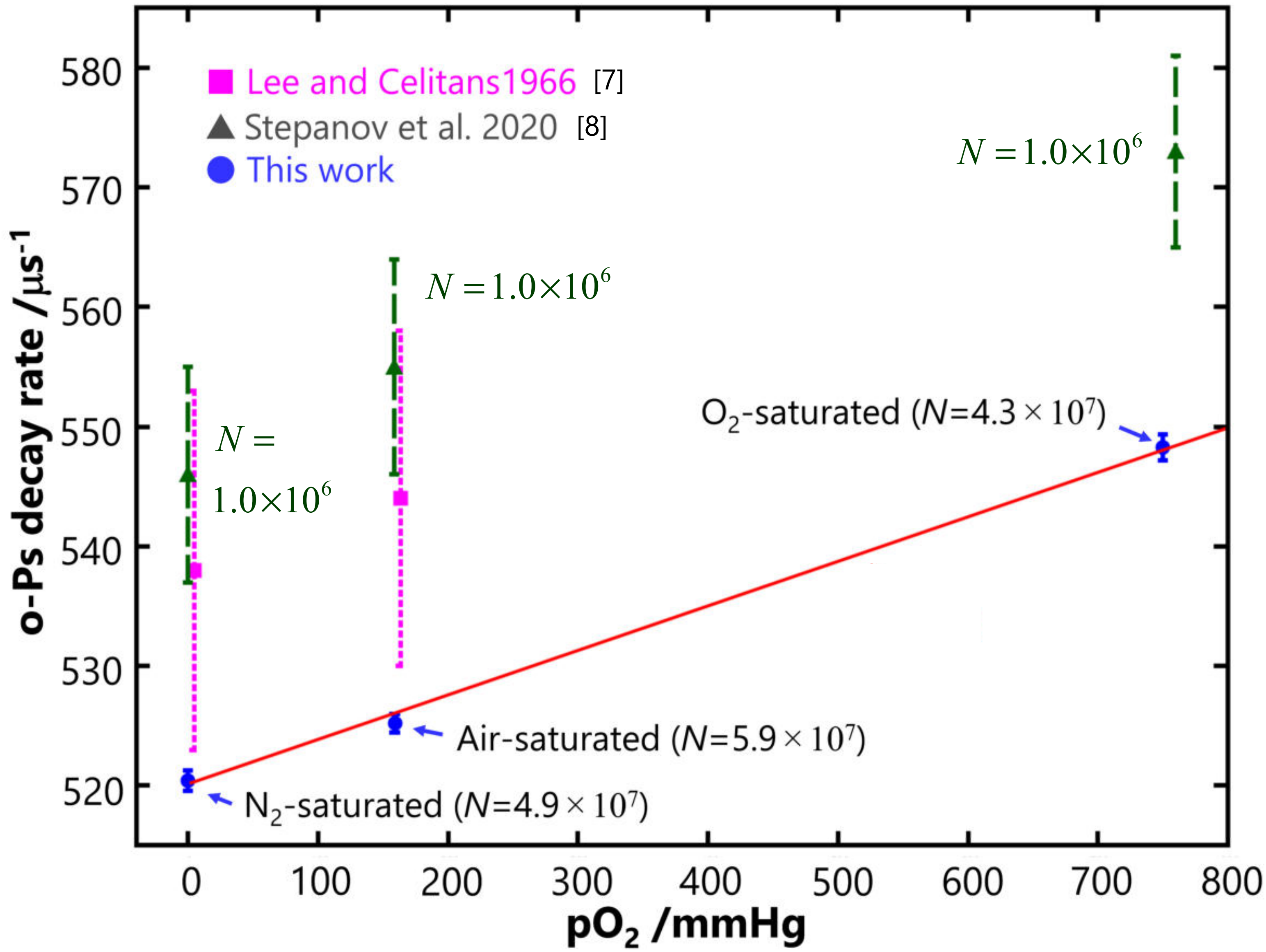
$$\Rightarrow \lambda_{\text{o-Ps}} + \lambda_{H_2O} + 296.0(3)\kappa_{O_2} + 556.1(5)\,\kappa_{N_2} = \frac{1}{\tau_{Air}} = 525.2(8)\ \mu s^{-1}$$




$$\tau_{O_2} = 1.8239(36)$$

$$\Rightarrow \lambda_{\text{o-Ps}} + \lambda_{H_2O} + 705.1(7)\kappa_{O_2} = \frac{1}{\tau_{O_2}} = 548.3(1.1)\ \mu s^{-1}$$

