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J-PET

Center for Theranostics

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6th Jagiellonian Symposium on Advances in Particle Physics and Medicine

Collegium Novodvorscianum, Kraków, July 5-10 2026

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DEVELOPMENT AND APPLICATIONS OF NEW NANOMATERIALS FOR HIGH SPEED, HIGH EFFICIENCY AND HIGH RESOLUTION RADIATION DETECTORS

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Abstract

This talk will describe proposed works towards a development and applications of new materials with superior secondary electron emission (SEE) and new class of detectors for radiation.

The SEE yield of heterostructures of ZnO nanoneedles coaxially coated with AlN or GaN has been studied for the first time using electron, ion, and X-ray beams. The SEE yield of the heterostructures is enhanced significantly by the intrinsic nanostructure of the ZnO nanoneedle templates as compared to the AlN and GaN thin films on Si substrates. These findings open up a way to develop new universal highly efficient radiation detectors based on the SEE principle by incorporating these one-dimensional (1D) nanostructures as a material of choice.

A new class of nanomaterials has been investigated by the Author with collaboration with several groups for the SEE properties and as candidate for highly efficient radiation detectors.

A similar idea was previously developed for carbon foils, boron-doped diamond and is now proposed for nanomaterials. Series of experiments have been performed with different radiation including electrons, ions and X-rays to better understand processes governing the SEE in 1D nanostructured materials. So far two international patents have been awarded for these works. Recently intensive works have been performed in collaboration with Cologne University and GSI in Germany on ZnO nanomaterials as possible candidates for radiation detectors for FAIR project.

Project was funded under the EC Horizon 2020 – Call: H2020-INFRAIA-2014-2015 - Proposal agreement No 654002 ENSAR2-PASPAG.

DEFECTS IN SEMICONDUCTORS AS SEEN BY POSITRONS

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Abstract

Positron annihilation spectroscopy is a powerful set of methods for the detection, identification and quantification of vacancy-type defects in semiconductors [1]. In the past decades, it has been used to reveal the relationship between (opto-)electronic properties and specific defects in a wide variety of elemental and compound semiconductors. In typical binary compound semiconductors, the selective sensitivity of the technique is at its best for vacancy defects on the cation sublattice (*e.g.*, Ga vacancies in GaN) that possess significant open volume and suitable charge: negative or neutral.

I will present recent advances in combining state-of-the-art positron annihilation experiments with *ab initio* computational approaches. The latter can be used to model both the positron lifetime and the electron-positron momentum distribution – quantities that can be directly compared with experimental results. In our laboratory, we have applied these methods to study a wide variety of semiconductor systems. I will give examples from group IV semiconductors such as Si and Ge [2], III-nitride semiconductors [3], as well as oxide semiconductors [4]. In all systems doping and alloying are used for tuning the fundamental parameters, leading to rich complexity in point defect related phenomena.

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FAST 3D POSITRONIUM LIFETIME ESTIMATION

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Abstract

Positronium lifetime imaging (PLI) extends conventional positron emission tomography by incorporating the time interval between positron emission and annihilation as an additional contrast mechanism. Estimating voxel-wise lifetime parameters in fully three-dimensional settings remains computationally challenging because the number of possible detectorstime channels grows rapidly while only a small subset is observed in practice. In this work we develop a scalable statistical framework for three-dimensional positronium lifetime estimation based on a time-of-flight–aware partial system matrix and a conjugate Bayesian inference scheme. The partial system matrix restricts the forward model to detector–time channels that are observed, substantially reducing memory and computational requirements while preserving the Poisson data model. Events are fractionally attributed to voxels through posterior weighting derived from the system matrix and reconstructed activity, enabling accumulation of weighted lifetime statistics directly from list-mode data. A conjugate Gamma–Exponential formulation then yields closed-form voxel-wise annihilation-rate estimates without iterative optimization. The framework is evaluated using both simulated data and a triple-coincidence dataset acquired with a J-PET prototype scanner and a NEMA image-quality phantom. Results demonstrate accurate recovery of activity and lifetime structure while achieving orders-of-magnitude faster lifetime estimation compared with iterative maximum-likelihood optimization. These results establish a computationally efficient foundation for large-scale three-dimensional positronium lifetime imaging.

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METASCINTILLATORS:
A DOOR OPEN TO THE 10 PS TIME-OF-FLIGHT PET CHALLENGE

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Abstract

The future generation of radiation detectors is more and more demanding on timing performance for a wide range of applications, covering a large energy spectrum from optical photons to high energy particles produced in collider physics experiments.

There is in particular a consensus for gathering a multi-disciplinary academic and industrial excellence around the ambitious challenge to develop a 10 ps Time-of-Flight PET scanner (TOFPET) [1]. The goal is to reduce the radiation dose (currently 5-25 mSv for whole body PET/CT), scan time (currently > 10 minutes), and cost per patient (currently ≈ 1000 € per scan), all by an order of magnitude, through the effective sensitivity gain related to the TOF performance. To achieve this very ambitious goal it is essential to significantly improve the performance of each component of the detection chain: light production, light transport, photodetection, readout electronics.

It has been shown that the possibility to reach 10 ps time-of-flight resolution at small energies, as required in PET scanners, although extremely challenging, is not limited by physical barriers.

One possible approach to overcome the intrinsic timing resolution limits of standard scintillators commonly used in PET scanners, such as BGO, LSO, LYSO, LGSO, etc… , is based on the metascintillator concept, a deep-tech approach, benefiting from recent important progresses in a number of disruptive technologies, to combine and optimize several functionalities in the same ionizing radiation sensor. This novel concept proposes a radical change of vision, addressing directly the scintillation mechanisms and light transport management with nanostructured scintillator heterostructures.

Indeed, such multi-functional heterostructures, combining the high stopping power of well know scintillators with the ultrafast photon emission resulting from the 1D, 2D, or 3D quantum confinement of excitons in nanocrystals, photonic crystals and/or photonic fibers for an optimum management of the scintillation light transport to the photodetectors, open the way to new radiation detector concepts with large design flexibility and unprecedented performance.

A first generation of metascintillators already demonstrated an improvement by a factor of 2 in time-of-flight resolution (and therefore in PET equivalent sensitivity) as compared to the state-of-the art with bulk scintillators, with commercially available photodetectors and readout electronics.

Perspectives for an ultimate gain of 20 (time-of-flight resolution of 10 ps) will be discussed.

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GENERATION OF EXOTIC IONS THROUGH THE COLLISION OF SLOW POSITRONS WITH SOLID SURFACES AND THEIR APPLICATIONS IN ATOMIC PHYSICS

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Abstract

Since its establishment in 2003, the positron research group at Tokyo University of Science has been conducting research focusing on exotic ions emitted from solid surfaces when slow positrons are incident upon them under ultra-high vacuum conditions. The research includes the efficient emission of positronium negative ions (Ps^-) from alkali metal-coated surfaces [1] and positron annihilation-induced ion desorption from solid surfaces [2]. In the former, we have investigated the properties of Ps^- [3-5] and succeeded in generating an energy-tunable positronium (Ps) beam by accelerating the generated Ps^- in an electric field and then converting it to Ps via laser irradiation [6]. Recently, we observed Ps diffraction through graphene thin layer using this Ps beam [7]. In the latter, we have observed the desorption of O^+ from TiO_2 surfaces and F_2^+ from LiF surfaces [8].

In this presentation, I will provide an overview of these research activities.

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Acknowledgements

This presentation is supported by JSPS KAKENHI Grants No. 25H00620.

ACCELERATOR BASED PET INNOVATIONS: POSITION SENSITIVE IMAGING AND ^{44}TI/^{44}SC GENERATOR DEVELOPMENT

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Positron emission tomography (PET) continues to benefit from parallel advances in detector instrumentation and radionuclide production, particularly in research environments where flexibility and innovation are essential. In this invited contribution, two complementary lines of work that address these challenges, spanning detector development for radiobiology and the feasibility of novel radionuclide production at accelerator facilities will be presented.

The first part of the presentation will focus on recent progress within the PANGoLINS [1,2] project toward the development of a compact, position-sensitive PET demonstrator tailored for radiobiological studies. The detector concept is motivated by the need for high spatial resolution and sensitivity when imaging radiotracer distributions in small samples and
experimental irradiation setups. The overall design philosophy, key choices in scintillator and photodetector technologies, and readout strategies, together with initial performance characterisation will be presented. Emphasis will be placed on how such systems can be
integrated into radiobiology and particle-therapy-related research workflows.

The second part will follow-up with a presentation of a feasibility study investigating the production of ^{44}Ti for a long-lived ^{44}Ti/^{44}Sc generator system, aimed at supporting PET research [3]. Owing to its favourable decay properties and growing interest for theranostic applications, ^{44}Sc represents an attractive PET radionuclide, provided a reliable supply can be established. We explore the prospects for a test irradiation at iThemba LABS, including considerations of target materials, irradiation conditions, expected yields, and radiological
constraints. This study represents an initial step toward assessing whether accelerator-based
production of ^{44}Ti could underpin a sustainable generator-based ^{44}Sc programme.

Taken together, these activities illustrate how coordinated developments in detector technology and radionuclide production can expand the capabilities of PET for medical physics and radiobiology. The presentation will also highlight opportunities for future experimental studies at accelerator-based facilities and the value of interdisciplinary collaboration in this field.

