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Ortho-Positronium Lifetime Spectroscopy for 2-D Liver Tissue Imaging

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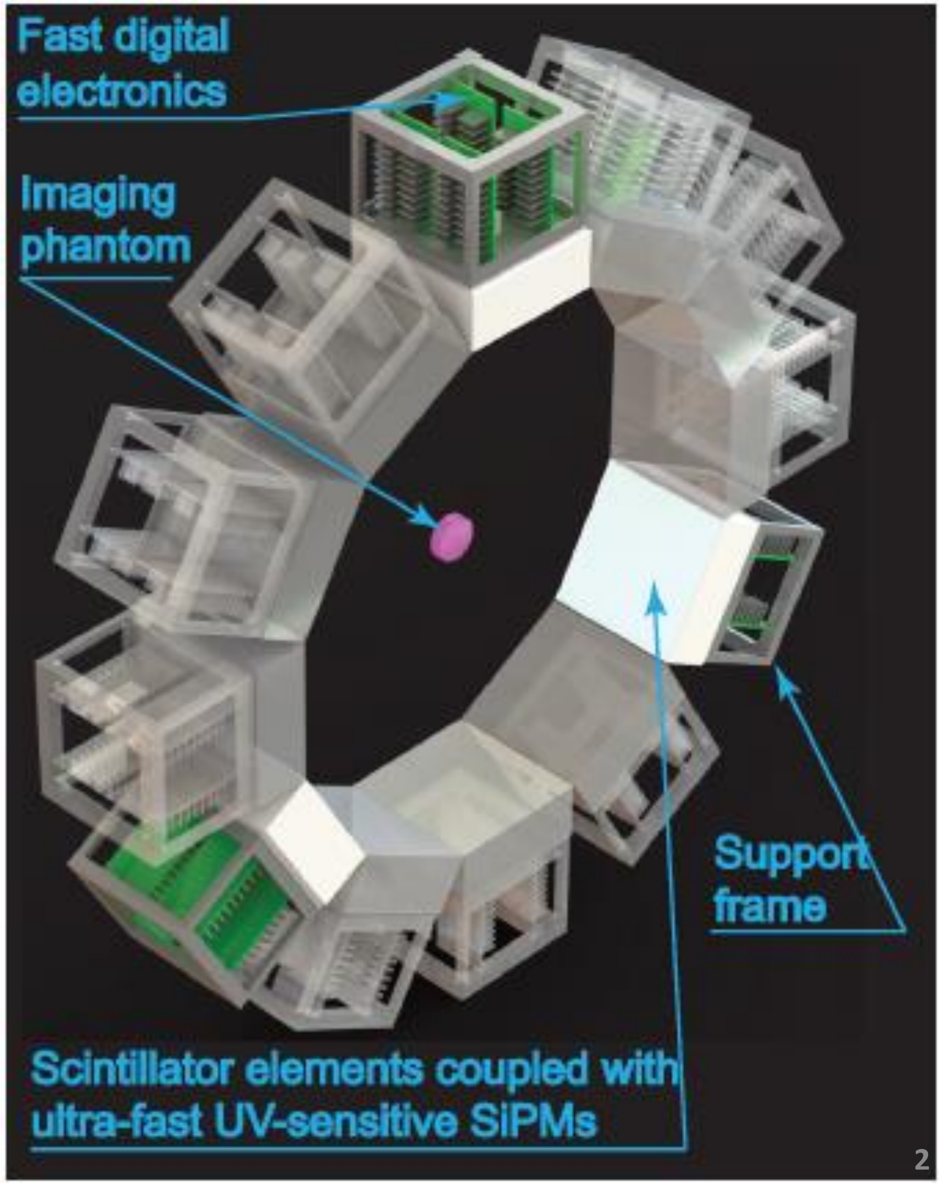
Motivation and objective

Objective: demonstrate a feasibility study to discriminate different types of soft tissue using positronium (Ps) lifetime spectroscopy and tomography.

- Ps is a subatomic particle formed as a combination of a positron and electron.
- Ps lifetime depends on the tissue structure.
- In highly dense tissues, Ps annihilates with surrounding electrons by emitting two 511-keV γ-rays (in the tens of nanoseconds time scale).
- Alternatively, Ps decays into 3 γ-rays with a longer lifetime.

The measurement of $2\gamma/3\gamma$ $(f_{3\gamma})$ can be used to measure the Ps lifetime in tissues and characterize the tissue microstructure.



Jasinska, B. & Moskal, P. A new PET diagnostic indicator based on the ratio of 3γ/2γ positron annihilation. Acta Phys.244 Polonica B 48, 1577–1582, DOI: 10.5506/APhysPolB.48.1577 (2017)
B. Jasińska et al., Acta Phys. Pol. B 48, 1737 (2017),

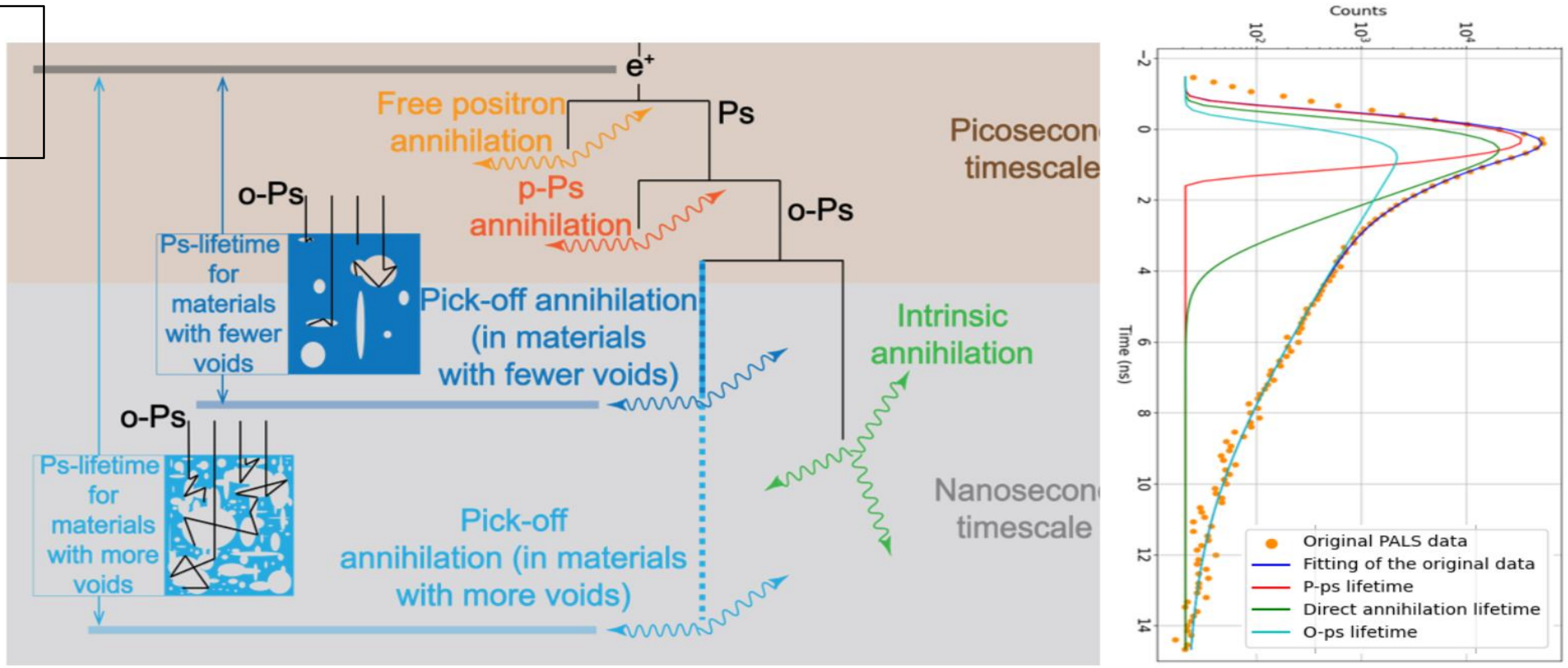
Positron and positronium physics

- Positron at rest directly annihilates with one of the surrounding electrons 60% of the time, while in the remaining 40% it forms Ps.
- Ps can be found in two states; para-positronium (p-Ps) and ortho-positronium (o-Ps).
- O-Ps lifetime depends on and the average void radius (R).

$$\tau_{o-Ps-medium} = \left(f_{3\gamma} - \frac{\left(-\frac{4}{3}P_{o-Ps}\right)}{370}\right)\left(\frac{\tau_{o-Ps-vacuum}}{P_{o-Ps}}\right)$$

$$\tau_{o-Ps-medium} = \frac{1}{\lambda_b}\left(1 - \frac{R}{R-\Delta} + \frac{1}{2\pi}\sin\left(\frac{2\pi R}{R+\Delta}\right)\right)^{-1}$$

P_{o-Ps} is the probability of o-Ps formation in the material, $\tau_{o-Ps-vacuum}$ is the o-Ps lifetime in vacuum, and the constant 370 is the computed ratio of cross sections of 2γ annihilation and 3γ annihilation for particles in free relative motion, $f_{3\gamma}$ the three-gamma fraction [1,2].
λ_b is the spin-averaged positronium annihilation rate and Δ is an experimentally measured parameter [1,2].