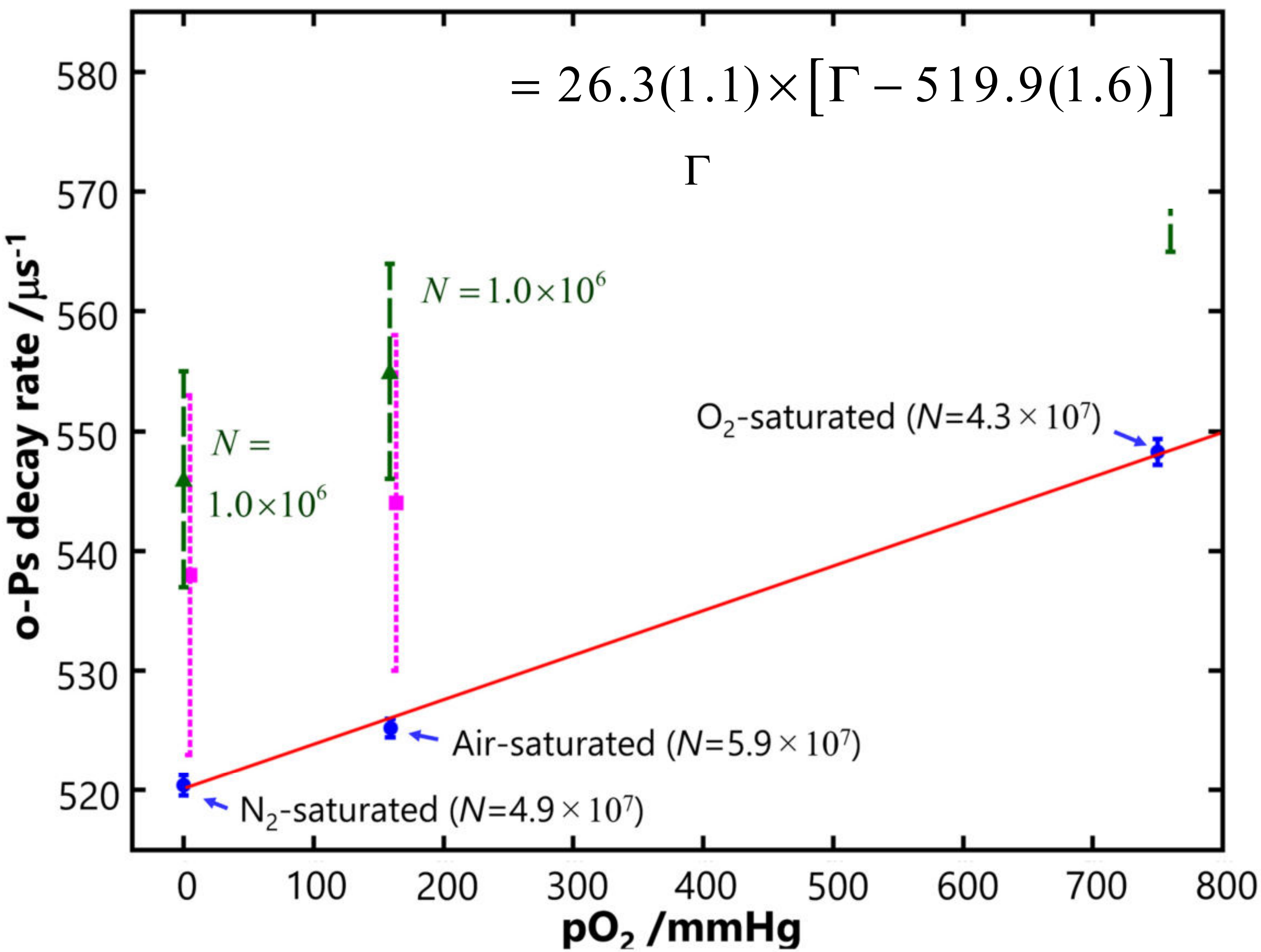
# $pO_2$ vs *o*-Ps Decay rate





[7] J. Lee & G. J. Celitans, *J. Chem. Phys.* **44** (1966) 2506.
[8] P. S. Stepanov et al., *Phys. Chem. Chem. Phys.* **22** (2020) 5123.