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OPERATIONAL SIGNATURES OF BELL PHOTONS BEYOND POLARIZATION FILTERS

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Abstract

At 511 keV, direct full polarization tomography of annihilation photons is not available. Even so, Compton scattering still makes it possible to infer polarization-dependent beam properties through statistical analysis. This talk presents an operational framework for identifying maximally entangled two-photon states in a high-energy regime beyond the reach of polarization filters. The starting point is a symmetry in the degree of polarization between a Compton-scattered signal beam and the corresponding coincidence-conditioned idler beam, first found for annihilation photons scattered by unpolarized electrons [1]. Later work showed that this symmetry is not restricted to a single annihilation-photon configuration, but is a general property of all Bell-equivalent two-photon states, with annihilation-photon pairs forming one member of that class [2]. Because the degree of polarization is an observable accessible through Compton polarimetry, this result opens a route to experimental discrimination of maximally entangled two-photon states. An explicit operational scheme will be presented in which signal-arm event selection defines coincidence-conditioned idler ensembles, azimuthal modulation in the idler arm is fitted in successive timing windows, and the resulting modulation levels are used for symbol inference. Relative to earlier work, the main contribution is therefore not a further state-classification result, but the construction of a single framework that links signal-arm selection, conditioned idler statistics, azimuthal fitting, and decoding. More broadly, this framework shows how polarization-dependent structure associated with entangled annihilation photons can be inferred operationally from coincidence-conditioned scattering observables, and it establishes a concrete Bell-state baseline for future studies of disturbance, effective channels, and nonideal measurement conditions.

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FLEXIBLE, MOBILE AND MODULAR PET IMAGING

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Abstract

Positron Emission Tomography (PET) is a powerful molecular imaging modality widely used in oncology, neurology, and cardiology. However, its broader clinical adoption is still limited by high system costs, restricted accessibility, and inflexible scanner geometries. The European Union's Horizon Europe research and innovation project PetVision aims to address these challenges by developing a next-generation, flexible, mobile, and modular PET imaging system based on limited-angle time-of-flight (TOF) technology.

In this contribution, I will present the underlying theoretical framework and simulation studies that guide the PetVision system design. The concept is based on a dual-panel detector geometry combined with ultra-fast timing performance, targeting a coincidence time resolution (CTR) of approximately 75 ps. Monte Carlo simulations demonstrate that such timing performance enables high-quality image reconstruction despite limited angular coverage, while significantly improving sensitivity and reducing system complexity.

Furthermore, I will provide the latest updates on detector development and experimental validation. These include advances in silicon photomultiplier (SiPM) technology, fast front-end ASIC electronics, and integrated photon detector modules, as well as recent timing measurements and prototype characterization results. Early experimental studies confirm that sub-100 ps CTR performance is achievable with current detector technologies, supporting the feasibility of the proposed system architecture.

The PetVision approach introduces a paradigm shift from conventional ring-based PET scanners toward adaptable flat-panel configurations that can conform to patient anatomy and clinical workflows. This flexibility enables new applications in point-of-care imaging, intensive care units, and image-guided interventions, while also reducing system cost and improving accessibility.

In conclusion, PetVision demonstrates that combining ultra-fast timing with modular detector design can enable clinically viable, cost-effective PET imaging systems with enhanced performance and broader applicability.

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Acknowledgements:

European Union's Horizon Europe research and innovation programme (grant agreement No. 101099896)

INTEGRATION OF COMPTON CAMERA WITH PET: A COMPTON-PET SYSTEM TOWARDS MULTI-ENERGY RADIONUCLIDE IMAGING

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Abstract

Integration of Compton cameras (CC) with PET (Compton-PET) can be advantageous for β^+-γ, and/or imaging radionuclides with multiple γ-energies. In the recent years, a few Compton-PET systems have been studied and are being developed [1-3], showing the potential of this technology to become a compact alternative to PET-SPECT systems [1], which faces challenges due to collimation in SPECT. CCs overcome this limitation and are more suitable for high-energy gamma emitting radiotracers [4, 5]. It has been previously shown by the IRIS group through simulations that joint CC and PET images of a Derenzo-like phantom filled with ^{89}Zr, ^{124}I, and, ^{18}F+^{95}T can be obtained successfully, demonstrating the capability of a Compton-PET system to image different radionuclides [6]. However, the simulations were performed in an ideal geometry where a CC is aligned axially perpendicular to a PET ring consisting of LSO crystals.

In the present work, simulation is performed based on a geometry that closely replicates our laboratory setup. Two detectors are positioned facing each other, while a CC is placed in the same plane, oriented perpendicular to the line connecting the back-to-back detectors. Coincidence data are collected with a source located at the center of the geometry, such that both PET detectors and the first plane of the CC are positioned equidistant from the source. Each of the four detectors consists of a $25.8 \times 25.8 \times 5$ mm^3 monolithic $LaBr_3$ crystal coupled to a SiPM (8x8 pixel array of 3.2 mm pitch). The image reconstruction algorithm has been developed and optimized by the IRIS group specifically for this imaging modality and is being applied to simulated data. We will present reconstructed images of point sources and/or a Derenzo phantom obtained using the simulated Compton-PET system. Successful imaging results will provide a strong basis for subsequent laboratory validation of the experimental Compton-PET system, enabling simultaneous β^+–γ and multi-energy radionuclide imaging.

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Preliminary In Vivo Mouse Imaging Study Using Quantum Entanglement-Based PET

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Abstract

Background and Objectives

Conventional PET suffers from scatter and random coincidences that cannot be fully suppressed by time or energy windows. Quantum Entanglement-based PET (QEPET) exploits the sinusoidal polarization correlation of entangled annihilation photon pairs (peaking at $\Delta\Phi \approx \pm 90°$), absent in noise events, enabling stronger noise rejection[1,2]. This study aims to experimentally verify the physical properties of QEPET and to demonstrate, for the first time, in vivo imaging of tumor-bearing mice using quantum entanglement information.

Methods

A custom triple-ring PET system was developed using Ce:GAGG scintillators with dynamic Time-over-Threshold (dToT) readout, achieving an energy resolution of 9.5% at 511 keV and a time resolution of 16.8 ns. Entangled pairs were extracted by identifying Compton scatter pairs from the same annihilation event and reconstructed with ML-EM. Physical validation used a single-rod phantom in real-system experiments and Geant4 simulations. For in vivo imaging, A431 xenograft BALB/c nude mice were administered ^{18}F-FDG (≈ 1.8 MBq) and scanned for 75 minutes.

Results

Sinusoidal modulation of $\Delta\Phi$ was confirmed in both experiment and simulation. The contrast ratio R was 1.91 (experiment) and 2.14 (simulation), both exceeding the classical limit of 1.63, confirming quantum entanglement detection. QEPET showed ~8% higher pair extraction accuracy than standard PET at high dose levels. Standard PET yielded higher Signal-to-Background Ratio (approximately 1.27× that of QEPET at 20 iterations), while QEPET yielded higher Signal-to-Noise Ratio (approximately 1.28× that of standard PET). In mouse imaging, normal organs including the thorax and bladder were correctly visualized, confirming proper system function.

Conclusions

Quantum entanglement in annihilation photon pairs was experimentally demonstrated, and the first in vivo QEPET imaging of tumor-bearing mice was achieved. Future work will focus on repeating the experiment under fasting conditions and developing a reconstruction algorithm integrating the complementary strengths of standard PET and QEPET.

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EXPLORING A HIMALAYAN INVASIVE PLANT: PHYTOCHEMICAL PROFILING, *IN SILICO* ANALYSIS, AND *IN VITRO* EVALUATION FOR ANTI-ACNE POTENTIAL

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Abstract

Background: Acne vulgaris is a multifactorial, immune-mediated inflammatory dermatosis affecting over 80% of the global population. Standard therapies (retinoids, benzoyl peroxide, and antibiotics) are constrained by adverse effects and rising antimicrobial resistance, motivating the exploration of phototherapeutics.

Objectives: To evaluate the anti-acne potential of selected Himalayan invasive plant species using an integrated approach that includes phytochemical profiling, *in silico* analysis (network pharmacology and molecular docking), and *in vitro* assays (antioxidant activity and anti-microbial potential).

Methodology – Three ethnopharmacologically relevant plant species – *Ageratum houstonianum, Bidens pilosa* and *Euphorbia hirta* (EH) were initially selected. Based on the preliminary phytochemical screening, EH was chosen for detailed investigation. Extraction was optimised using ultrasonication-assisted extraction, varying solvent ratios. The optimised extract was subject to qualitative/quantitative analyses; LC-MS and HPLC were used to identify and quantify phytoconstituents. The identified compounds were further analysed using network pharmacology and molecular docking against acne-associated molecular targets. The biological activity of the extract was assessed through *in vitro* antioxidant assays (ABTS and FRAP) and antimicrobial assays against common bacterial strains, including *S. aureus, E. coli, P. aeruginosa*, and *B. subtilis*.

Results – Phytochemical screening and quantitative estimation of total phenolic and flavonoid contents revealed that the 85% methanol:15% water extract of EH exhibited the highest levels of phenols and flavonoids (123.52 mg gallic acid equivalent/g and 43.38 mg rutin equivalents/g), respectively. The LC-MS identified key flavonoids, including quercetin and kaempferol, which were further quantified by HPLC. Network pharmacology (NP) analysis identified 87 common targets between phytoconstituents and acne-related genes, including key proteins TNF, AKT1, STAT3, SRC, NR3C1, AR, and CYP19A1. Pathway enrichment indicated significant involvement in steroid hormone biosynthesis pathways. Molecular docking (MD) demonstrated strong binding affinities between phytochemicals and key target proteins of the disease, including TNF and AKT1. The extract exhibited significant antioxidant activity, with 97.6% inhibition in the ABTS assay and a FRAP value of 46.3±12.84 mg AAE/G at 100 µg/mL. Additionally, broad-spectrum antibacterial activity was observed against common bacterial strains.