(Left) is the positron and positronium physics process corresponding to each PALS time spectrum (right). The time spectrum in (b) is the time difference between the detection time of prompt gamma and the annihilation photons

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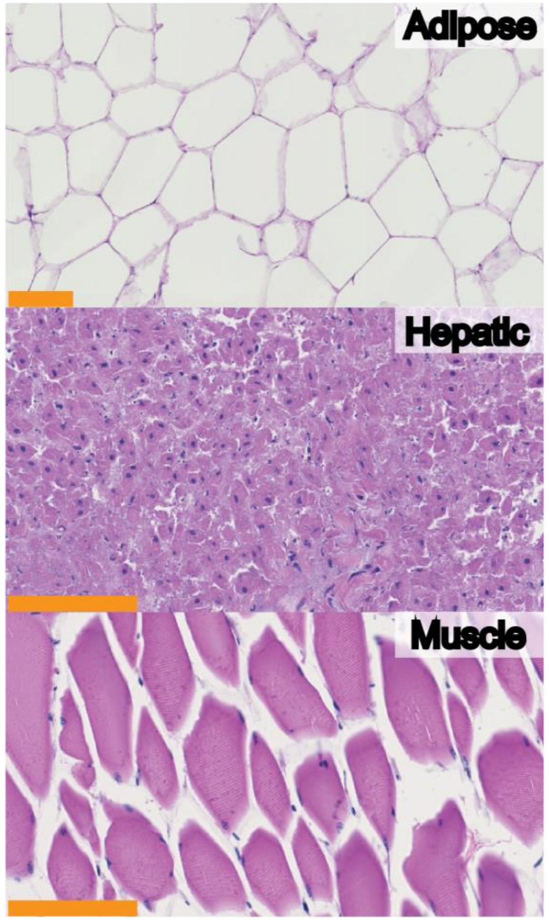
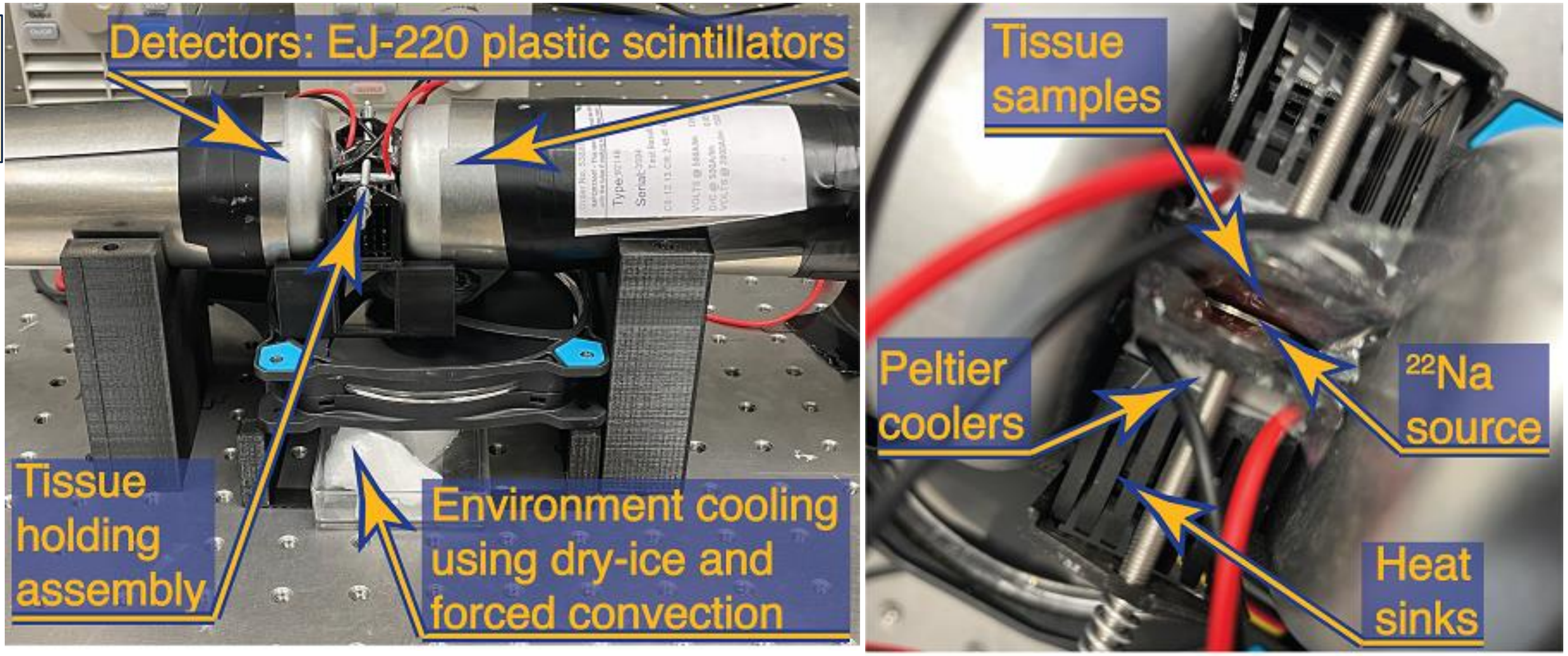
[1] Bozena, Jasinska & Moskal, Pawel. (2017). A New PET Diagnostic Indicator Based on the Ratio of 3γ /2γ Positron Annihilation. Acta Physica Polonica B. 48. 1577. 10.5506/APhysPolB.48.1577.
[2] D. W. Gidley, H. G. Peng, R. S. Vallery, Positron annihilation as a method to characterize porous materials, Annual Review of Materials Research 36 (2006) 337 49–79. doi:10.1146/annurev.matsci.36.111904.135144.

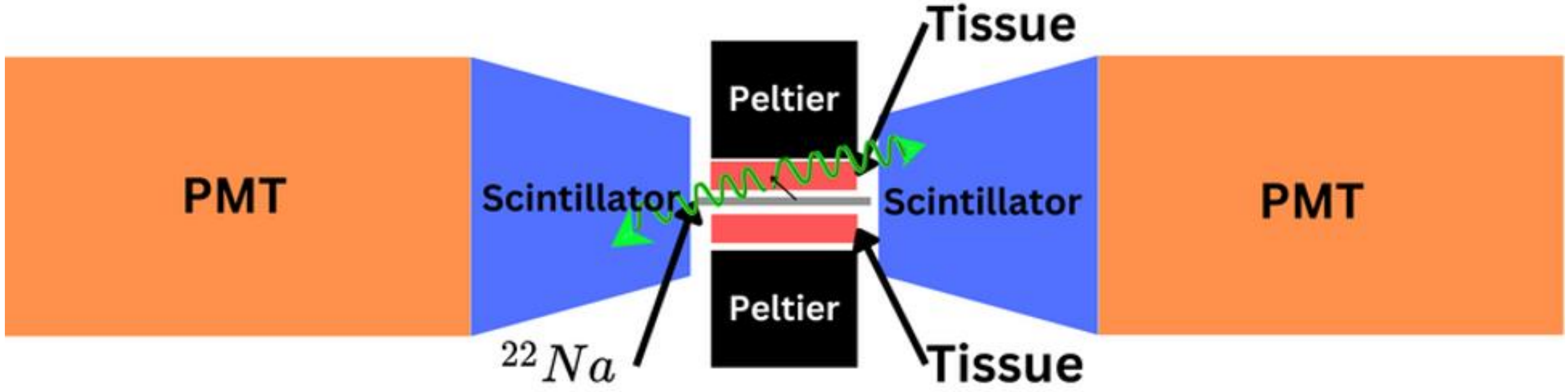
Positron Annihilation Lifetime Spectroscopy (PALS)

We measured the o-Ps lifetime using PALS in three types of soft tissues; adipose, hepatic, and muscles.





PALS experimental setup for Ps measurements in biological tissue



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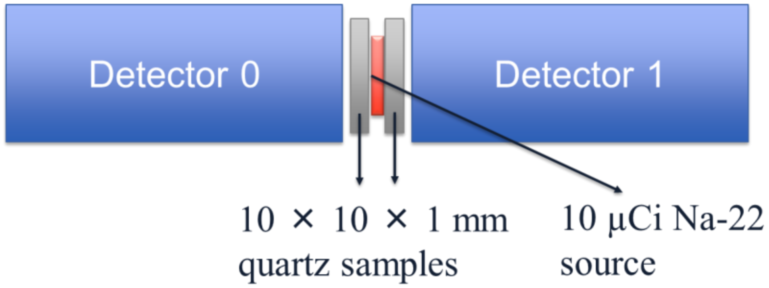
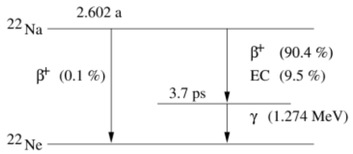
Positron Annihilation Lifetime Spectroscopy (PALS)

Experimental setup



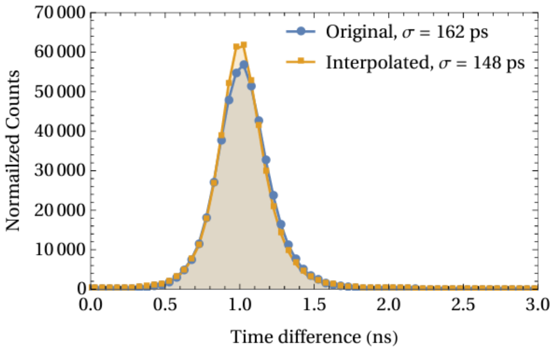


- We first interpolated the digitized pulses based on Shannon's interpolation formula.
- We used the terminated *sinc* function instead of sinc to reduce Eq.(1) to a finite sum

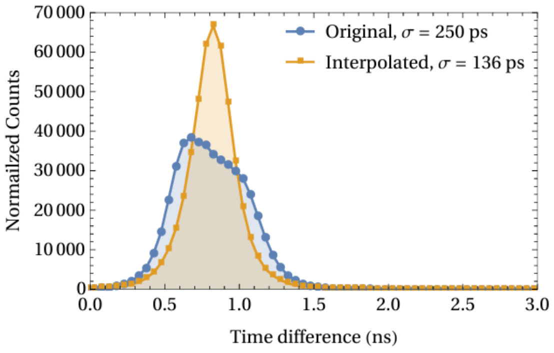
$$g(j,k) = \sum_{i=-\infty}^{+\infty} g_s(j-i)\,\text{tsinc}(iN+k) \quad (1)$$

- We applied a digital version of the constant-fraction discrimination (CFD) algorithm to each interpolated pulse.