# $pO_2$ vs *o*-Ps Decay rate



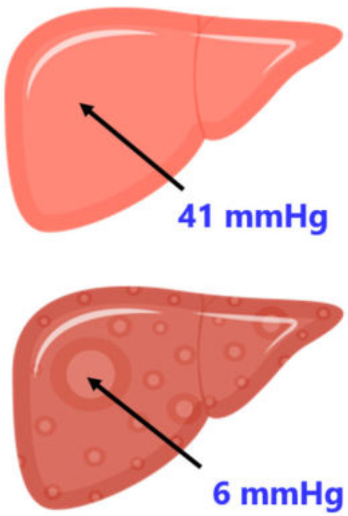


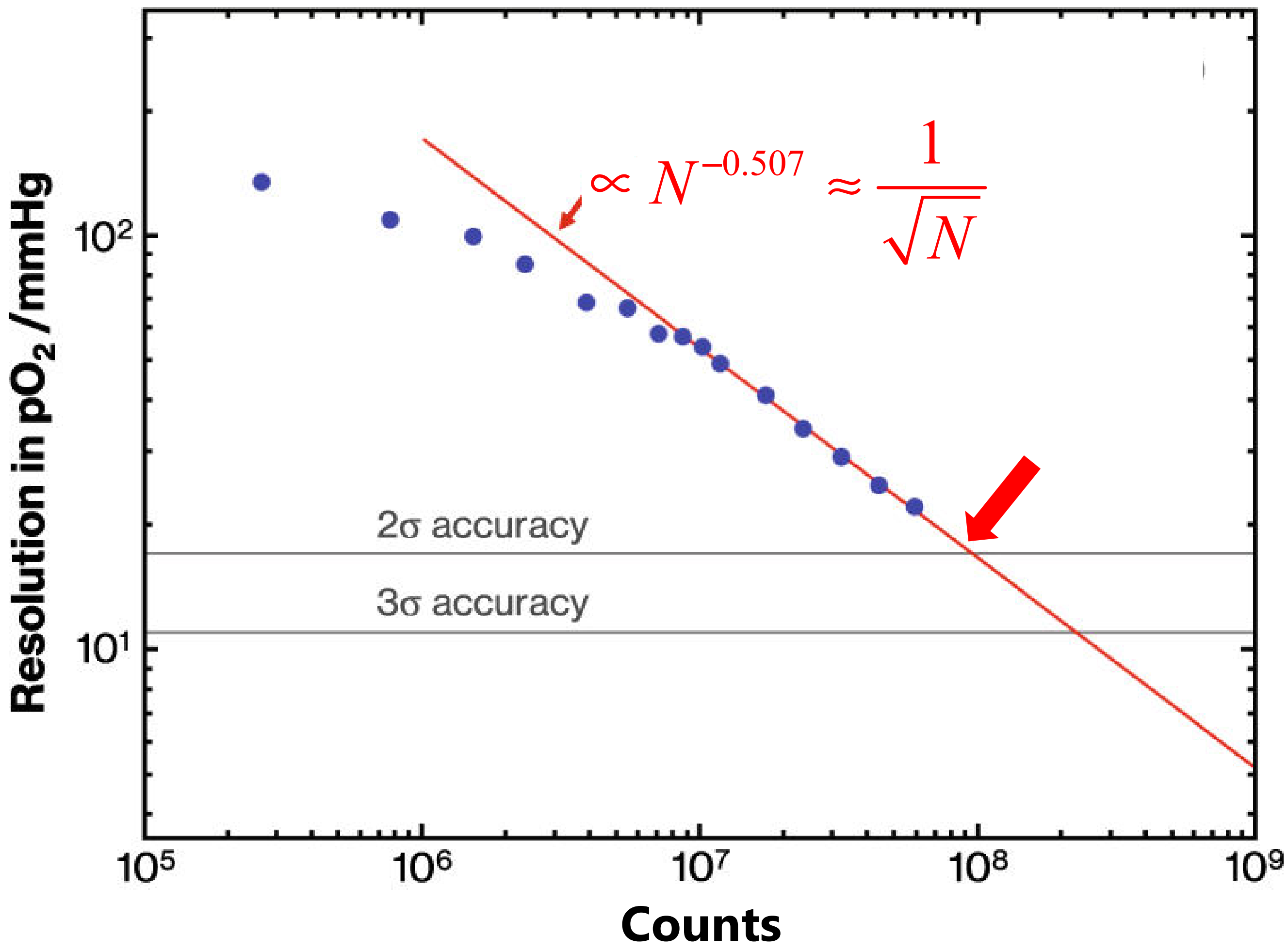
[7] J. Lee & G. J. Celitans, *J. Chem. Phys.* **44** (1966) 2506.

[8] P. S. Stepanov et al., *Phys. Chem. Chem. Phys.* **22** (2020) 5123.

# Counts vs $pO_2$ Resolution

## Resolution



# Discussion

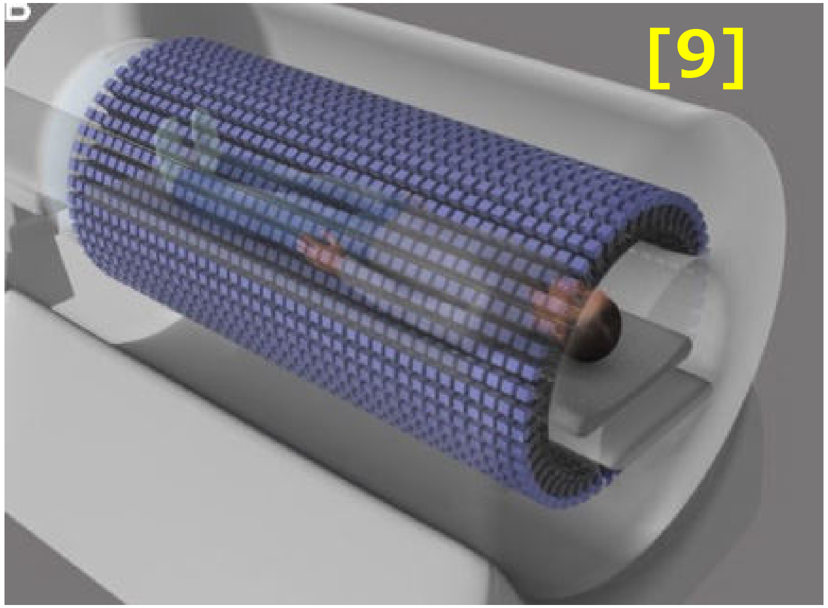
# $10^8$ counts possible?