Conclusion – The findings indicate that EH possesses significant anti-acne potential, supported by its rich phytochemical profile, potent antioxidant and antimicrobial activities, and mechanistic plausibility from NP and MD. Further work will focus on improving the therapeutic performance of the extract by incorporating it into lipid-based nanocarrier systems to overcome stability and skin permeation limitations, as well as on its biological evaluation.

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PERFORMANCE EVALUATION OF A BRAIN PET PROTOTYPE WITH CROSSHAIR LIGHT-SHARING DETECTORS

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Abstract

Background and objective. For accurate brain positron emission tomography (PET) imaging, high spatial resolution is essential. Improving spatial resolution requires reducing the ring diameter and using scintillators with a finer pitch [1]. In addition, depth-of-interaction (DOI) capability is necessary to achieve uniform spatial resolution across the entire field-of-view (FOV). We developed a crosshair light-sharing (CLS) detector using 1.6 mm-pitch scintillators that enables both time-of-flight (TOF) and DOI measurements [2]. In this study, we evaluated a brain PET prototype with CLS detectors in accordance with the NEMA NU2-2024 standards [3]. *Methods.* Using 252 CLS detectors, we developed a brain PET prototype. The ring diameter and axial FOV are 29.6 cm and 18.3 cm, respectively. The prototype can scan both sitting and lying positions by adjusting the angle and height via side handles. A custom-made hollow-ring phantom was used for normalization. For the performance evaluation, we measured filtered back-projection (FBP) spatial resolution, count rate performance, image quality with a brain-sized image quality phantom, and TOF resolution, following NEMA NU2-2024 standards. For imaging performance, we measured the rod phantom and the hemispherical Hoffman phantom with the ordered-subset expectation-maximization (OSEM) algorithm. *Main results.* The FBP spatial resolution was 2.1 mm at a 1 cm offset of the FOV center. 1 mm rods were visualized at both the center and offset positions. The peak noise-equivalent count rate (NECR) was 16.8 kcps at 7.2 kBq ml^{-1}. The scatter fraction and TOF resolution at the NECR peak were 22.6% and 271.4 ps, respectively. The best TOF resolution was 241.2 ps at 0.42 kBq ml^{-1}. The image contrast of 4 mm hot spheres was about twice as good as that of a hemispherical brain PET, VRAIN [4], at a similar noise level. We confirmed clearly separation of gyri and sulci in the Hoffman phantom. *Conclusion.* We demonstrated that the brain PET prototype with CLS detectors has excellent image quality for small structures.

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NUCLEAR MEDICINE IMAGING WITH ANGULAR CORRELATION MEASUREMENT FOR LOCAL MICROENVIRONMENT SENSING

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Abstract

Nuclear medicine can provide highly sensitive molecular imaging (~pmol/L) inside the body by visualizing the distribution and kinetics of radiotracers using X-rays and gamma rays. However, conventional modalities such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) are limited to imaging tracer accumulation and cannot obtain microenvironmental information (e.g., pH, temperature, intermolecular interactions). Here, we propose and demonstrate a novel nuclear medicine imaging approach based on cascade gamma-ray angular correlation measurements for local microenvironment sensing[1)].

Cascade radionuclides such as ^{111}In, widely used in SPECT, emit multiple gamma rays sequentially, which exhibit angular correlation. This correlation is perturbed by the precession of the nuclear spin in the intermediate state under local electromagnetic fields, resulting in a modification of the angular correlation. Angular correlation measurement has been commonly used in material science[2)] as perturbed angular correlation (PAC) spectroscopy. ^{111}In is also a PAC probe due to the 85 ns mean lifetime of its intermediate state. We combined double-photon coincidence imaging, which localizes radionuclides using directional detectors, with angular correlation measurements, and demonstrated both imaging of ^{111}In accumulation and pH sensing using a measurement system with a time resolution of approximately 9 ns and time-integrated angular correlation analysis[1)].

Recently, we also developed a higher time resolution measurement system with a time resolution of approximately 300 ps, consisting of eight 8×8 array GFAG pixel scintillators arranged in a ring, enabling full angular coverage. Using this system, we performed time-differential angular correlation analysis using all angles. The results obtained for $^{111}InCl_3$ solutions at different pH levels are consistent with previous reports based on coincidence detection at only 90° and 180° [2)]. In the presentation, we will introduce the details of our measurement system and recent results of fundamental studies on angular correlation for biomedical applications.

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POSITRON ANNIHILATION IN BIONANOTECHNOLOGY: DESIGN PRINCIPLES FOR POLYMER-BASED BIOSENSORS

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Abstract

This work presents a comprehensive and quantitatively oriented analysis of the role of polymer microstructure and free volume in governing the performance of electrochemical biosensors. Particular emphasis is placed on the application of positron annihilation spectroscopy (PAS) as a uniquely sensitive technique for probing sub-nanometer free-volume characteristics and establishing direct structure-function relationships. By integrating results from organic-inorganic hybrid ureasil-based and photocross-linked polymers, a consistent correlation is demonstrated between free-volume parameters (size, distribution, and thermal expansion) and key biosensor characteristics, including sensitivity, mass transport efficiency, and enzyme activity. It is shown that variations in free-volume cavity size and connectivity systematically control analyte diffusion, enzyme accessibility, and reaction kinetics within polymer matrices. Furthermore, the combined influence of network topology (crosslinking density, phase separation) and chemical functionality (polymer composition, photoinitiator effects) on free-volume evolution during polymerization and aging is elucidated. In-situ PAS studies of photopolymerization reveal that kinetic pathways directly determine the final microstructure and, consequently, the functional performance of biosensing platforms. Based on the relationships identified between polymer structure and biosensor performance, several general design principles can be formulated [1]: (i) optimization of free volume is critical to balance enzyme accessibility with structural stability; (ii) crosslinking density should be carefully controlled to regulate diffusion and mechanical integrity; (iii) minimizing structural heterogeneity improves reproducibility, while polymer chemistry governs electrostatic interactions that influence substrate transport; and (iv) finally, surface-confined immobilization enhances sensitivity by maximizing the effective enzyme concentration at the electrode interface. These principles collectively provide a framework for the rational design of high-performance electrochemical biosensors.

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A DEEP LEARNING FRAMEWORK FOR WATER-EQUIVALENT PORTAL DOSE RECONSTRUCTION AND TREATMENT ERROR DETECTION USING EPID IMAGING FOR PHANTOMS AND PATIENTS

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Background and Objective: Electronic portal imaging devices (EPID) enable transit in vivo dosimetry (IVD), but their widespread clinical use is limited by non-linear detector response and the associated labor-intensive calibration procedures [1]. To overcome this, we developed a deep learning (DL)-model, that can reconstruct water-equivalent portal dose (PD) directly from EPID images. The goal of this work is to evaluate the accuracy of our DL model for portal dose reconstruction in various phantom and patient scenarios, and to assess the sensitivity of the framework to detect different types of dose errors.

Methods: A dataset of over 300 EPID measurements and corresponding portal dose simulations from the Monaco treatment planning system (TPS) was generated using various phantoms and irradiation fields, as well as patient data. A 2D U-Net model was trained to convert EPID images into portal dose images. To assess error detection sensitivity, additional EPID measurements were acquired while introducing intentional delivery errors in phantoms, including monitor unit variations, setup shifts, gantry angle deviations, and anatomical changes. Model performance was evaluated using mean absolute error (MAE), gamma-index (γ) analysis (1%/1 mm, 2%/2 mm, 3%/3, 4\%/mm, and 5%/5 mm), and dose difference-based metrics.

Main results: The DL model achieved high accuracy in PD reconstruction. Mean γ passing rates were 94.2% for phantoms and 97.0 3% for pre-treatment patient images, respectively, with predictions computed in under 1 second. For error detection, monitor unit variations of 3% were identified (γ passing rates <95%). Sensitivity to setup and gantry errors depended on field size and phantom, with improved sensitivity for larger fields. Tissue thickness variations of approximately 3 mm were detectable. Combining γ-index analysis with dose difference metrics enhanced the overall sensitivity of the framework.

Conclusions: The proposed DL framework enables fast and accurate reconstruction of water-equivalent portal dose from EPID images while providing reliable detection of clinically relevant delivery errors. The data-driven and TPS-based approach is unique with respect to existing studies. By eliminating the need for complex calibration procedures and integrating multiple alert metrics, our framework supports efficient, safe, and compliant radiotherapy treatments.

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Acknowledgements. This research was partly funded by the InTrEPID project (MUR PRIN 2022CWXR8K - CUP I53D23000520006)217 and the ARTEMIS project (INFN, CSN5).

μPPET DETECTOR SYSTEM

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Abstract

In the astroparticle community, the longstanding discrepancy between model predictions and experimental measurements of the muon count at ground level remains unresolved — the muon puzzle. The μPPET project investigates a possible solution based on QCD corrections arising from polarisation effects induced by the geomagnetic field during atmospheric shower development [1]. The predicted signature is an anisotropy in the muon trajectory distribution relative to the primary cosmic-ray direction.

To test this hypothesis, μPPET repurposes J-PET detectors: the Big Barrel (BB) [2] acts as a muon tracker, while the Modular detector [3] is reconfigured as a rooftop array — the Modular Array (MA) — at the Department of Physics, Astronomy, and Applied Computer Science at Jagiellonian University, for shower reconstruction.

In this talk, we present the current status of the detector system. We cover BB calibration for muon identification, the MA design and synchronization architecture, the definition of event classes, and the future analysis framework — including the neural network architectures planned for improving reconstruction and classification performance.