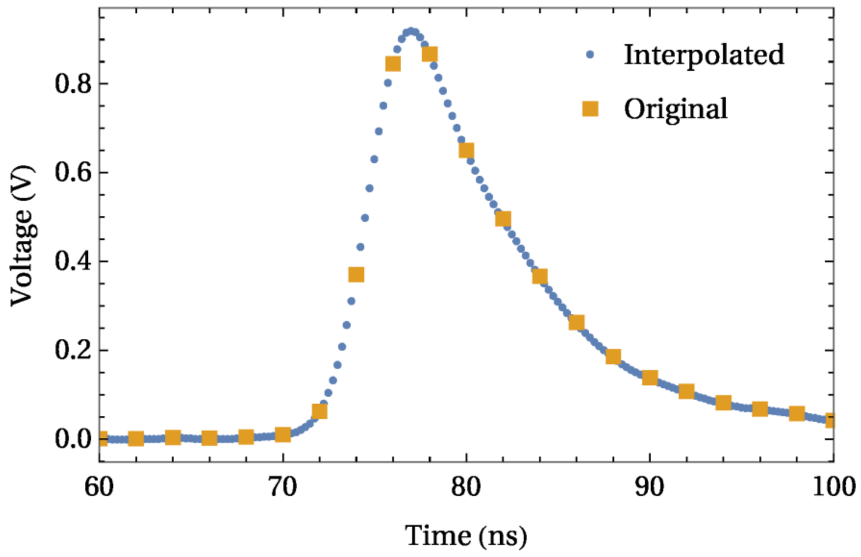
$$\text{CFD}(i) = F \times S(i) - S(i-\boldsymbol{\Delta}) \quad (2)$$

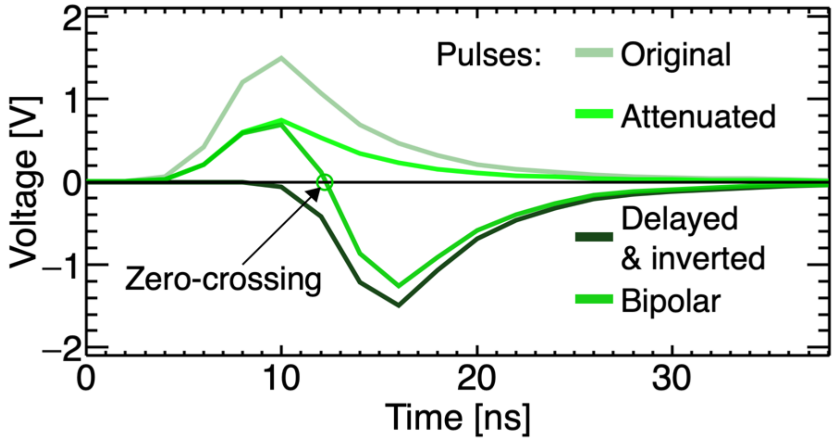


(a) F = 0.75, Δ = 6 ns



(b) F = 0.4, Δ = 6 ns





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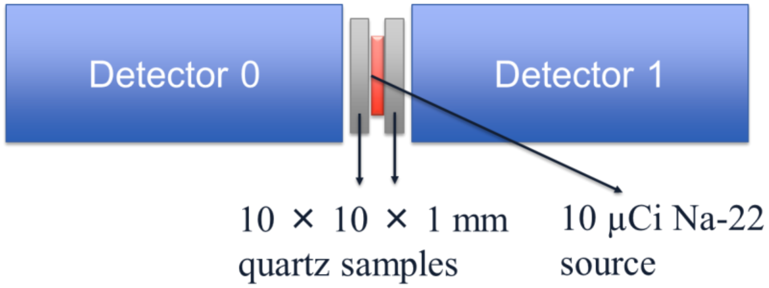
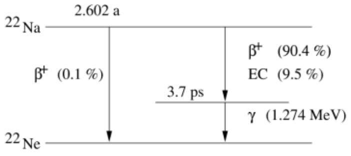
Fang, M., Bartholomew, N., and Di Fulvio, A. (2019). Positron annihilation lifetime spectroscopy using fast scintillators and digital electronics. Nuclear Instruments and Methods in Physics Research Section A 943:162507

Positron Annihilation Lifetime Spectroscopy (PALS)

Experimental setup





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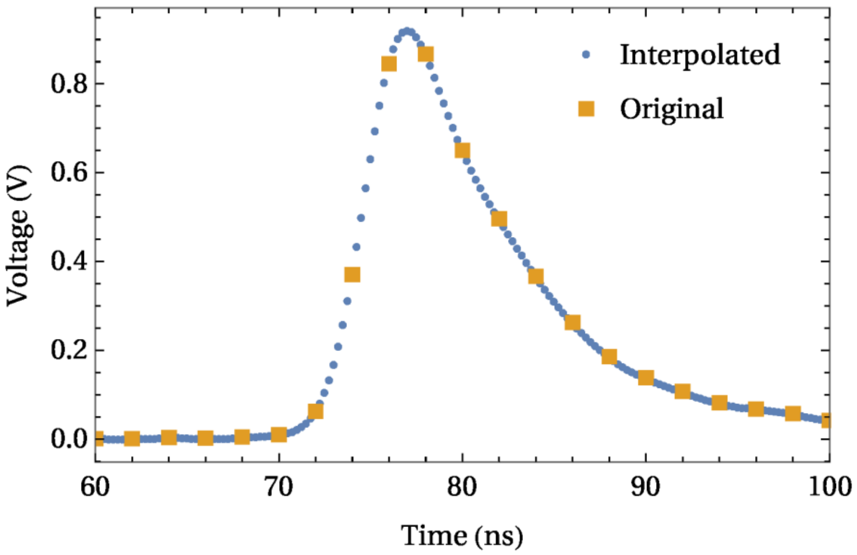

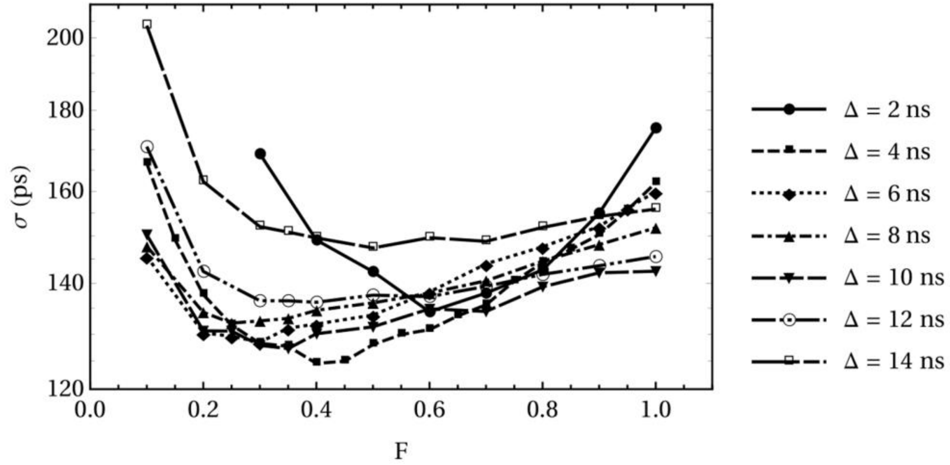

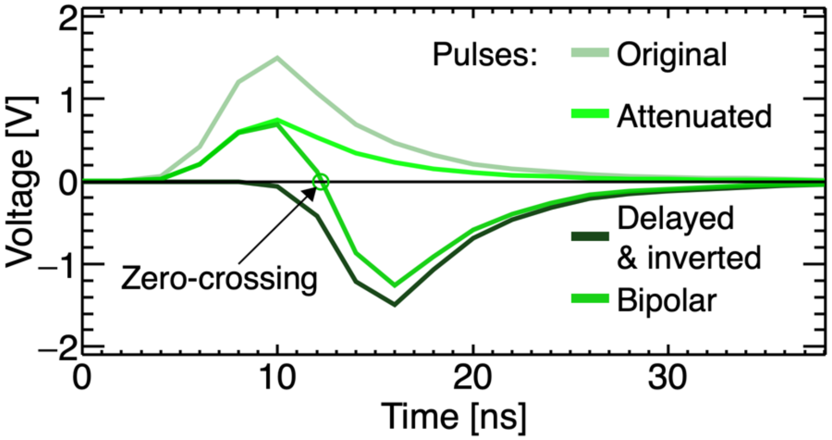

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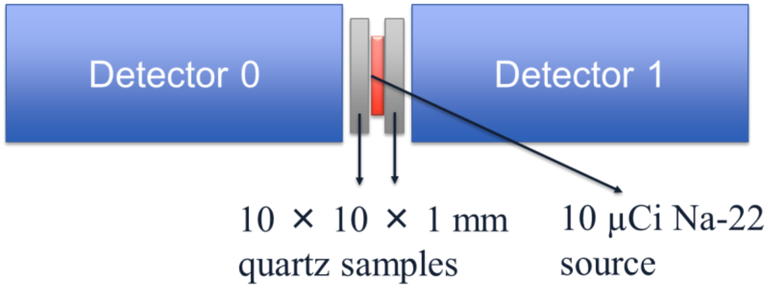