↑Activity
- this measurement: 200 kBq
- FDG-PET scan: 200 MBq

↑Solid angle
- this: ca 5%
- whole-body scanner: >60%

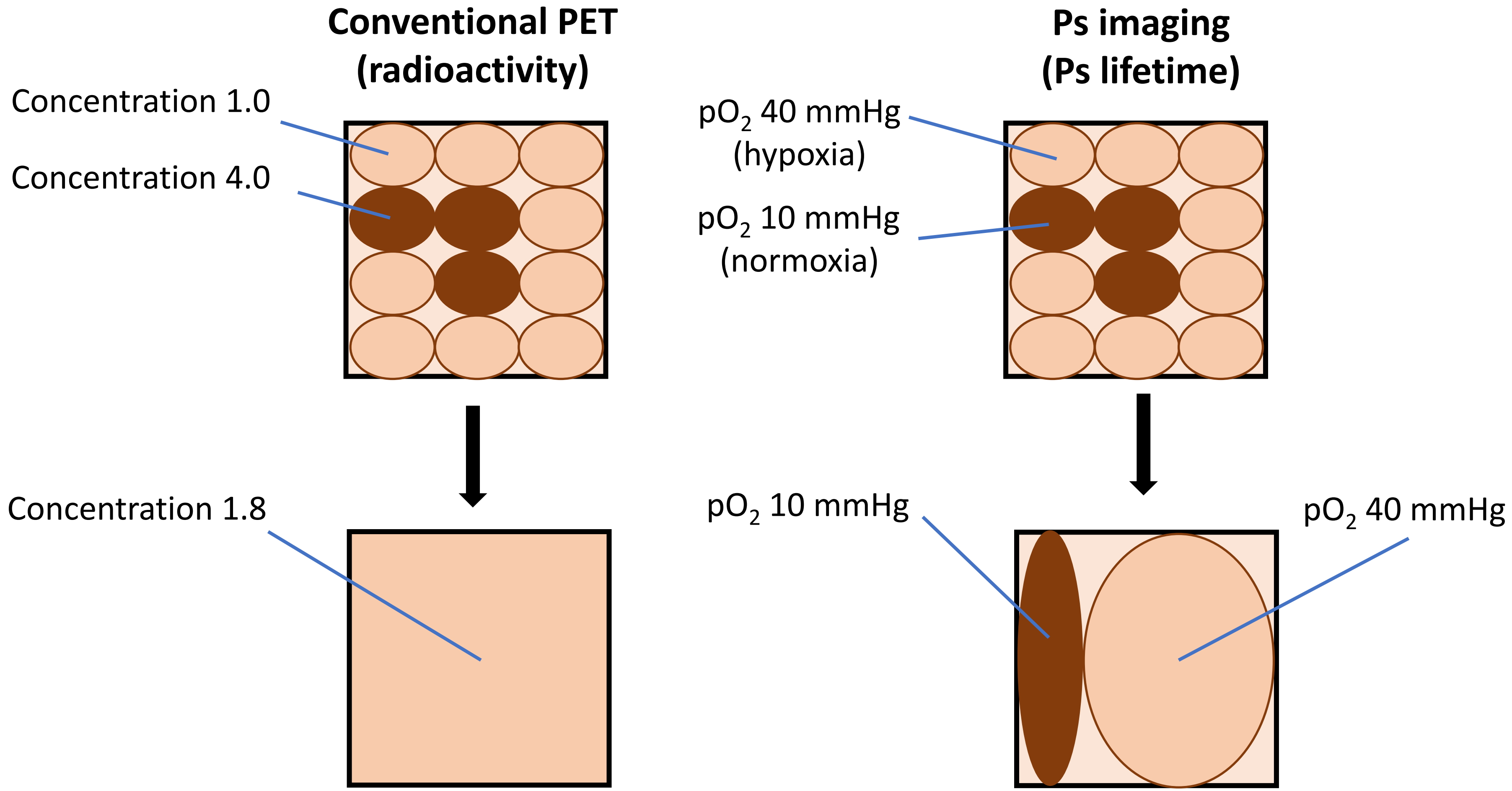
↓Triple coincidence required

↓Within 30 min




[9] S. R. Cherry, et al. *J. Nucl. Med.* vol. **59,** pp. 3–12 (2018).

# Larger voxel available

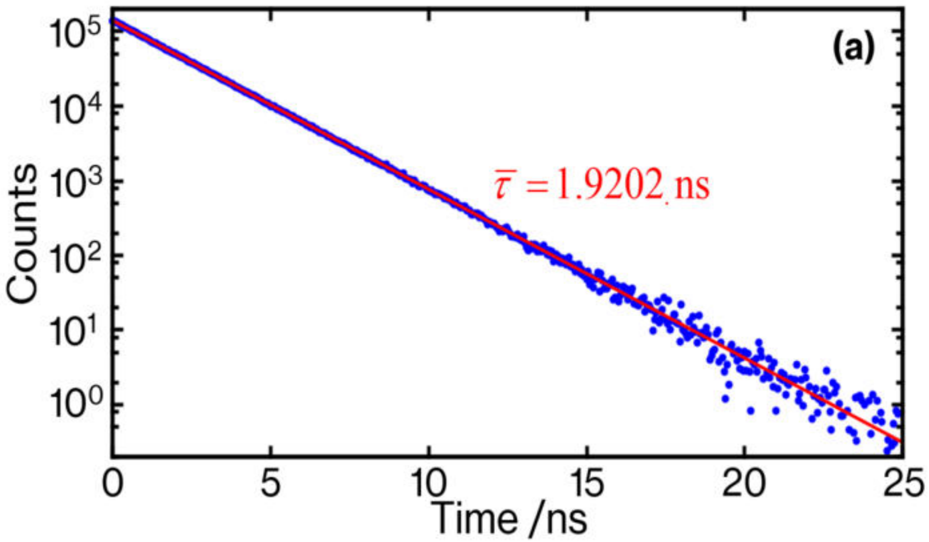



The interior of the voxel is assumed to be uniform, and no information other than the averaged concentration is outputted.