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AI-DESIGNED MINI-PROTEINS FOR TARGETED IMAGING AND THERAPY

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Abstract

Recent advances in computational methods such as AlphaFold and RFdiffusion enable the de novo design of small, stable proteins (“mini-proteins”) with precisely defined structures and binding properties. These molecules are significantly smaller than antibodies and can be engineered to bind specific targets with high affinity.

Their size places them in a favorable regime for in vivo applications: rapid tissue penetration, tunable blood clearance, and reduced background signal. When labeled with radioactive or fluorescent probes, they provide high-contrast imaging. The same scaffolds can be adapted to carry therapeutic payloads, allowing direct translation from target detection to intervention.

From a physical standpoint, mini-proteins act as programmable carriers that control the spatial distribution of signal or energy at the molecular level. Their behavior can be tuned through design- modulating binding affinity, stability, and pharmacokinetics - to achieve predictable system-level outcomes.

This talk will introduce the basic design principles behind AI-generated mini-proteins and highlight their emerging role as a flexible platform for targeted imaging and therapy.

Acknowledgements

Funding: ERC Advanced No. 1011998074, NCN 2021/42/A/ST2/00423 for P.M and NCN 2022/47/I/NZ7/03112 for E.S.

STUDIES OF THE PHI-NUCLEON INTERACTION USING FINAL-STATE INTERACTIONS

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Abstract

A hadron is composed of quarks and gluons, the elementary particles responsible for the strong interaction, and constitutes most of the visible matter in the universe. Elucidating hadron–hadron interactions is therefore essential for understanding the origin and evolution of matter. The force generated by meson exchange, in which each hadron transfers one quark to the other, is well established through scattering experiments of hadrons and spectroscopic studies of excited hadrons. However, much less is known about gluon dynamics in hadron–hadron interactions and reactions. When the two hadrons do not share quarks of the same flavor, meson exchange is forbidden, and the interaction is expected to be dominated at leading order by gluon exchange. Gluon-mediated mechanisms are essential for understanding reactions in which new quarks are produced, as well as the properties and production mechanisms of exotic hadrons containing $ccc\bar{c}$ and $b\,b\,b\bar{b}$ pairs.

To elucidate gluon dynamics in hadron–hadron interactions, we investigate low-energy scattering between a nucleon NN ($uuuuuu$ or $uuuuuu$) and a $\phi\phi$ meson ($sss\bar{s}$). The strength of the $\phi\phi NN$ interaction remains controversial. While near-threshold $\phi\phi$ photoproduction assuming the vector-meson dominance (VMD) model suggests a weak interaction [1], analyses of the nuclear mass-number dependence of incoherent $\phi\phi$ photoproduction from nuclei [2], momentum correlation in high-energy proton-proton collisions [3], and lattice QCD calculations [4] indicate stronger attraction.

To clarify this issue, we analyze $\gamma\gamma uu \rightarrow \phi\phi\pi\pi^0 pppp$ data obtained in the LEPS experiment at SPring-8 together with new near-threshold $\pi\pi^- pp \rightarrow \phi\phi pp$ data from the planned E45 experiment at J-PARC, thereby enabling the extraction of the low-energy $\phi\phi NN$ scattering parameters without relying on the VMD framework. These studies of $\phi\phi NN$ interaction using final-state interactions will be presented.

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Acknowledgements

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PROBING THE NUCLEAR PERIPHERY VIA THE COLD ANNIHILATION OF ANTIPROTONIC ATOMS

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Abstract

The density distribution at the surface of atomic nuclei is still not well known, particularly the halo and neutron skin which are almost invisible to electromagnetic probes. Measurements of the nuclear surface are of particular interest as they help test our understanding of the fundamental nuclear forces [1] and allow us to explore the density dependence of the nuclear symmetry energy, which links to the properties of neutron stars [2]. In this respect, the antiproton is a particularly valuable tool, as it is notoriously sensitive to regions of low hadronic density [3]. In an antiprotonic atom, the antiproton can be bound in radially localized Rydberg states. If the annihilation takes place at the outer nuclear periphery, then the high-energy mesons released during the annihilation can miss the residual nucleus entirely, resulting in a 'cold' nuclear fragment with only one less nucleon [4,5].

In this respect, we are presenting a new technique which could probe these cold annihilation fragments. Building on recent proof-of-principle studies that successfully demonstrated the capture and identification of annihilation-induced ions in a Penning-Malmberg trap [6]. This work outlines a method to perform TOF spectrometry of cold nuclear annihilation fragments, which will enable us to explore the lifecycle of antiprotonic atoms and give access to a new tool to probe the composition of the nuclear stratosphere.

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IN-BEAM PET FOR FIRST IN VIVO PROTON RANGE ASSESSMENT IN SMALL-ANIMAL THERAPY WITH ONLINE IMAGE RECONSTRUCTION

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Introduction: The first precision image-guided in vivo intensity modulated proton irradiation (IMPT) of small animals was performed at the Danish Center for Particle Therapy (DCPT), with a dedicated platform developed within the SIRMIO project [1]. Online image reconstruction was achieved using an in-house designed in-beam positron emission tomography (PET) system [2].

In Vivo Experiments: Two sets of experiments were conducted delivering up to 60 Gy (RBE) using IMPT plans with 20 to 40 MeV proton beams in one or two fractions.

Detector Technology: The in-beam PET scanner, developed at LMU (Germany) in collaboration with QST (Japan), comprises 56 scintillator modules arranged in a spherical geometry. Each module integrates 3 LYSO crystal layers to provide depth-of-interaction (DOI) and sub-mm spatial resolution [3].

Online Reconstruction and Simulation: A dedicated computational framework was developed to compensate for automated mouse translation and rotation during in-beam PET data acquisition. This approach emulates multi-field IMPT beam scanning using a fixed, focused beam of variable energy [4]. The framework combines positron emitter production maps from the research version of RayStation (RaySearch Laboratories AB, Sweden) treatment planning system [5] with a motion-aware online reconstruction algorithm. This enables co-registration of dynamic PET events to a static CT reference frame, facilitating direct comparison of predicted and measured activity distributions during irradiation.

Results: Preliminary data show the capability of the PET system to visualize, during irradiation, the activity maps produced by beam activation in biological tissue. After sensitivity and motion corrections, a strong correlation was found between experiment and simulation, confirming the sub-mm accuracy of the model and imaging system. Additionally, washout of positron emitter nuclei during irradiation was observed, providing insight into tissues types and washout dynamic [6].

Discussion: The development of the first spherical, high-resolution in-beam PET scanner for small animals represents a fundamental advance, particularly for tracking short-lived positron emitters such as ^{15}O, which are difficult to observe with off-beam PET due to their short half-life.

Conclusions: This proof-of-concept study supports the feasibility of online range verification with an in-beam PET scanner during proton irradiation of small animals. The combination of Monte Carlo simulations and online reconstruction allows for quick feedback on delivery accuracy and may enable biological interpretation. These findings pave the way for advanced preclinical proton therapy research and the integration of online biological information into precision radiation oncology.

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Acknowledgements ERC SIRMIO ID: 725539

IN VIVO POSITRONIUM RATIO IMAGING VIA DIRECT LOCALISATION OF O-PS THREE-PHOTON ANNIHILATION

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Abstract

1. Introduction

In positron emission tomography (PET), a fraction of positron forms a metastable bound state called ortho-Positronium (o-Ps), then decay into 3γ or 2γ. The o-Ps $3\gamma/2\gamma$ decay ratio depends on tissue oxygen partial pressure and microstructural voids, offering a novel approach to evaluate tumour hypoxia and microenvironments. We developed a "3-photon PET" system to directly image o-Ps 3-photon annihilations and propose "Positronium Ratio Imaging (PRI)" to visualise the $3\gamma/2\gamma$ distribution [1]. Here, we report its fundamental performance and proof-of-principle results using phantoms and tumour-bearing mice.

2. Methods

Using a ring-type HR-GAGG/SiPM detector and ^{18}F-FDG, we implemented a direct event reconstruction algorithm based on 3-photon decay kinematics. After evaluating spatial resolution, we compared the $3\gamma/2\gamma$ ratios among a porous material (XAD-4), hypoxic water, and pure water.
Furthermore, we performed in-vivo imaging of subcutaneous tumor model mice to evaluate the $3\gamma/2\gamma$ distribution.

3. Results

The system achieved a spatial resolution (FWHM) of <1.1 cm without relying on time-of-flight or conventional tomographic reconstruction. Phantom studies demonstrated significantly higher $3\gamma/2\gamma$ ratios in both porous and hypoxic regions compared to pure water. In-vivo experiments revealed a heterogeneous $3\gamma/2\gamma$ distribution across the body. Detailed analyses and clinical feasibility will be discussed.