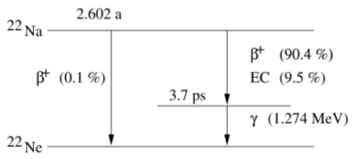

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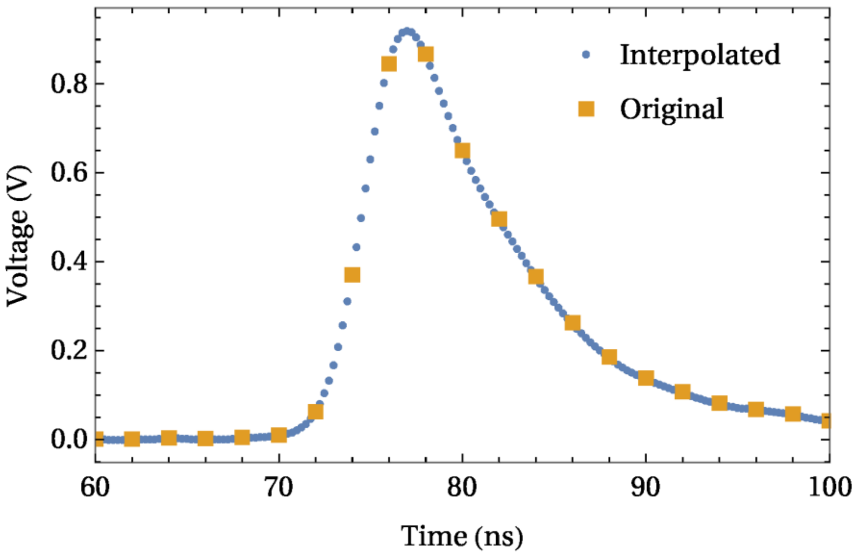
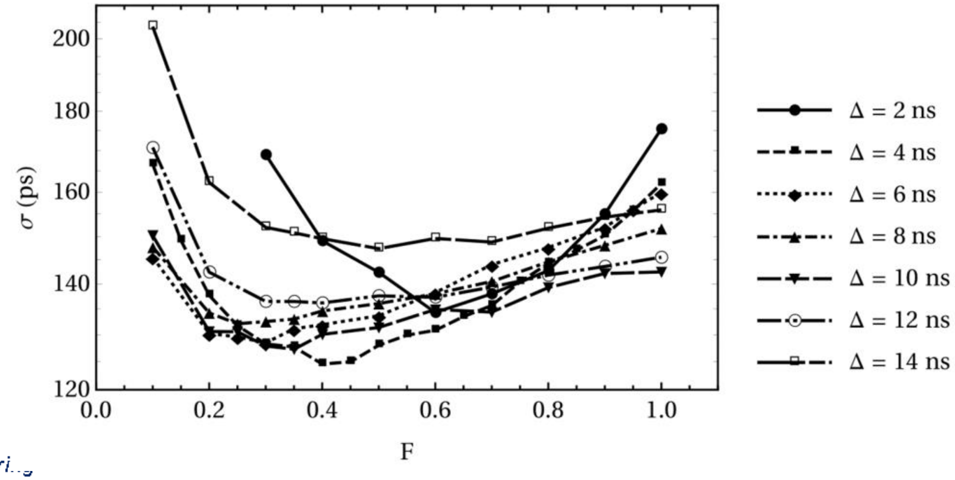
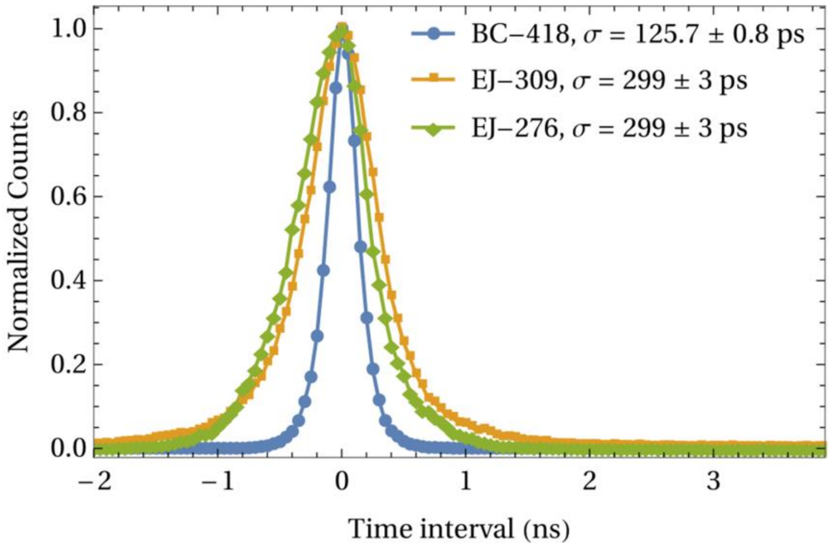
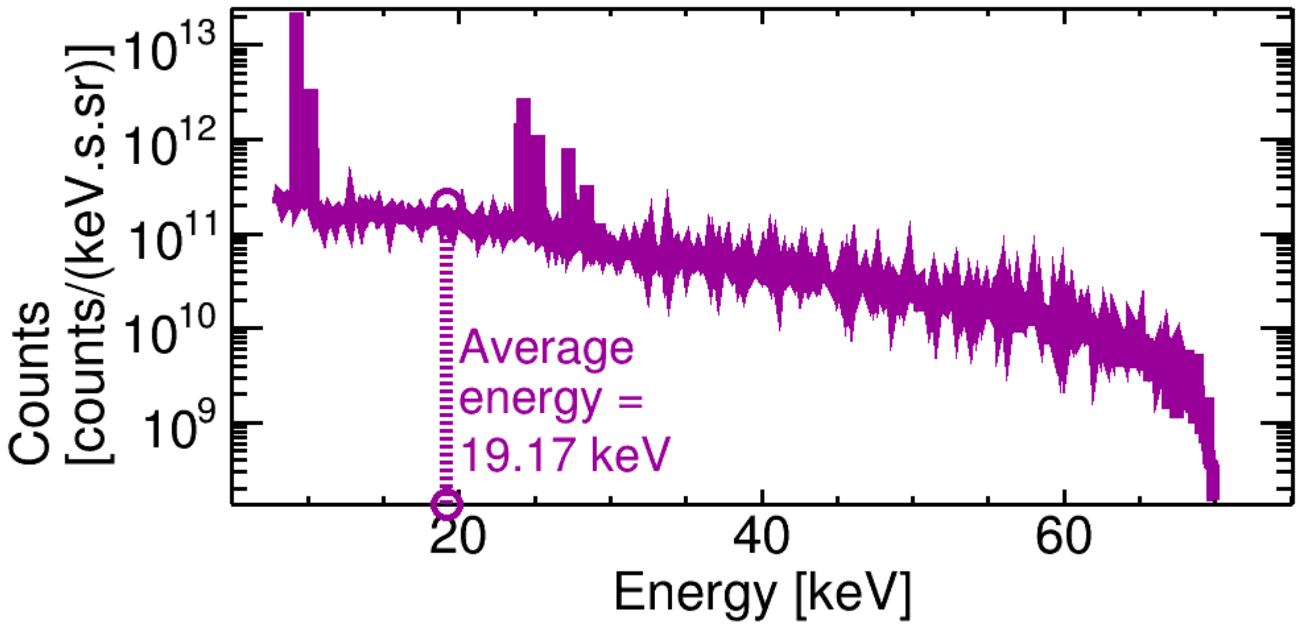


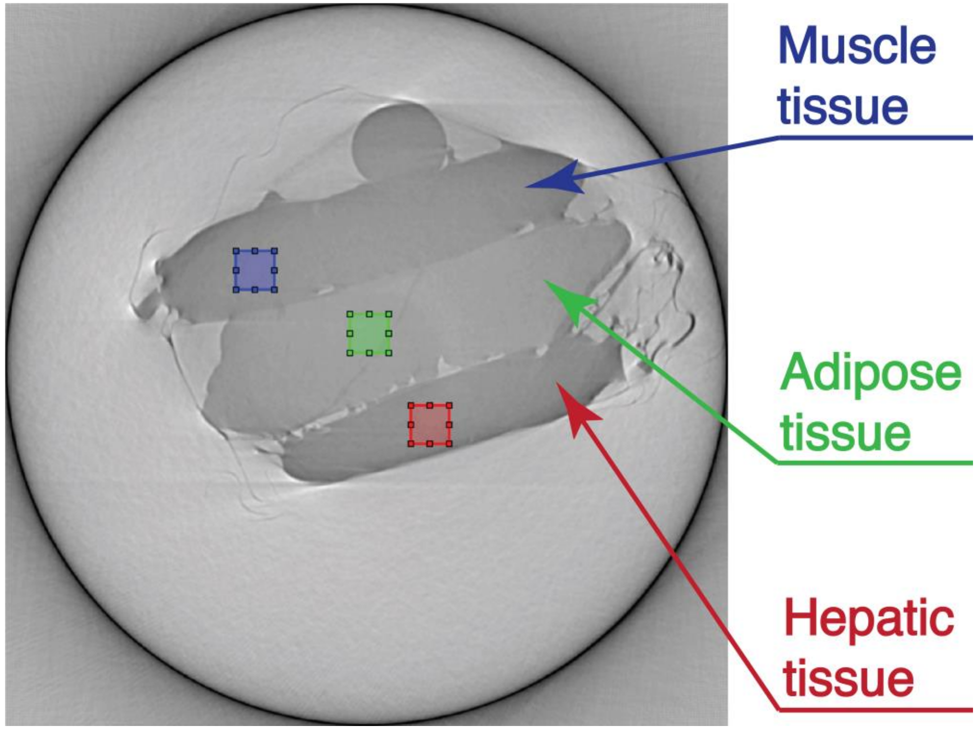




Comparative X-ray Phase Contrast Tomography Analysis

- A propagation distance (object-to-detector distance) of approximately 2.15 m was utilized to enhance the phase effects. This propagation distance, paired with the source-to-object distance of approximately 1.85 m, resulted in a magnification of 2.16 and a Fresnel number of approximately 2.82
- Average X-ray energy of our liquid-metal-jet-based X-ray source is 19.17 keV for the 70 kVp X-ray energy spectrum