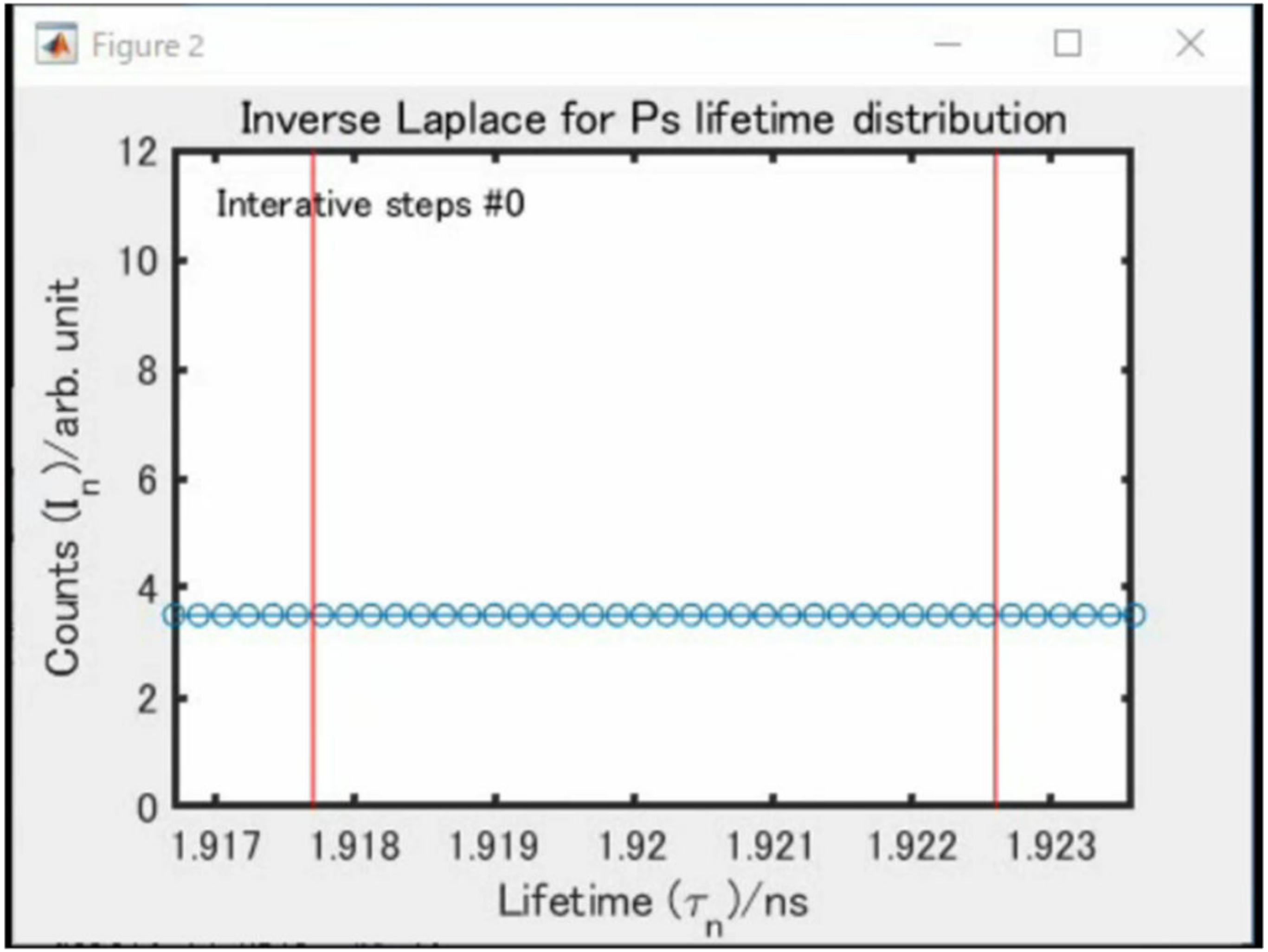
The lifetime components are separatable to output the lifetime and the amount of each component.

# Inverse Laplace transform (CONTIN[10])

$$\begin{cases} F(t) = \exp(-\lambda t) \\ f(x) = {}^{-1}\{F(t)\} = \delta(x-\lambda) \end{cases}$$



# CONTIN (Video)



# Evaluation function

system matrix | solution | data

$$J_0 \equiv \left| \begin{pmatrix} \exp\left(-\frac{t_1}{\tau_1}\right) & \exp\left(-\frac{t_1}{\tau_2}\right) & \cdots & \exp\left(-\frac{t_1}{\tau_n}\right) \\ \exp\left(-\frac{t_2}{\tau_1}\right) & \exp\left(-\frac{t_2}{\tau_2}\right) & \cdots & \exp\left(-\frac{t_2}{\tau_n}\right) \\ \exp\left(-\frac{t_3}{\tau_1}\right) & \exp\left(-\frac{t_3}{\tau_2}\right) & \cdots & \exp\left(-\frac{t_3}{\tau_n}\right) \\ \vdots & \vdots & \ddots & \vdots \\ \exp\left(-\frac{t_\mathrm{m}}{\tau_1}\right) & \exp\left(-\frac{t_\mathrm{m}}{\tau_2}\right) & \cdots & \exp\left(-\frac{t_\mathrm{m}}{\tau_n}\right) \end{pmatrix} \begin{pmatrix} \frac{I_1}{\tau_1} \\ \frac{I_2}{\tau_2} \\ \frac{I_3}{\tau_3} \\ \vdots \\ \frac{I_n}{\tau_n} \end{pmatrix} - \begin{pmatrix} S_n(t_1) - B \\ S_n(t_2) - B \\ S_n(t_3) - B \\ \vdots \\ S_n(t_\mathrm{m}) - B \end{pmatrix} \right|^2$$