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PROGRESS IN DEVELOPING A SMALL TWO-HEAD PROTOTYPE SCANNER FOR RECONSTRUCTION-FREE DIRECT POSITRON EMISSION IMAGING

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Abstract

Positron emission tomography (PET) maps the three-dimensional distribution of radiolabeled tracers by measuring coincident 511 keV annihilation photon pairs. As in all tomographic modalities, recovering the source distribution requires a mathematical reconstruction step, which introduces geometric constraints that ultimately dictate the system design. In time-of-flight (TOF) PET, the arrival time difference of the two annihilation photons constrains the annihilation locus along the line of response. Commercial systems today achieve coincidence timing resolutions (CTR) of ~200 ps FWHM, improving image signal-to-noise but falling far short of event-by-event localization. Once the CTR reaches the few-tens-of-picoseconds level, each detected coincidence can be directly placed in space from its TOF difference alone, making image reconstruction unnecessary. We call this direct positron emission imaging (dPEI). Being free from the reconstruction step, dPEI scanner geometry is no longer constrained to the conventional closed-ring design, allowing more flexible configurations tailored to specific imaging purposes. The first demonstration [1] was conducted using two single-channel Cherenkov-radiator integrated microchannel plate photomultiplier tubes (CR-IMPs), which emit and detect Cherenkov photons only. As a next step, we are developing a small two-head prototype scanner, comprising the following key developments. First, the pure Cherenkov radiator has been replaced with BGO, which emits both Cherenkov and scintillation photons [2]. Second, for scaling up, we are developing multi-anode BGO-IMPs to provide spatial and energy information, both of which are required for quantitative imaging. Third, to process ultrafast signals from these detectors, we are developing a high-precision digitizer based on time-to-digital converters implemented on FPGA [3]. Finally, CNN-based timing estimation is also being developed. These innovations bridge the gap between a proof-of-principle experiment and a first full system using dPEI. This talk presents the status of our development, including preliminary results from each component, and discusses strategies toward the first multi-channel prototype system.

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Acknowledgements

This work was supported by the National Institutes of Health grant R01 EB033536.

POSITRONIUM IMAGING THROUGH ENERGY MEASUREMENTS IN 3-GAMMA ANNIHILATION EVENTS

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Abstract
Positron Emission Tomography (PET) is a non-invasive and widely researched medical imaging technique used to monitor physiological functions in the body with diagnostic applications in fields such as oncology and neurology. PET relies on detecting gamma rays from positron-electron annihilations to estimate the location of radioactive tracers within a patient's body. In tissue, over 40% of annihilations proceed from the formation of positronium, an unstable positron-electron bound state, with about 0.5% of positronium self-annihilating into the rare emission of three gamma rays. Recently, positronium imaging has emerged as a promising complementary diagnostic tool to PET [1], with the first in-vivo positronium image of the human brain published in late 2024 [2]. Positronium imaging involves tomographic imaging of parameters characterizing the properties of positronium in tissue. These parameters can include positronium formation probabilities, annihilation lifetimes, or the 3-gamma to 2-gamma annihilation ratios. Because the characterizing parameters of the annihilation are sensitive to the surrounding tissue environment, positronium imaging can be correlated with hypoxia and structural voids in tumors. Such correlations can provide diagnostic information that conventional medical imaging modalities such as PET, Computed Tomography (CT), or Magnetic Resonance Imaging (MRI) cannot offer. Furthermore, since positronium imaging measures positron annihilations, it can potentially be performed in parallel with conventional PET, providing complimentary diagnostic information without delivering any additional radioactive dose to the patient.

The present work demonstrates an approach for imaging 3-gamma positron annihilations from β^+ decays of ^{18}F [3]. The isotope is produced through a novel method of neutron activation of a polytetrafluoroethylene (Teflon) disk. Measurements were performed using the 8π gamma-ray spectrometer, a highly efficient and selective ball array of 72 Bismuth Germanium Oxide (BGO) detectors arranged in an icosahedron geometry with ~95% solid-angle coverage. Coupled with a digital data acquisition system, the 8π spectrometer provides waveform digitization and online multiplicity filtering capabilities, enabling efficient and selective measurement of rare 3-gamma positron annihilations. An energy-based reconstruction method was applied to produce three-dimensional 3-gamma PET images with a FWHM point spread of 4.0 cm at the center of the array.

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Acknowledgements
We acknowledge the support of the Natural Sciences and Engineering Research Council of Canada (NSERC). Nous remercions le Conseil de recherches en sciences naturelles et en génie du Canada (CRSNG) de son soutien.

INHALABLE DRUG DELIVERY SYSTEMS BASED ON LIPIDS AND POLYMERS TO TREAT LUNG DISEASES

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Abstract

Advanced drug delivery systems (DDS) have recently been engineered to provide accurate tissue targeting and controlled release of active pharmaceutical ingredients to the defined place in the body to minimize systemic exposure. DDS in the form of dry powder for inhalation play an important role in the management and treatment of pulmonary diseases. Lipids, degradable polymers, e.g. polyanhydrides, are excellent candidates for producing such advanced DDS [1]. In our group, we have developed inhalable stimuli-sensitive drug carriers that are intended to improve the efficacy of lung cancer therapy through guided accumulation directly at the tumour site and controlled drug release triggered by an alternating magnetic field, resulting in a local increase in temperature. Such DDS are in the form of solid lipid microparticles composed of fatty acids loaded with superparamagnetic iron oxide nanoparticles (SPIONs) and paclitaxel. Microparticles meet various criteria, including suitable aerodynamic properties, high drug loading efficiency, sufficient mobility in the magnetic field, melting temperature under hyperthermia conditions, and enhanced *in vitro* efficacy as studied in contact with healthy and malignant lung epithelial cells [2,3]. Furthermore, we developed polyanhydride DDS of antibiotics and quorum sensing inhibitors (QSi) for the treatment of bacterial infections in patients with chronic obstructive pulmonary disease (COPD) exacerbations. These DDS are microparticles made of poly(sebacic acid) derivatives loaded with antibiotics (gentamycin, tobramycin, and azithromycin) and QSi (curcumin, linolenic acid) that have a synergistic effect [4]. Microparticles have a suitable size for inhalation (aerodynamic diameter in the range of 1-5 µm), degrade in a few days and release drug cargo, which is capable of killing pathogenic bacteria in planktonic form and preventing biofilm creation. The system is cytocompatible with lung epithelial cells and lung tissue, as shown by *in vitro* and *ex vivo* tests, respectively [5-6]. More recently, we are working on pollen-like DDS polymeric microparticles containing lipid nanoparticles (LNPs) loaded with ensifentrine for the treatment of chronic obstructive pulmonary disease. Our results show that DDS based on lipids or polyanhydride microparticles can be useful in the treatment of life-threatening lung diseases.

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This study was supported by the NCN project (No 2025/56/Q/ST5/00240) and by the Program „Excellence Initiative – Research University" and the Subsidy for AGH University of Krakow, Poland

AI-ENHANCED IN VITRO AND IN VIVO IMAGING OF PRECLINICAL CANCER MODELS

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Artificial intelligence is increasingly transforming preclinical cancer research by enabling quantitative analysis in both in vitro and in vivo models. We propose an integrated AI framework covering the full imaging pipeline, from acquisition and reconstruction to segmentation, classification, and biomarker discovery. In *in vitro* studies, AI enables automated segmentation of single cells, cell colonies, and 3D spheroids, using planimetric quantification of area, perimeter, circularity, growth kinetics, and structural heterogeneity, providing objective readouts for clonogenic assays and treatment-response studies. Machine learning can also classify cellular phenotypic states and predict culture conditions, including hypoxia versus normoxia, using morphological, textural, and time-resolved features from label-free microscopy or high-content imaging.

In in vivo studies, AI substantially improves longitudinal imaging of murine tumor models. In ultrasound, deep learning-based segmentation of serial 2D frames enables reproducible volumetry and shape-agnostic 3D reconstruction of irregular tumors, reducing operator dependence and supporting objective therapy monitoring [1]. Automated ultrasound segmentation combined with voxel-based 3D reconstruction also enabled cross-sectional and cross-modal validation against calipers, micro-CT, and tumor weight, supporting AI-assisted volumetry in preclinical oncology. Beyond ultrasound, AI can further enhance electron paramagnetic resonance imaging (EPRI) through denoising, reconstruction, registration with complementary anatomical modalities, and quantitative analysis of oxygen maps. EPRI provides quantitative *in vivo* tumor oxygenation imaging with approximately millimeter-scale spatial resolution and near-absolute pO_2 mapping, making it valuable for identifying hypoxic subregions associated with therapy resistance [2].

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This work was funded by NCN (grants 2022/45/B/NZ4/01215, 2022/45/B/NZ5/01695) and NCBiR (grant ENM3/IV/18/RXnanoBRAIN/2022). The Vevo F2 ultrasound system was funded by the Jagiellonian University, within the Strategic Programme Excellence Initiative.

FROM SYNGENEIC TO HUMAN MELANOMA MODELS: LONGITUDINAL MICROCT TRACKING OF METASTATIC PROGRESSION IN MICE

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Abstract

Longitudinal monitoring of metastatic progression is critical for advancing preclinical oncology. Robust melanoma models are essential to capture the complex dynamics of tumor dissemination. In vivo micro-computed tomography (micro-CT) provides an innovative, standalone modality to track these processes non-invasively, offering vital insights into both structural tumor burden and functional respiratory metrics.

Early syngeneic studies utilizing the B16-F10 murine cell line validated micro-CT for characterizing macroscopic lung metastases and corresponding declines in aerated volume. However, recent efforts have shifted toward aggressive humanized models. Specifically, the WM-266-4 melanoma cell line established in immunosuppressed SCID mice offers a unique platform to closely study human tumor metabolism and phenotype.

Following intravenous injection of WM-266-4 cells, longitudinal respiratory-gated micro-CT tracked systemic disease progression over 24 days. The model exhibited profound cachexia, evidenced by continuous body weight reduction and a 15.3% loss of body fat. Concurrently, functional respiratory capacity severely deteriorated; aerated lung volume (ALV) declined by 23.5%, significantly increasing respiratory effort. This deterioration was accompanied by a transient compensatory hyperinflation in total lung volume prior to a steep terminal decline.