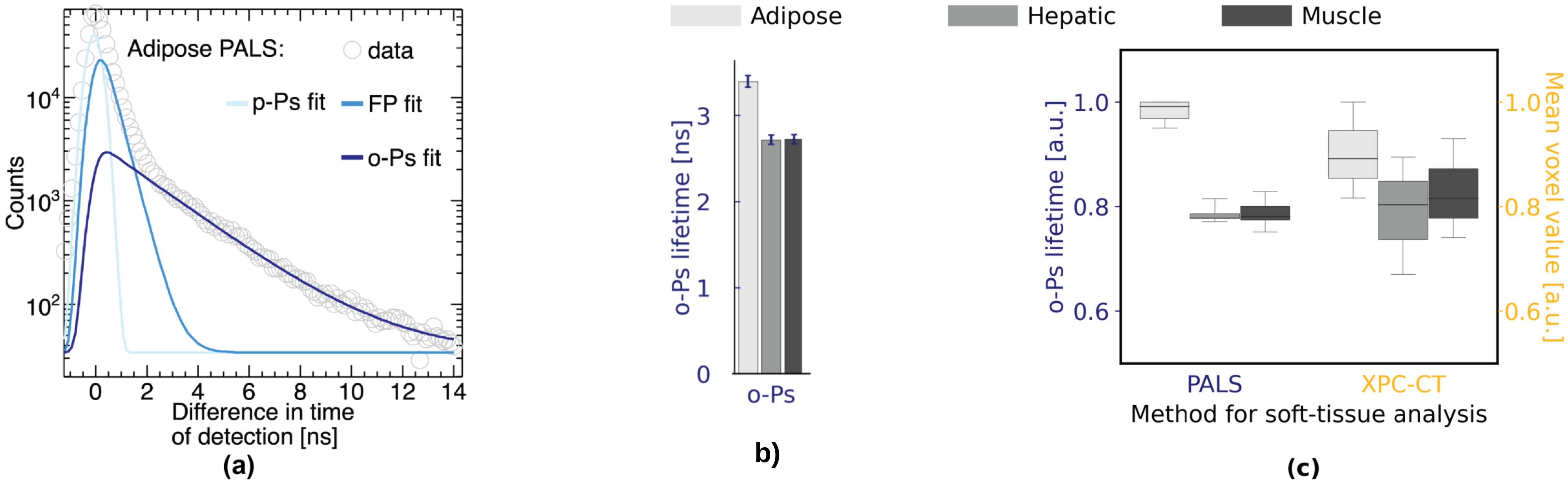




This XPC-CT system included: a liquid-metal-jet-based X-ray source (MetalJet195 D2, Excillum) operated at 70 kVp, 130 W power, and about 14 μm focal spot size; a CsI(Tl) scintillator-based X-ray imager with a pixel pitch of 13 μm, active area of about 54^2 mm^2, and 2x2 binning (4k × 4k X-Ray GSENSE SCMOS, Photonic Science); and an object manipulation system to rotate the imaging samples.

Ps lifetime results in biological tissue

- We found that the o-Ps lifetime in adipose tissues (3.4±0.01 ns) was approximately 25% longer than in hepatic (2.71±0.01 ns) and muscle (2.72±0.1 ns) tissues.
- The adipose tissue was discriminable from hepatic and muscle tissues using o-Ps lifetime.



Results of PALS analysis and its benchmarking with XPC-CT. (a) PALS spectrum and its three lifetime components; p-Ps, free-positron (FP), and o-Ps lifetimes (b) The comparison of three components of the PALS spectrum for the three soft tissue (c) Comparison of PALS as a method for soft-tissue analysis with the current state-of-the-art, XPC-CT.

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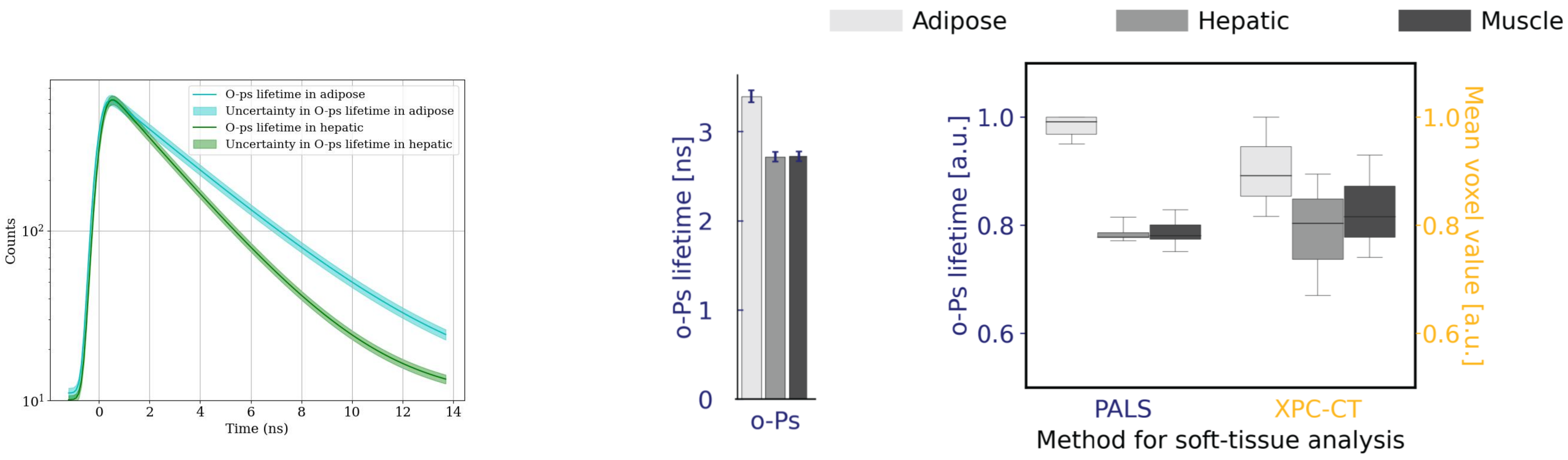


b)

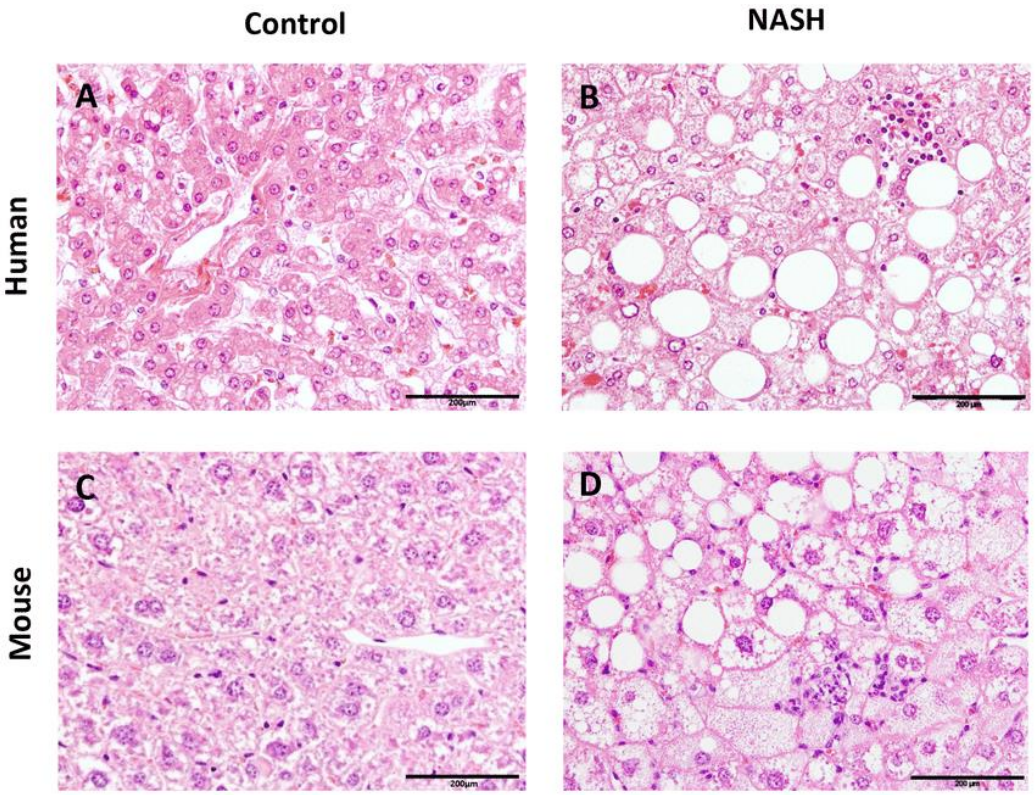
(c)

Results of PALS analysis and its benchmarking with XPC-CT. (a) PALS spectrum and its three lifetime components; o-Ps lifetimes (b) The comparison of three components of the PALS spectrum for the three soft tissue (c) Comparison of PALS as a method for soft-tissue analysis with the current state-of-the-art, XPC-CT.

Preliminary results on NASH samples

- Controls and non-alcoholic steatohepatitis (NASH)-diet-fed small animals (total of 12 + 12 samples).
- Samples were in 10% formalin.

	O-Ps lifetime (ns)
A3 & A4	3.81±0.27
D5 & D7	3.80±0.27
Control 1	3.50±0.26
Control 2	3.42±0.24



Liang, Wen & Menke, Aswin & Driessen, Ann & Koek, Ger & Lindeman, Jan & Stoop, Reinout & Havekes, Louis & Kleemann, Robert & van den Hoek, Anita. (2014). Establishment of a General NAFLD Scoring System for Rodent Models and Comparison to Human Liver Pathology. PloS one. 9. e115922. 10.1371/journal.pone.0115922.