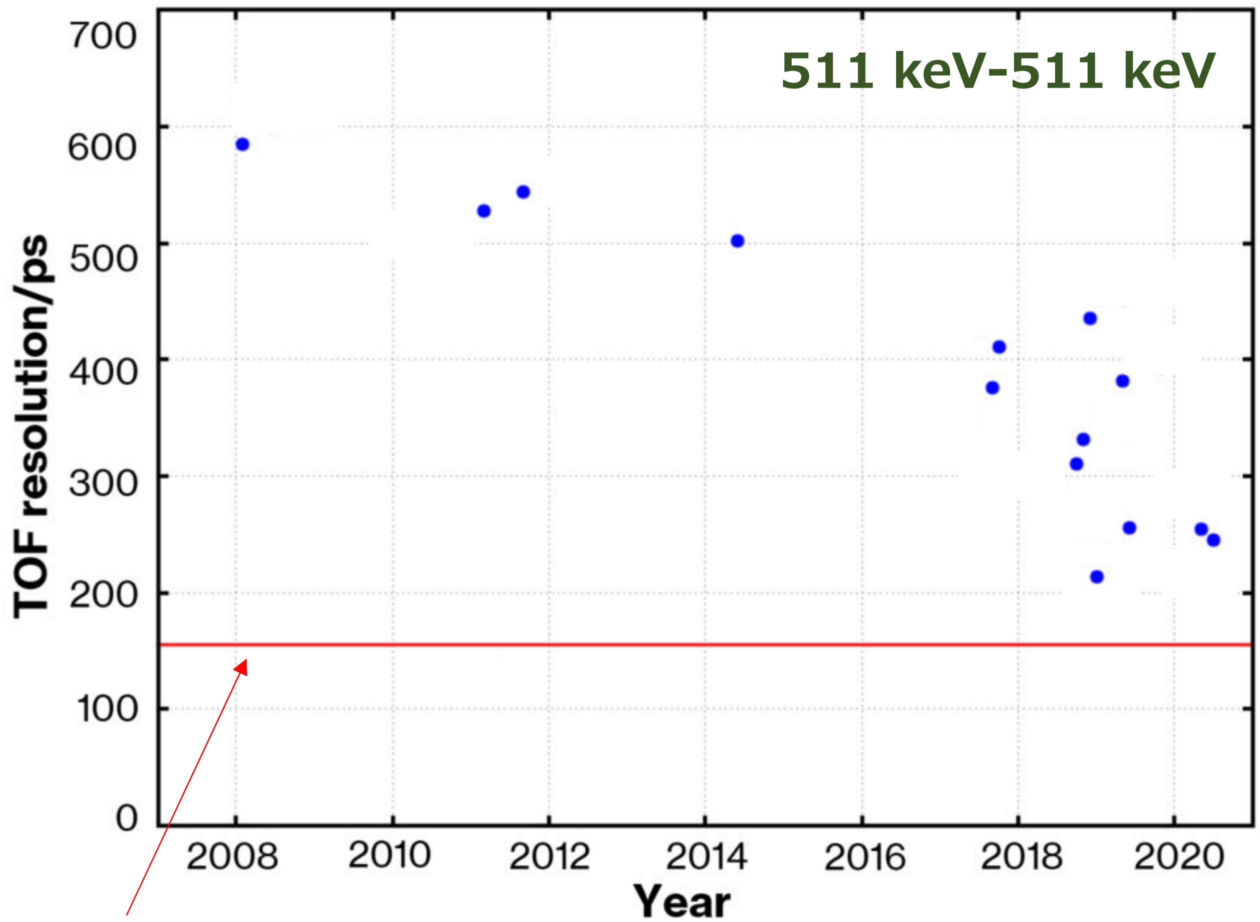
$$+ \alpha^2 \left[ \left(\frac{I_1}{\tau_1}\right)^2 + \left(\frac{I_2}{\tau_2}\right)^2 + \cdots + \left(\frac{I_n}{\tau_n}\right)^2 \right]$$

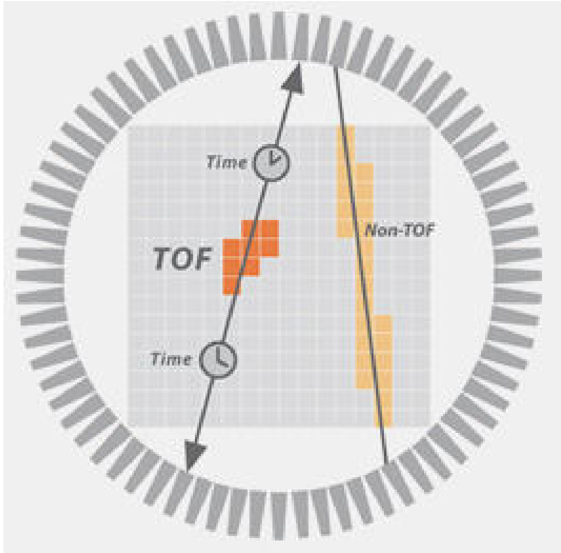
regularizer (general)

$$J_1 = \sum_{j=1}^{\mathrm{m}} \left\{ \frac{\left[\sum_{i=1}^{n} \frac{I_i}{\tau_i} \exp\left(-\frac{t_j}{\tau_i}\right)\right] - \left[S_n(t_j) - B\right]}{\sqrt{S_n(t_j)}} \right\}^2 + \alpha^2 \sum_{i=1}^{n-2} \left( \frac{I_i}{\tau_i} - 2\frac{I_{i+1}}{\tau_{i+1}} + \frac{I_{i+2}}{\tau_{i+2}} \right)^2$$

regularizer (CONTIN)

# Timing resolution for lifetime spectroscopy




[11] H. Saito, et al, *Nucl. Instrum. Methods A* **vol. 487**, pp. 612–617 (2002).