Strikingly, despite the severe systemic decline and respiratory impairment, no discrete tumor nodules were detectable in the lungs, liver, or brain via in vivo or high-resolution ex vivo micro-CT. This radical divergence from traditional macroscopic metastasis models suggests that WM-266-4 dissemination manifests primarily as diffuse micro-metastases, infiltrative growth, or tumor dormancy falling entirely below the spatial resolution threshold of micro-CT.

These findings highlight the critical value of functional micro-CT imaging. By capturing systemic metabolic shifts and respiratory decline independent of macroscopic nodule formation, micro-CT enables nuanced, longitudinal evaluations of complex human melanoma phenotypes, micro-metastatic infiltration, and tumor dormancy in living systems.

LIGHT-INDUCED DESORPTION OF POSITRONIUM

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Abstract

When a positron is implanted into a solid and stops in a subsurface region, it can diffuse back to the surface before it is annihilated. This positron may either be re-emitted from the solid into a vacuum, become trapped in a surface image potential (known as a surface state), or interact with an electron on the surface to form positronium (Ps). Re-emitted positrons do not contribute to the main part of positron lifetime spectra; instead, they create structures in the background at longer timescales. Conversely, positrons annihilated in the surface state contribute to the positron lifetime spectrum with a component that typically has a lifetime in the range 300 - 400 ps. This surface component, along with a long-lived Ps contribution, is observed in positron lifetime spectra measured using low-energy positrons across all materials.

Positrons that are trapped in the surface state can escape by capturing a valence electron and forming Ps. This desorption of Ps is a thermally activated process, limited by the binding energy of the positron in the surface state, and is observed as a significant increase in Ps contribution after heating the sample to elevated temperatures.

Furthermore, our work demonstrates that the release of positrons from the surface state through the emission of Ps can also be triggered by incident photons with energy equal to or greater than the binding energy of the surface state. Since this binding energy typically ranges around a few eV, light-induced Ps desorption can occur when the sample is illuminated with infrared or visible light.

In this report, we present low-energy positron lifetime measurements of metals and semiconductors. The samples were analyzed both in the dark and during irradiation with light of various wavelengths. A notable increase in Ps yield on the surface due to light illumination was observed for all samples using positrons with incident energies below 1 keV, providing direct evidence for light-induced Ps desorption.

ADVANCED COMPUTATIONAL MODELS FOR THERANOSTIC DIGITAL TWINS

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Abstract

Cancer research is going through a paradigm shift, transitioning towards exploring and treating malignancy as a systemic disease through multi-scale modelling of cancer diagnosis and therapy. Yet, the bulk of research in the field is directed towards understanding the genetic and molecular characteristics of this disease. A holistic approach is adopted through cancer systems biology to comprehend the behavior of malignancies. The role of multimodality precision imaging in the management of cancer patients is well-established. Costly and time-consuming animal testing and human clinical trials are limiting factors in clinical research. A new concept in the field of radiopharmaceutical therapies (RPTs) of cancer, referred to as computational nuclear oncology, involving the use of theranostic digital twins (TDTs) and *in silico* virtual clinical trials, which is the central topic of this talk, has recently emerged and is expected to result in a major breakthrough in theranostics. Computational models, such as DTs—virtual patient replicas created from but not limited to imaging and clinical data, have emerged as tools to generate synthetic data and simulate radiopharmaceutical kinetics to guide *in silico* treatment planning. The theoretical foundations and ethical aspects have been described at some level of detail; yet the methodological basis and translational underpinning remain unexplored. Its implications will be far reaching, with substantial potential impact in basic science, clinical practice, and biomedical research. At the same time, TDTs will open up a new direction in the field of cancer treatment and theranostics that will revolutionize the way clinical trials are performed today. The role of artificial intelligence in building sophisticated DT models will be explored in detail.

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This work was supported by the Swiss National Science Foundation under grant No. 30030–231742 and Geneva League Against Cancer under grant LGC 2402.

IMAGING TECHNOLOGY DEVELOPMENTS FOR THERAPEUTIC RADIOPHARMACEUTICALS

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Abstract

Optimizing the efficacy and safety of therapeutic radiopharmaceuticals may greatly benefit by moving away from fixed dosing toward personalized, quantitative strategies [1]. Direct imaging of therapeutic radionuclides is a desired capability for calculating lesional doses and monitoring patient response as well as assessing normal tissue toxicities from radiation damage. In this presentation, hardware and software approaches for direct imaging of therapeutic radionuclides at all scales from human to tissue/cell levels will be described. For example, we analyzed the performance of dodecagonal SPECT systems using cadmium zinc telluride (CZT) detectors and low, medium, and high energy tungsten collimators. We also evaluated a novel imaging method based on positrons generated from pair productions, not positron emissions, for direct imaging of the Pb-212 decay chain using a conventional PET technology with potential pathways for improving this imaging performance. Also, we used Monte Carlo simulations to model DNA double strand breaks at the cellular and DNA levels for various therapeutic radionuclides with the primary objective of correlating the modeling to observational. The dodecagonal CZT-SPECT scanner, with newly designed high-energy collimators, improved the detection of high energy gamma emissions from I-131 and Ac-225. Pair production tomography enabled high-resolution localization of Tl-208 in the decay chain of Pb-212 [2]. Cell/DNA-level Monte Carlo simulations showed that the distance between the radionuclide's energy release and the DNA target significantly affects the amount of complex damage, the primary mechanism of therapeutic effect observed in radiopharmaceutical therapy. In conclusion, advanced imaging and biological modeling are key to improving radiopharmaceutical therapy outcomes, and there are ample opportunities to develop novel technologies that can combine experimental and observation studies to provide mechanistic understanding of how this important therapeutic modality works.

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BEYOND SCALE: DETECTOR PHYSICS PERSPECTIVES ON THE FUTURE OF PET

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Abstract

"Bigger is better" is not always true in positron emission tomography (PET) because of angular deviation in coincidence detection. A larger detector ring leads to degraded spatial resolution as well as higher production costs. Therefore, cost-effective application-specific or organ-dedicated systems can sometimes be ideal in terms of imaging performance. However, in practice, detectors must be equipped with depth-of-interaction (DOI) capability to achieve uniform spatial resolution, and the development of DOI detectors with excellent time-of-flight (TOF) resolution has been attracting increasing attention in the field of nuclear medicine physics.

In this talk, after reviewing various DOI-TOF detector development efforts [1], the Crosshair Light-Sharing (CLS) detector is introduced as an example of a successful DOI-TOF detector [2]. In the CLS concept, U-shaped light paths formed within a scintillator block bridge neighboring photodetectors in the north, south, east and west directions, enabling discrimination of crystals with half the pitch of the photodetector array. The developed CLS detector consists of fast LGSO crystals with a width of 1.45 mm and a length of 15 mm.

The first realization of this technology as a PET system is Mirai-PET, an animal PET system for rodents and nonhuman primates, which demonstrated 0.75 mm rod separation and 242 ps TOF resolution with a 170 mm ring diameter and a 156 mm axial field of view (FOV) [3]. Following this success, a brain-dedicated PET prototype, CLS-7, with a 296 mm ring diameter and a 183 mm axial FOV was developed and achieved 1 mm rod separation and 241 ps TOF resolution [4]. Potential applications of the CLS detector to whole-body PET will be discussed in this talk.

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Acknowledgements

The author gratefully acknowledges the support and contributions of all members of the Imaging Physics Group at QST (https://www.qst.go.jp/site/imaging-physics/report-on-pet-imaging-physics-research-en.html).

WHY STANDARDIZATION MATTERS IN RADIATION MEDICINE: THE PERSPECTIVE OF THE INTERNATIONAL COMMISSION ON RADIATION UNITS AND MEASUREMENTS (ICRU)

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Abstract

Radiation medicine—encompassing diagnostic imaging, radiation therapy, and nuclear medicine—depends fundamentally on precision, consistency, and safety. The ICRU, established at the First International Congress of Radiology in London in 1925, was founded to develop and disseminate scientifically rigorous recommendations that harmonize the use of radiation in medicine and science. Its standards provide a common language for clinicians, physicists, researchers, and regulatory bodies.

One of the ICRU's major contributions is the standardization of absorbed dose reporting and treatment prescription in radiotherapy. Reports such as ICRU 50[1] have established frameworks for defining target volumes, organs at risk, and dose distribution parameters. These guidelines allow radiation oncologists worldwide to design and compare treatment plans using consistent metrics, which is essential for evidence-based practice and multicenter clinical trials. In particle therapy, following ICRU Report 93 on Prescribing, Recording, and Reporting Light Ion Beam Therapy[2], similar reports on proton therapy and Boron Neutron Capture Therapy are currently in preparation.

In diagnostic radiology and nuclear medicine, ICRU recommendations support accurate dosimetry, optimization of image quality, and radiation protection. Standard units such as the gray (Gy), sievert (Sv), and becquerel (Bq) facilitate the safe communication of exposure levels and biological risk. One of the major steps toward a unified approach in nuclear medicine was ICRU Report 96[3], which emphasized that absorbed dose, rather than isotope activity alone, should be used in radiopharmaceutical therapy.

Ultimately, standardization in radiation medicine is not merely a technical requirement—it is a cornerstone of patient-centered care. As radiation technologies continue to evolve, the ICRU's mission remains to ensure that innovation is matched by consistency, safety, and scientific integrity.

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SUSTAINABLE INORGANIC-ORGANIC HYBRIDS AS DRUG DELIVERY SYSTEMS

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Abstract

Inorganic-organic nanohybrids have currently attracted widespread attention due to their beneficial properties and versatile applications in many biomedical areas. Phenolic compounds and other natural molecules can be used as powerful reducing agents of metal ions, and at the same time, excellent stabilizers of the resulting nanostructures. Nevertheless, this bottom-up approach of nanoparticle engineering requires a fine balance between the intrinsic supramolecular forces of assembly and the subsequent interfacial and stabilizing interactions, and it represents still an ongoing challenge.