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Ps lifetime modeling (I)

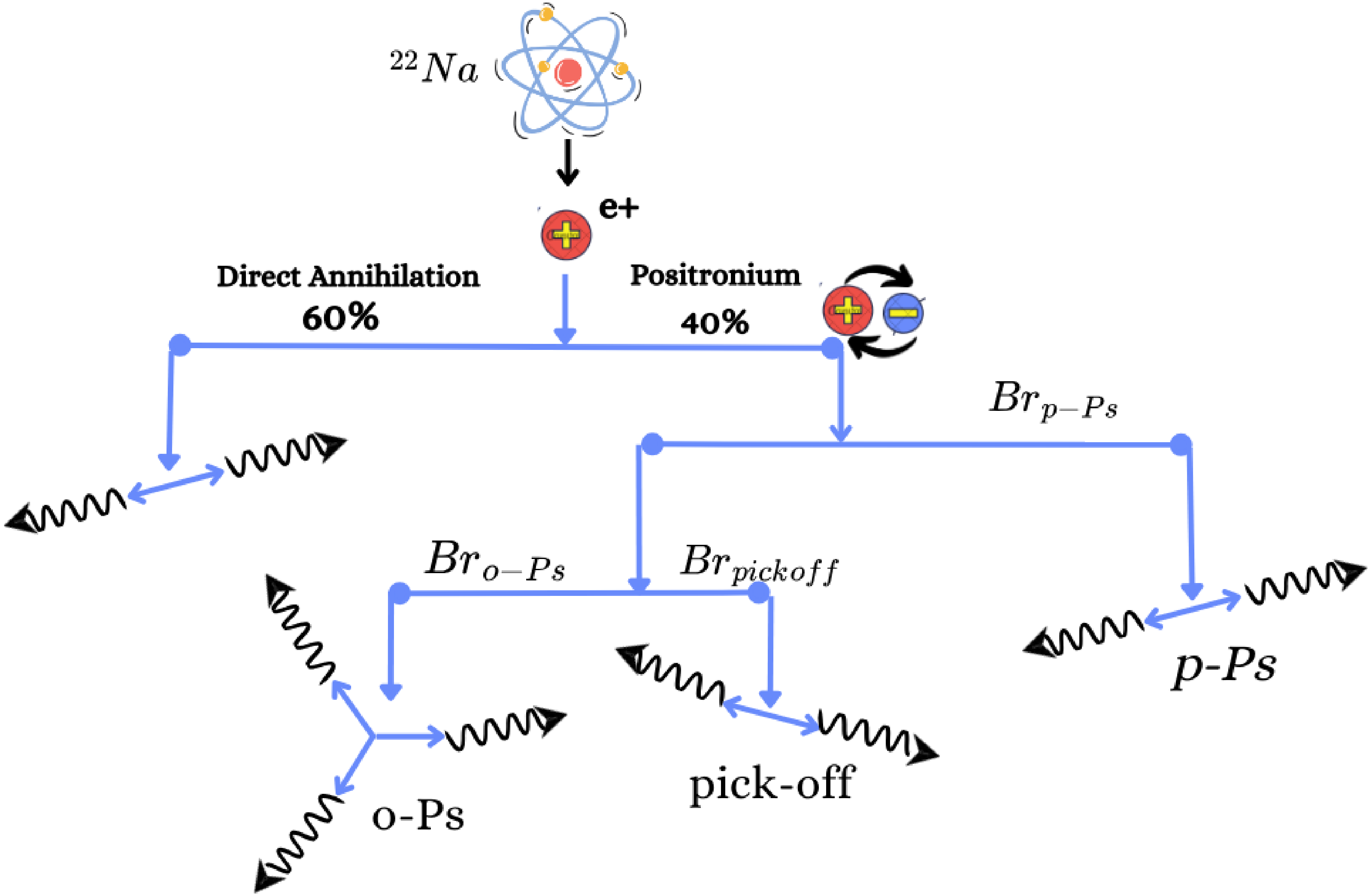
Pick-off-annihilation-rate= $4\pi r_o^2 c N_e$

$Br_{pickoff} = \frac{pick-off\ annihlation\ rate}{total\ annihilation\ rate}$

Br_{o-Ps} = 1- ($Br_{pickoff}$ + Br_{p-Ps})

Where N_e is the surrounding electron density, r_o the classic electron radius 2.8×10^{-13} cm, and c the speed of light.

$Br_{pickoff}$ is the pick-off Branching ratio, Br_{o-Ps} is the o-Ps branching ratio and Br_{p-Ps} is the p-Ps Branching ratio.



Ps lifetime modeling (II)

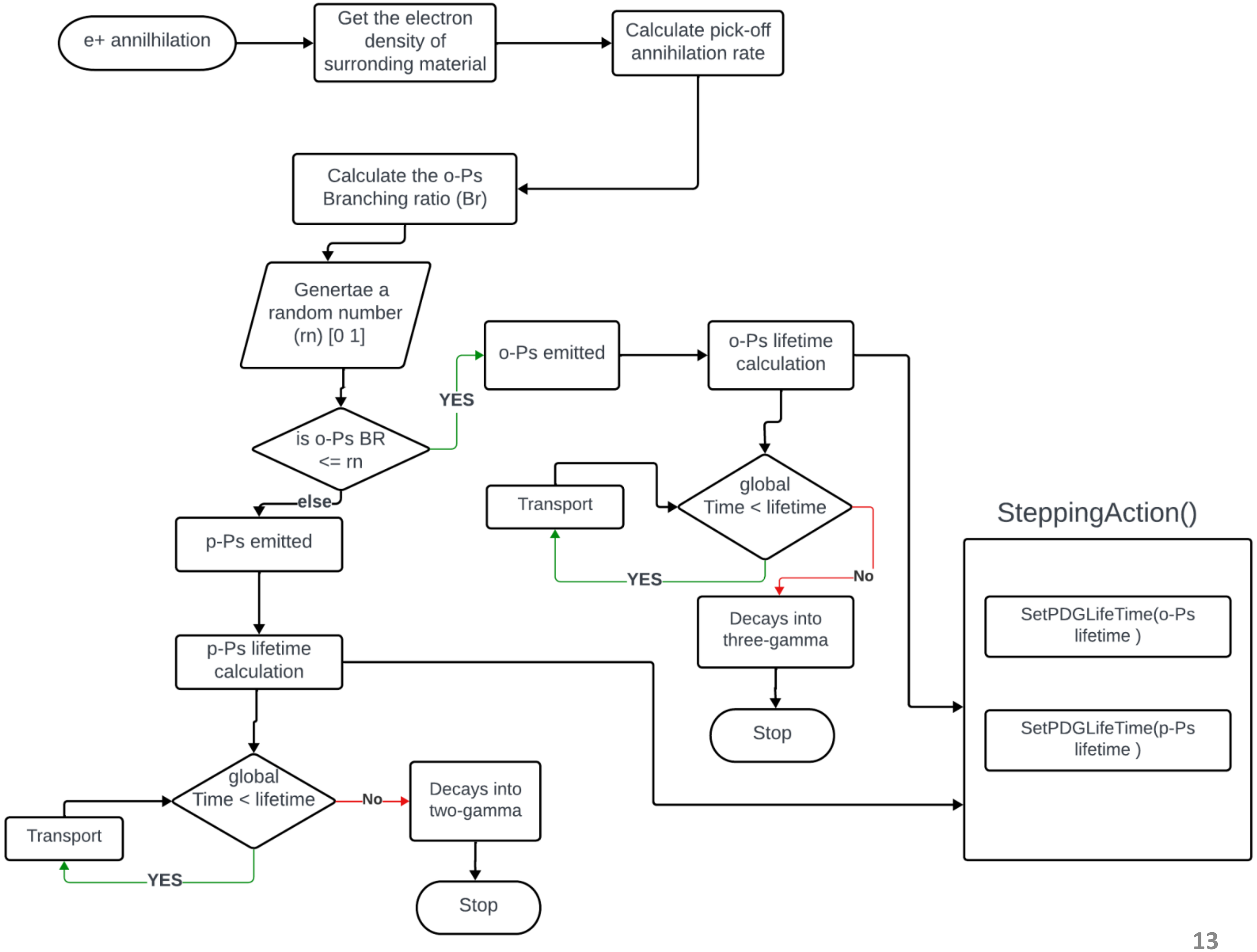
Pick-off-annihilation-rate= $4\pi r_o^2 c N_e$

$$Br_{pickoff} = \frac{pick-off\ annihlation\ rate}{total\ annihilation\ rate}$$

$$Br_{o-Ps} = 1 - (Br_{pickoff} + Br_{p-Ps})$$

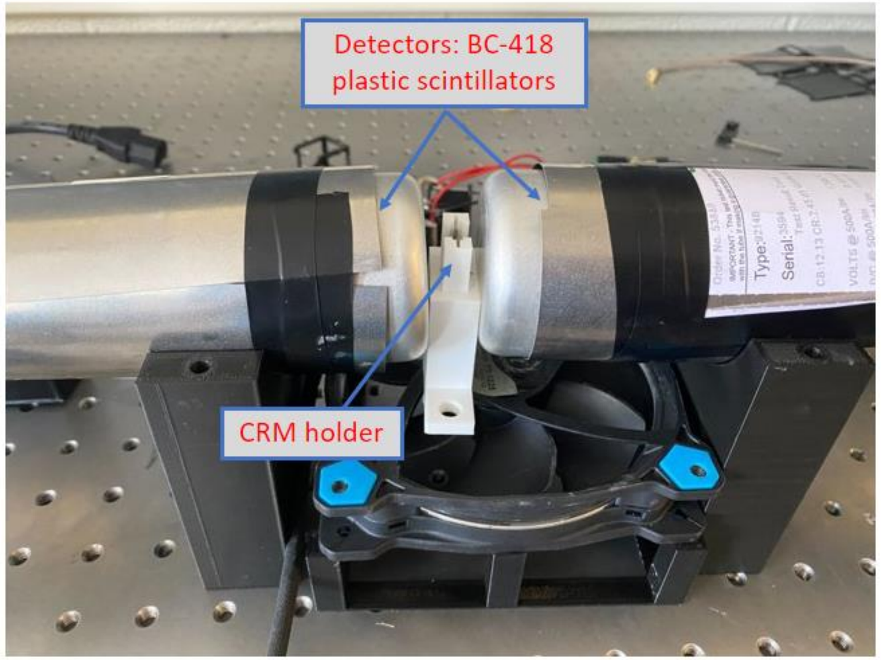
Where N_e is the surrounding electron density, r_o the classic electron radius2.8×10^{-13}, and c the speed of light.