# Background (random coincidence)

high quality delay cable. For the direct and inverted spectra there is a loss of signal due to conversion of signal events into randoms, so that the *measured* spectrum for a single exponential signal with decay constant $\lambda$ as a function of time $t$ has the form

$$(A\, e^{\pm\lambda t} + B)\, e^{-nt} \quad (1)$$

where $A$ and $B$ are constants, $n$ the stop rate and the positive sign for $\lambda$ applies to the inverted spectrum. The usual approximation $e^{-nt}=1$ is not sufficiently accurate when $n$ is large.

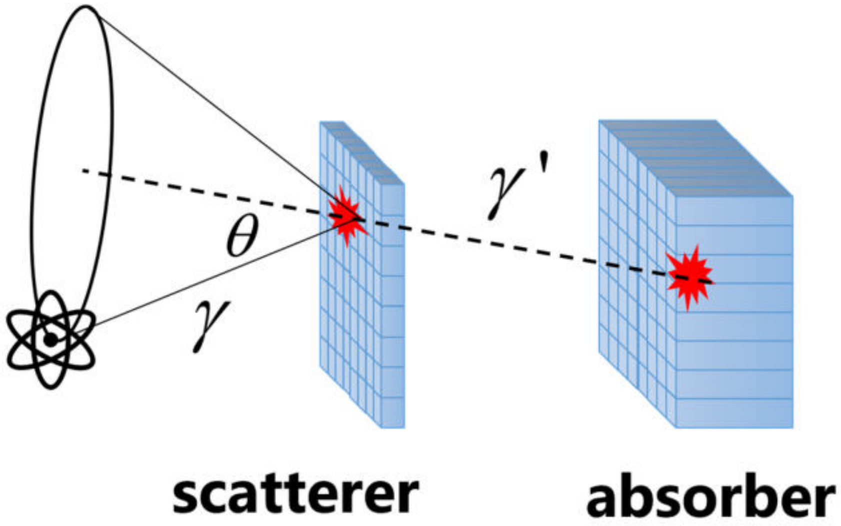
[12] P. G. Coleman *et. al*, *J. Phys. E*, **5** (1972) 376.

With the stop couting rate, $\eta$, the probability having no stop until time, $t$, and having the stop in the next $\Delta t$ :

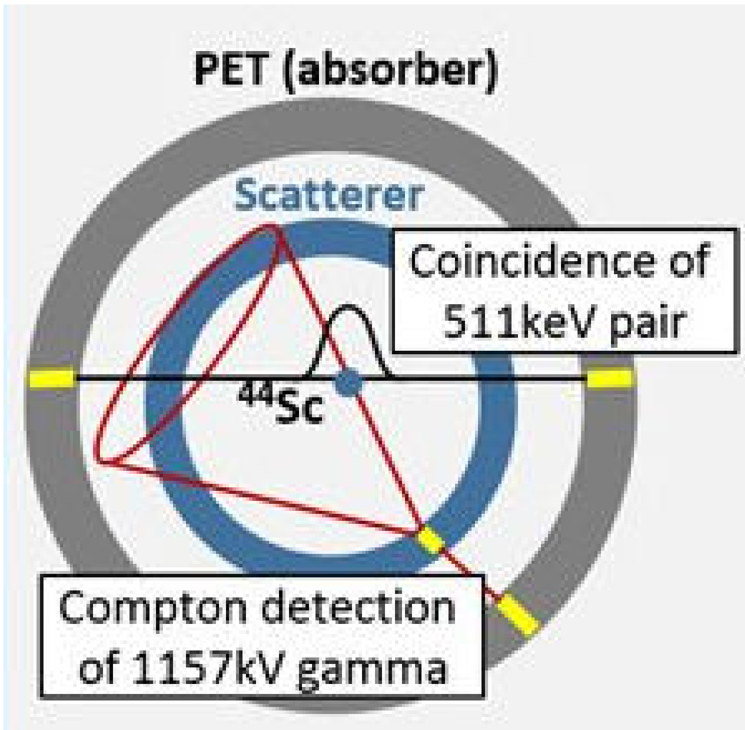
$$\lim_{\Delta t \to \infty} (1-\eta\Delta t)^{\frac{t}{\Delta t}} \cdot \eta\Delta t \to C_1 \exp(-\eta t) \qquad \because \lim_{n\to\infty}\left(1+\frac{1}{n}\right)^n = e$$

# Compton camera technique

**Compton camera**




$$\theta = \cos^{-1}\left[1 + m_e c^2 \left(\frac{1}{E_\gamma} - \frac{1}{E_{\gamma'}}\right)\right]$$

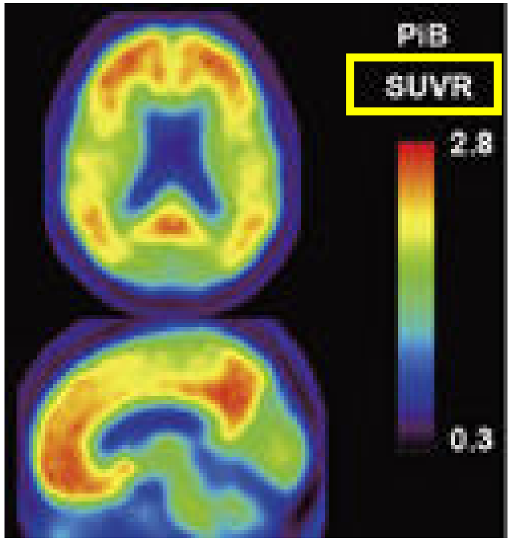




[13] E. Yoshida, Phys. Med. Biol., vol. 65, pp. 125013 (2020).