Inorganic-organic hybrids of different spatial and modular dimensionalities and drug delivery characteristics will be presented: *i*) surfaced functionalized mono- and bimetallic Ag, Au nanoparticles (OD) of different morphologies (i.e., nanospheres, nanostars), and *ii*) polymeric nanofibers (1D) and films (2D) with metal nanoparticles and bioactive components (caffeic acid, rosmarinic acid, ellagic acid, *Roses* extracts). For instance, Au or Ag nanoparticles modified with tannic acid (TA) and coordinated with Fe(III) or Cu(II) ions (e.g., Au@TA_Fe(III), Ag@TA_Cu(II)) were investigated as novel chemodynamic platforms for tuned autocatalytic self-Fenton reactions. In addition, Au nanostars modified with small phenolic compounds (gallic, caffeic, tannic acids) with surface plasmon resonance above 650 nm were proposed for photothermal therapy (PTT). Finally, plasmonic (Ag, Au, Ag/Au NPs) and non-plasmonic (ZnO NPs) nanostructures were examined as chemodynamic antibacterial agents accelerating tissue regeneration *via* induction of cellular immune response.

The versatility of the inorganic-organic hybrids with surface supramolecular assemblies, combined with the intrinsic bioactivity of particular components, resulted in efficient biological activity. The results envisage a high potencial for biomedical applications of the resulting materials, among others, as biocompatible delivery systems of small biomolecules, metal ions or other reactive species with improved therapeutic efficacy and reduced toxicity.

Acknowledgements

The research was financed under the National Science Center project OPUS-22 (2021/43/B/ST4/02833).

BEYOND THE EXPONENTIAL LAW: WHAT FLUORESCENCE REVEALS ABOUT QUANTUM DECAY

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Abstract

The exponential decay law is widely used in atomic and particle physics, providing a simple universal description of unstable systems. Yet, quantum mechanics predicts that this behaviour is only approximate and must eventually break down at very short and very long times [1,2]. At late times, the decay is expected to follow a power-law behaviour [3].
In this talk, we explore these deviations in a experimental setup using fluorescence decay of organic dyes. By monitoring the emitted photons over extended time scales, we observe a power-like behaviour, consistent with earlier experimental observations in molecular systems [4].
A particularly intriguing aspect of our results is that this late-time behaviour is not universal. While the characteristic lifetime of the system remains unchanged, different spectral bands reveal distinct long-time decay patterns. This indicates that the decay process retains a form of memory that depends on how it is probed.
We interpret these findings within a quantum framework that connects the observed behaviour to the structure of the energy distribution and to the presence of multiple decay channels.

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STEM CELL IMAGING FOR CARDIOVASCULAR CELLULAR THERAPIES

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Abstract

Background: Cellular therapies brought a promise of medical revolution among civilization untreatable diseases. Variety of cells were applied with different plasticity allowing them to adapt to conditions of recipient organ. However, majority of them yielded to apoptosis or migrated out of delivery site. Tracking system seemed to be essential to optimize stem cells preparations differentiating between type of cells and their viability.

Objective: To find and optimize experimental system allowing to track applied stem cells in target organ *in situ* (heart) applying human stem cells of different origin while emphasizing their viability.

Methods: Superparamagnetic iron oxide nanoparticles (SPIONs) were used for direct cell labeling together with magnetic resonance imaging (MRI) versus bioluminescence while using human skeletal muscle-derived stem/progenitor cells (SkMDS/PC). In another approach molecular probes as well isotopic labeling (Technetium Tc-HMPAO) were used to track huSkMDS.PCs or mesenchymal stem cells (MSC) in mouse post-infarction myocardium *in situ.* Next attempts involved dual molecular molecular probes aiming to use promotor/reporter probes serving 2 deoxy-18F-fluorodeoxyglucose for heart viability estimarted and isotopic Fluor (4-18F-fluoro-3-[hydroxylmethyl]butylguanine using PET/CT for huSkMDS/PC/MSC dual cell intervention to post-infarction heart. Finally, we evaluated dual promoter/reporter system to differentiate between huSkMDS/PCs and MSCs retention in post-infarction heart as well as to estimate chemoattraction (SDF-1) with the use of nanoparticles and/or anti-TGF beta heart pre-treatment.

Main results: Although the used SPION's versus bioluminescence imaging were able to visualize the cells for two-weeks imaging - SPIONs did not differentiate viability/proliferation status of applied cells. Quantitative labeling with Technetium of different cell population applied for cell intramyocardial delivery brought into light superior capability at early phase (24hrs) retention of huSkMDS/PCs transfected with Connexin43 which possibly mediated gap junction formation. Dual applicability of molecular probe Multimodal reporter gene conataining the elongation factor (EF1) promoter controls herpes simplex thymidine kinase (HSV-TK) which could link analogues of guanosine indicating both heart viability with either accumulation in tissues fluoroglucose (PET, heart viability) while on the other labeled FHBG when phosphorylated by HSV-TK could trap inside of the stem cells giving PET/CT images. Dual product reporter probes providing two types of bioluminescence using MSCV-fluc-GFP lentiviral vector (firefly luciferase for SkMDS/PCs) and EF-1-mkate-nanoluc (for MSC) synthetic luminescent product differentiated well between the applied stem cells for cell intervention and additional optimization protocols while using nanoparticles or anti-fibrotic agents in post-infarction heart.

Conclusions: Dual purpose/application molecular promoter/reporter probes either with isotopic or non-isotopic imaging may serve well to track applied cell populations in *in situ* conditions allowing for further optimization of cellular therapies in non-treatable civilization diseases (failing heart).

Study was supported by grant No – NCN 2020/37/B/NZ5/00

RANGE MONITORING IN PROTON THERAPY USING THE J-PET SCANNER: EXTENDED EXPERIMENTAL STUDIES

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Abstract

A method for experimental determination of the proton beam range using the modular J-PET detector will be presented. Measurements were performed in a water-equivalent phantom and supplemented with irradiations of PMMA and anthropomorphic head phantom to assess the feasibility of proton range verification under conditions relevant to clinical proton therapy. A series of 4×4×4 cm^3 dose volumes were irradiated with proton beams delivering uniform doses of up to 16 Gy at varying penetration depths and for different proton beam energies. In the case of the head phantom, measurements were performed for two proton beam ranges while PMMA phantom was irradiated with a few different energies of pencil beam.

Data acquisition was carried out using a dual-head configuration of the J-PET prototype, with each head composed of three layers of four detection modules. The system operated in a triggerless acquisition mode during irradiation and in the post-irradiation phase. For image reconstruction, only data collected after irradiation were used, reconstruction was performed with the CASToR framework.

The reconstructed PET images represented the spatial distributions of β^+ emitters produced by nuclear interactions of protons within the irradiated media. Activity profiles were extracted along the beam axis and fitted using a sigmoidal function to determine the distal fall-off position. A linear correlation was observed between the simulated dose ranges shifts and those derived from PET activity distributions in the water-equivalent phantom.

Additionally, the dependence of the extracted activity range on proton beam energy was investigated in the water-equivalent phantom. The results showed the expected monotonic increase of penetration depth with increasing proton energy, demonstrating the sensitivity of the J-PET-based method to energy-dependent range variations. The head phantom reconstruction results were used to assess the effectiveness of applied reconstruction corrections.

Lower dose scenarios were studied by randomly rejecting a fraction of the acquired data. For a delivered dose of 4 Gy, the mean range shift error was approximately 1 mm for a 5-minute acquisition window and decreased to below 1 mm when 30 minutes of post-irradiation data were used. These results demonstrate the feasibility of precise proton range verification using the J-PET system and indicate its potential applicability for proton therapy monitoring.

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Calculations were performed on the Ziemowit computer cluster in the Laboratory of Bioinformatics and Computational Biology, Silesian University of Technology, created in the EU Innovative Economy Programme POIG.02.01.00–00-166/08 and expanded in the POIG.02.03.01–00-040/13 project.

We acknowledge support from the National Science Centre (NCN), grant nos. 2021/42/A/ST2/00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, and 2023/50/E/ST2/00574; the Polish Ministry of Science and Higher Education (MNiSW), grants no. IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Areas; and the ERC Advanced Grant POSITRONIUM (no. 101199807).

VALIDATED OPTICAL PHOTON MODELING OF LONG PLASTIC SCINTILLATORS FOR PRECISION TIMING APPLICATIONS

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Abstract:

Plastic scintillators are widely used in radiation detection due to their fast response, mechanical flexibility, and cost-effectiveness, making them attractive for large-area timing detectors in both fundamental physics [1-3] and applied instrumentation [4,5]. In particular, long scintillator geometries offer the possibility of extended detection coverage. However, as the scintillator length increases, the interplay between geometry and light propagation becomes increasingly critical to detector performance. Optical photon transport in such systems is strongly influenced by position-dependent effects, surface properties, and photosensor response [6]. These factors significantly affect light-collection efficiency and timing performance, especially when signals are read out from the ends of the scintillator.

In this work, we present a comprehensive characterization of optical photon transport in long plastic scintillator detectors using detailed Monte Carlo simulations based on Geant4 [7], validated with experimental measurements. Two scintillator bars of different lengths are investigated to validate the simulation model, with particular emphasis on extended detector configurations. The simulation incorporates key optical processes, including scintillation emission, bulk absorption, reflection, and photon propagation, along with realistic photosensor response. The main key observables, such as light yield, attenuation profiles, and photon arrival-time distributions, are studied as functions of interaction position along the scintillator [8]. The results provide quantitative insights into the interplay between optical photon transport and timing behavior in long scintillators and establish a validated framework for predicting detector response in extended geometries.