$Br_{pickoff}$ is the pick-off Branching ratio, Br_{o-Ps} is the o-Ps branching ratio and Br_{p-Ps} is the p-Ps Branching ratio.

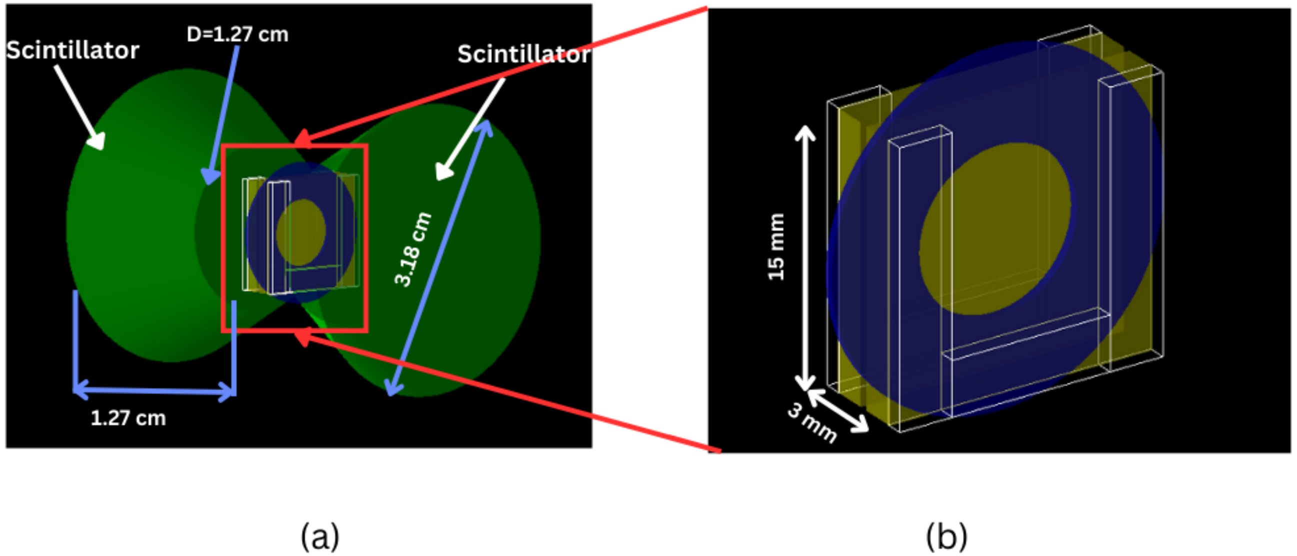


Ps lifetime modeling (III)

- We utilized a Monte Carlo method to investigate the capability of generating a Ps lifetime image using the three-gamma fraction.
- We built a Geant4 model to simulate the Ps lifetime as a function of electron density and validated our model experimentally.
- To validate our model, we compared the measured o-Ps lifetime of Certified Reference Materials (CRMs) in the PALS experiment with the calculated value from the simulation.



PALS experimental setup of CRMs



(a) Geant4 model of PALS experiment for CRMs, (b) Two samples of polycarbonate RM (yellow), ^{22}Na disk source (blue) and CRM holder (white).

Material	Simulated o-Ps lifetime	Measured o-Ps lifetime	Relative error
Polycarbonate	2.10 ± 0.07 ns	2.10 ± 0.05 ns	< 0.01%
Quartz	1.47 ± 0.07 ns	1.53 ± 0.05 ns	3.92%
Fused silica	1.71 ± 0.04 ns	1.62 ± 0.05 ns	5.56%

Ps lifetime image in biological tissue

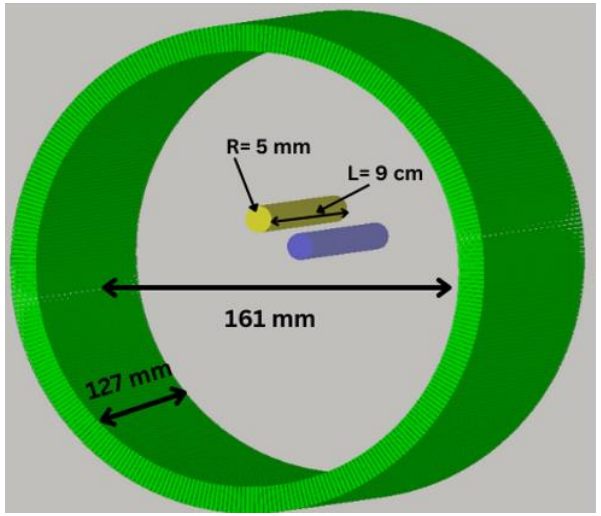
We employed a Geant4 replicated model of the Inveon Small-Animal PET scanner 182 to study the feasibility of producing a Ps lifetime image.
The scanner comprises of :

- Four rings, with 16 blocks in each ring.
- Each block consists of 20 × 20 Lutetium-based (LYSO) crystals measuring 1.5 × 1.5 × 10 mm^3 each.

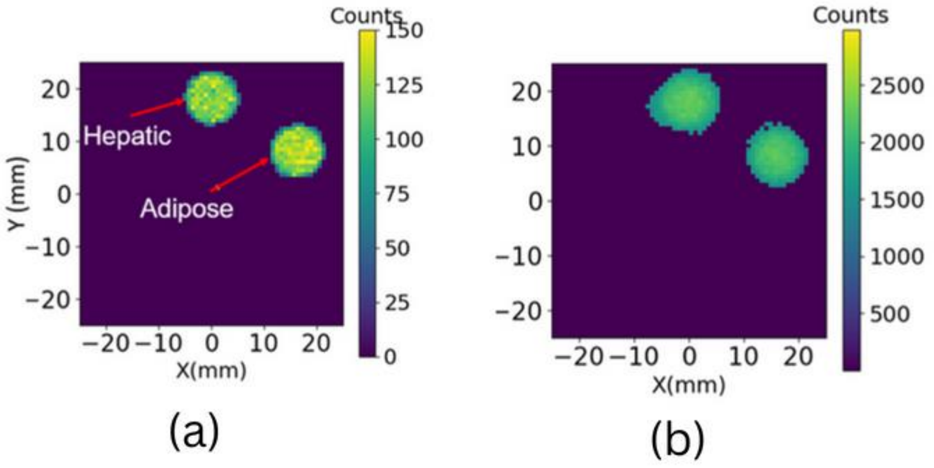
The two-gamma image is reconstructed using the Time-Of-Flight (TOF) technique, and the three-gamma image using the three-gamma imaging technique.

The three-gamma fraction image is obtained by the ratio between the three-gamma image and the total number of annihilation. Subsequently, the o-Ps lifetime image is generated from:

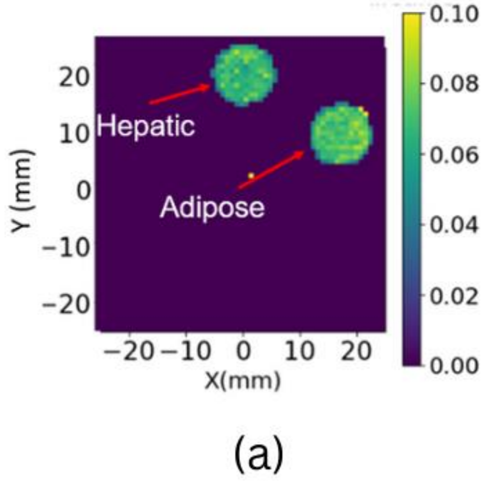
$$\tau_{o-Ps-medium} = \left(f_{3\gamma} - \frac{\left(-\frac{4}{3} P_{o-Ps}\right)}{370} \right) \left(\frac{\tau_{o-Ps-vacuum}}{P_{o-Ps}} \right)$$



Simulated Inveon small-animal PET scanner with two tissue cylinders; adipose (blue) and hepatic (yellow).



(a) Reconstructed two-gamma image (TOF) , (b) reconstructed three-gamma image

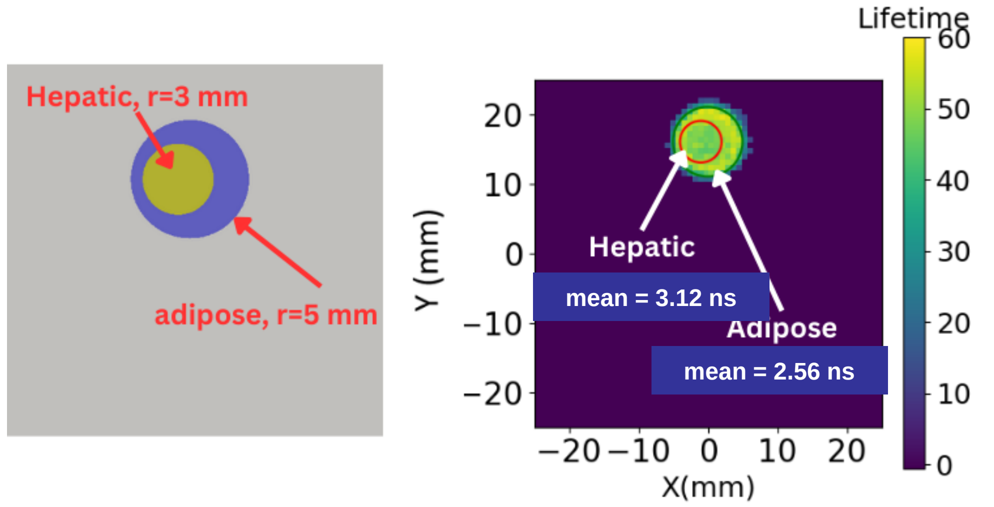


Simulated positronium images (a) Three-gamma fraction image

Krzysztof Kacperski, Nicholas M. Spyrou, and F. Alan Smith. Three-gamma annihilation imaging in positron emission tomography. IEEE Transactions on Medical Imaging, 23:525–529, 4 2004.