# Absoluteness (SUV vs mmHg)

- **SUV** (standardized uptake value) depending on
  - scanner
  - protocol
  - corrections
  - reconstruction algorism
  - other situations.




GE Healthcare

SUV=1:
average radioactive concentration

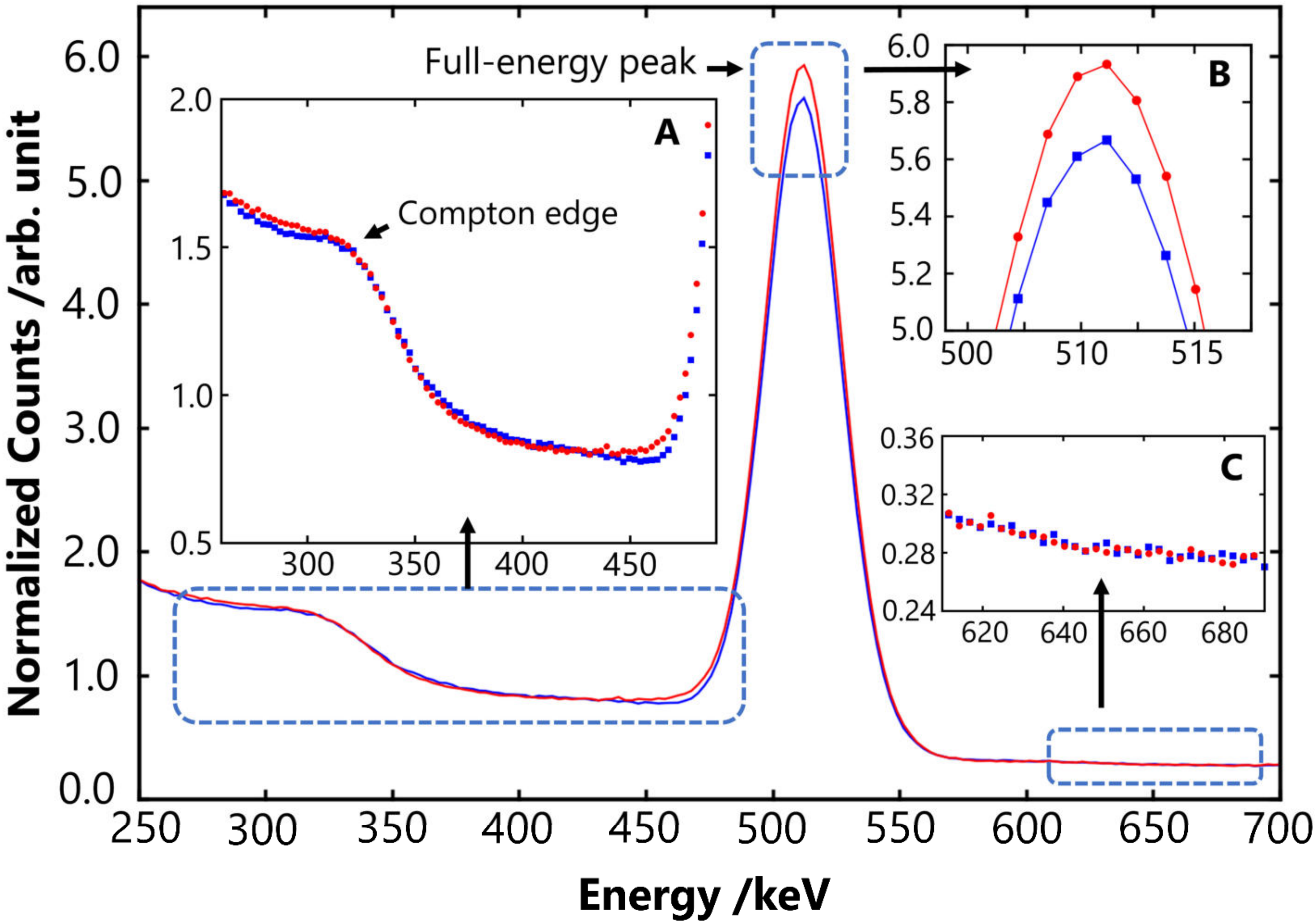
- **$pO_2$ in mmHg**
  - enable comparison data between deferent protocols.

# Summary

- A linearity between $pO_2$ and o-Ps decay rate was observed. (proportionality: 26.3±1.1 mmHg/μs$^{-1}$)
- 100M counts provides $pO_2$ resolution of 17 mmHg which is enough to discriminate hypoxia from normoxia.
- An inverse Laplace transform may divide Ps lifetime components for a larger voxel in Ps imaging.
- We are planning to combine PET with Compton Camera technique for Ps lifetime imaging.

[12] K. Shibuya, *et al.*, *Commun. Phys.* **3,** 173 (2020).
[OPEN ACCESS]

# Backup Slides



Normalized Counts /arb. unit
Energy /keV
Full-energy peak
Compton edge
A
B
C