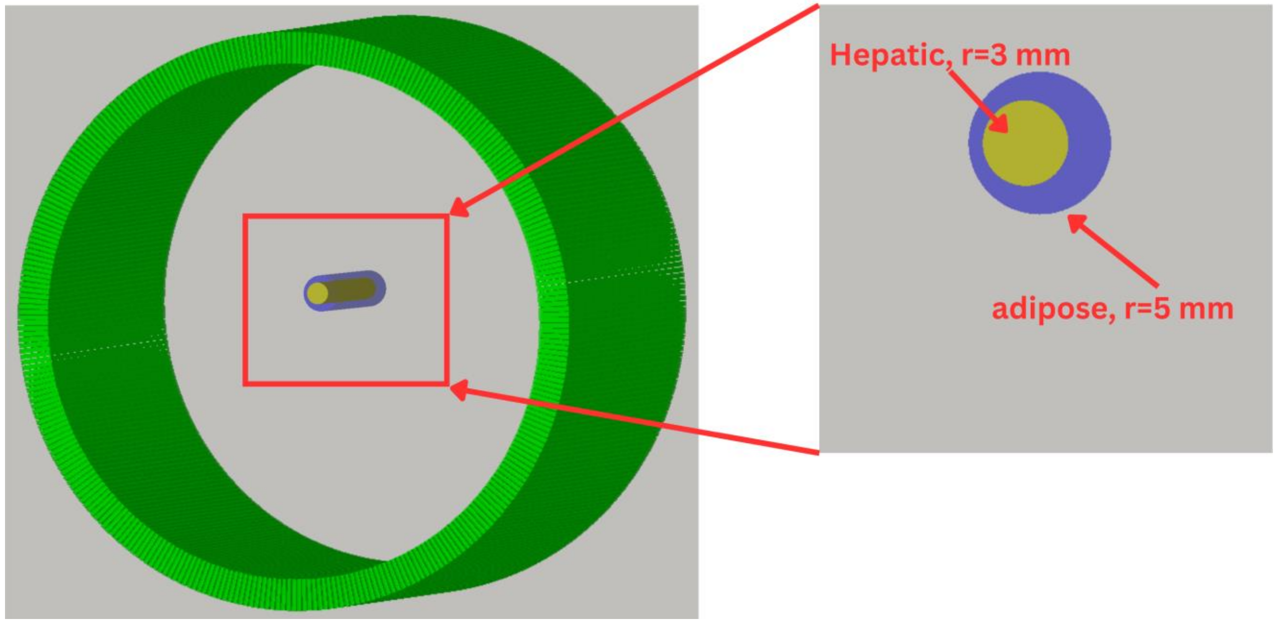
Ps lifetime image in biological tissue

We extended our model by simulating a phantom with tissues that overlap to investigate the capability of producing a contrast Ps lifetime image.



(a) (b)

(a) The Geant4 simulated phantom (b) Ps lifetime image.



Geant4 simulation of Inveon small-animal PET scanner imaging two overlapping cylindrical volumetric sources of adipose and hepatic tissues (blue is adipose and yellow is hepatic).

Conclusions

- We conducted an experiment to classify different types of soft tissues based on their o-Ps lifetime.
- We performed a feasibility study to create a Ps lifetime image using a commercial PET scanner and the three-gamma fraction.
- This method allows the creation of the Ps lifetime image without the need to measure the prompt gamma. Isotopes commonly used in PET do not emit a prompt gamma.
- This expands the PET diagnostic capability using traditional positron emitters.
- The resulting Ps lifetime image of hepatic and adipose tissues showed a higher lifetime in adipose compared to hepatic tissue, which is in line with the expected theory.
- These results could have relevant applications for diagnosing liver medical conditions where adipose tissue is intermixed with hepatic tissue.

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Prof. Ashish V. Avachat – University of Pittsburgh

Dr. Jiajie J. Xud, Prof. Mark A. Anastasio, Dr. Mayandi Sivaguru - UIUC

Thank you for your attention!

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Void size

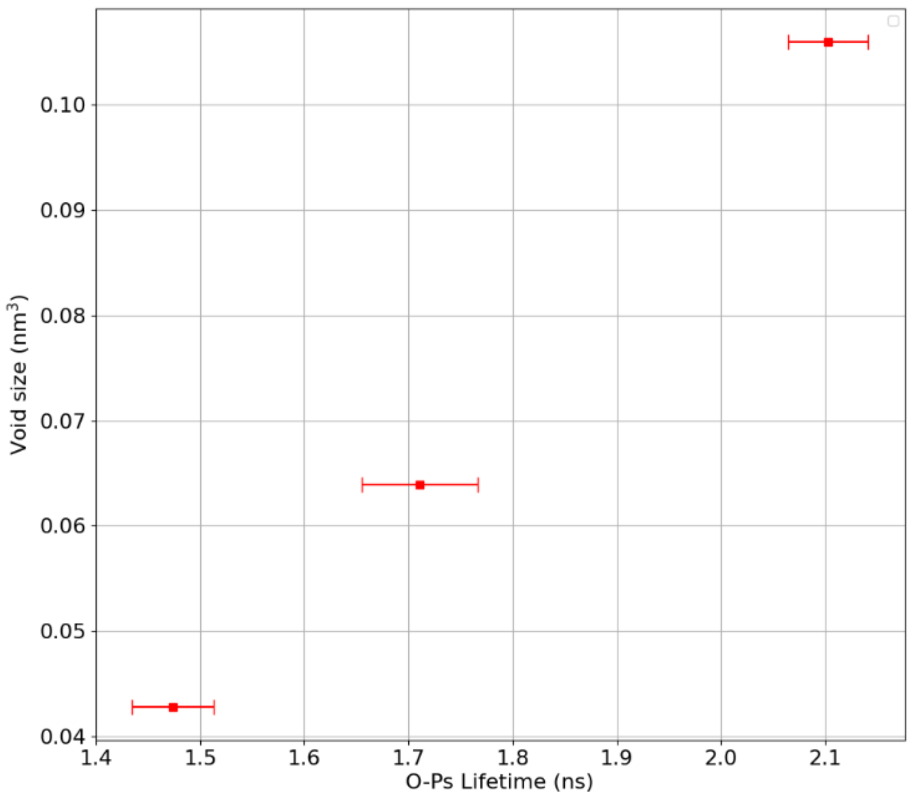
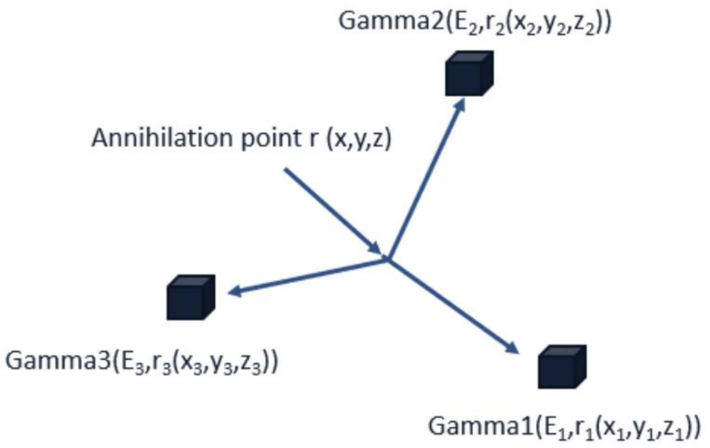


Figure 3.7: The o-Ps lifetime as a function of the void size.

Three-gamma reconstruction



Consider a three-gamma decay taking place at point r (x,y,z) and detected in coincidence by three detectors at r_1 r_2 r_3 respectively, where r_i (x_i,y_i,z_i). Each detected gamma-ray can have an energy between 0 and 511 keV corresponding to E_1, E_2, E_3. Applying the conversation of momentum and energy laws, we get the following three nonlinear relations. The conservation of momentum equations are:

$$p_x = \frac{E_1}{c}\frac{x - x_1}{|r - r1|} + \frac{E_2}{c}\frac{x - x_2}{|r - r2|} + \frac{E_3}{c}\frac{x - x_3}{|r - r3|} = 0 \tag{4.2}$$

$$p_y = \frac{E_1}{c}\frac{y - y_1}{|r - r1|} + \frac{E_2}{c}\frac{y - y_2}{|r - r2|} + \frac{E_3}{c}\frac{y - y_3}{|r - r3|} = 0 \tag{4.3}$$

$$p_z = \frac{E_1}{c}\frac{z - z_1}{|r - r1|} + \frac{E_2}{c}\frac{z - z_2}{|r - r2|} + \frac{E_3}{c}\frac{z - z_3}{|r - r3|} = 0 \tag{4.4}$$

The conversation of energy is given by:

$$E_1 + E_2 + E_3 = 2m_e c^2 \tag{4.5}$$

where m_e is the electron rest mass and c is the speed of light.