This work contributes to the development of large-area, high-precision timing detectors and provides a foundation for future applications in areas such as time-of-flight measurements and medical imaging systems [9,10].

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POSITRONIUM RATIO IMAGING, QUANTUM ENTANGLED PET AND DOUBLE PHOTON EMISSION IMAGING WITH A RING-TYPE COMPTON-PET SCANNER

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Abstract

Compton-PET method we proposed [1] realizes the multi-nuclide imaging by combining PET imaging and Compton imaging with a single device. Here we introduce three recent applications in quantum enhanced nuclear medical imaging, positronium ratio imaging (PRI), quantum entangled PET (QEPET) and double photon emission imaging (DPEI). PRI utilizes the ratio of positronium decay into three gamma (ortho-Ps) or two gamma (para-Ps) and can be used for detecting microenvironment with electron-positron spin alignment via pure positron emitter ^{18}F-FDG. The first PRI images[2] with different oxygen and porosity will be introduced. QEPET[3] utilizing Compton scattering events could enhance SNR in the image[4][5][6] and our first results with a small animal 3 ring-type scanner results will be presented. DPEI is another MeV-regime quantum sensing method using nuclear spin and double photon emitting nuclide. The demonstrated pH sensing and imaging[7] will be shown in the symposium.

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NEMA PHANTOM CHARACTERISTICS OF SIMULTANEOUS DOUBLE ISOTOPE IMAGING WITH J-PET USING ^{55}CO + ^{18}F AND ^{52}MN + ^{18}F ISOTOPES

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Abstract

Simultaneous double-isotope PET imaging has several advantages over single-isotope imaging since multiple scans are undergone at the same time [1, 2]. The principle is that if one isotope is a pure β^+ emitter and the second emits a $\beta^+ + \gamma_p$, then the conven-tional 2γ reconstruction contains contributions from both, while $2\gamma + \gamma_p$ events would originate exclusively from the second isotope [3, 4]. Then the subtracted images based on the efficiency of triples-to-doubles give the image from the pure β^+ emitter.

For the study, the NEMA-NU2-2018 phantom was utilized with ^{55}Co + ^{18}F and ^{52}Mn + ^{18}F pairs. The phantom was used for a quantitative and qualitative study of two isotopes, ^{55}Co + ^{18}F and ^{52}Mn + ^{18}F, by filling the three largest spheres with ^{55}Co with a concentration of 0.09 MBq/ml or ^{52}Mn with a concentration of 0.22 MBq/ml and the three smallest spheres with ^{18}F with a concentration of 2.03 MBq/ml for ^{55}Co + ^{18}F measurement and 8.2 MBq/ml for ^{52}Mn + ^{18}F measurement, and data was collected.

The data was grouped into 30-minute time frames with six data groups. The grouped data were analyzed for two types of events with the event selection criteria of stranded 2γ events and the extended $2\gamma + \gamma_p$. However, in the case of $2\gamma + \gamma_p$ events, ^{55}Co and ^{52}Mn isotopes emit three deexcitation photons with the energy of ^{55}Co (477 keV, 931 keV, and 1408 keV) and ^{52}Mn (744.22 keV, 936 keV, and 1434 keV) with different branching ratios and levels; the deexcitation gamma experiences a strong Compton tail in the lower TOT region. The likelihood of the annihilation and deexcitation photons in the TOT range was calculated, and the best triplets were selected based on the combinations of two annihilation and one deexcitation photon.

The selected events from 2γ and $2\gamma + \gamma_p$ candidates were processed for reconstructing the emission point using TOF; the reconstructed images were analyzed to calculate the recovery coefficient, noise level, activity concentration, and count rates as a function of sphere diameter by choosing the ROI. From the 2γ reconstructed images for each time frame for three smaller spheres, which were filled by ^{18}F, drops faster than the largest three spheres, which were filled by ^{55}Co and ^{52}Mn, since ^{18}F has a shorter half-life compared to them. In the case of $2\gamma + \gamma_p$ reconstructed images, the three largest spheres showed activity images.

Acknowledgment

We acknowledge support from NCN (grants 2021/42/A/ST2/00423, 2021/ 43/B/ST2/02150, 2022/47/I/NZ7/03112, 2023/50/E/ST2/00574), MniSW (IAL/SP/596235/ 2023 and SPUB/SP/627733/2025), SciMat and qLife Priority Research Areas, ERC Advanced Grant POSITRONIUM no. 101199807, PRISMAP (Project 1729020993 aniX3), and PLGrid infrastructure (PLG/2024/017688, PLG/2025/018762).

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EXOTIC CASE: POSSIBLE OBSERVATION OF A BOUND DIPROTON AND IT'S DECAY IN AN UNBOUND DEUTERON

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For years we have studied exotic two-nucleon nuclei: the dineutron [1] and the diproton [2]. It is known that these nuclei are unbound by definition. However, if such nuclei can be contained in a potential well of nuclei with sufficiently large radii, as was theoretically shown in [6], then we could observe their decays and seek an estimate of the binding energy. The binding energy can manifest itself in the occurrence of nuclear reactions with the formation of residual nuclei and the emission of two neutrons or two protons in a bound state for energies on the incident particles below the thresholds of such reactions. This energy range between the threshold and the energy of the incident particles for which the formation of a dineutron and a diproton in a bound state will be complete to give us either a point or an interval estimate of the binding energy. From our previous experiments, we have obtained a recent interval estimate of the dineutron binding energy, which is now [1.6÷2.8] MeV [1]. For the diproton, or ^{2}He nucleus, we have assumed that the binding energy is in the range [0.35÷1.440] MeV depending on the purely nuclear or atomic-nuclear characteristics of the decay [2]. In both dineutron and diproton decays, the product nucleus will be a deuteron, which is expected to be produced in the singlet or triplet state. The latter is well known, and the former is also under investigation [4].

In this work, we conducted an experimental search for the formation of a singlet diproton in a bound state and its subsequent decay to a singlet deuteron state via the positron emission regime after irradiation of 91 micron thick 159Tb foils with protons with energies of [2.7÷5.8] MeV. As a result of our search, the binding energy of a diproton due to decay via the positron emission state into a bound or unbound singlet deuteron state has a lower bound of the interval exceeding 3.47 MeV for the atomic-nuclear process. This result establishes the following hierarchy of binding energies of nuclei bound with two nucleons: $B_d < B_{dn} < B_{dp}$, where B_d, B_{dn} and B_{dp} are the binding energies of the deuteron, dineutron and diproton, respectively, and contradicts all our previous available ideas about the formation of systems bound with two nucleons in a bound state, and requires an explanation taking into account unknown yet assumptions and knowledge.

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TOWARD POSITRONIUM IMAGING: BODY TEMPERATURE DEPENDENCE AND GAMMA-RAY-INDUCED POSITRON IMAGING

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Abstract

The time it takes for a positron to annihilate (positron lifetime) varies depending on the surrounding electron density. This property has been used in material analysis for a long time. By utilizing this property, it may be possible to add new in vivo information derived from positron lifetime to PET (known as positronium (Ps) imaging [1]). We have been conducting positron lifetime measurement studies using the commercially available clinical PET system "VRAIN", developed by QST, aiming at applications such as visualization of intratumoral oxygen partial pressure [2] and in vivo radical-related information [3]. In this presentation, we report in detail on the following two topics.

1. Influence of body temperature on positron lifetime

Positron lifetime is also known to depend on the temperature of the liquid; therefore, evaluating the influence of body temperature is essential for clinical applications. Using pure water samples, positron lifetime measurements were performed with VRAIN at temperatures of 25 °C, 36 °C, and 44.5 °C. The results suggest that the positron lifetime in water changes by approximately 3.5 ps/°C. This finding indicates that corrections for body temperature distribution are required when comparing lifetime values between different regions of the body or between spatially distant sites in vivo.

2. Proposal of γ-ray-induced positron lifetime imaging analysis

To realize Ps imaging, it is necessary to construct a database of positron lifetime values for biological samples. However, a major limitation of conventional positron-based material analysis is that it is sensitive only to near-surface regions. Recently, a technique to irradiate samples with a 6.6 MeV gamma-ray beam has been developed at UVSOR [4]. This beam can penetrate deep inside samples and induce positrons via pair production. Therefore, we propose a novel technique termed γ-ray-induced positron lifetime imaging analysis, in which these induced positrons are imaged based on the PET principle. If realized, this technique would enable in vivo analysis of biological samples as well as three-dimensional analysis of relatively large materials. In the initial experiment, we succeeded in observing the differences in spatial distribution and positron lifetime components of standard samples (Si and SiO_2) with different lifetime values, in two-dimensional imaging with a pair of PET detectors.

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SUBTYPE-SPECIFIC INSIGHTS IN BREAST CANCER RADIOTHERANOSTICS

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Abstract

Background

Breast cancer (BCa) is the most common cancer in women and represents a highly heterogeneous disease driven by marked variability in surface receptor expression. Four major molecular subtypes are recognized based on the status of estrogen receptor α (ERα), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2).

Objectives

Personalized healthcare enables the selection of optimal treatment for each patient by considering the tumor's molecular profile and disease stage. In this context, major advances have been achieved in nuclear medicine through the use of radioligands for diagnostic molecular imaging and targeted radionuclide therapy. Accordingly, the objective of this study is to develop, and evaluate a series of radioligands for different BCa subtypes, including ERα+, PR+, HER2+, and triple-negative (TNBC).

Methods

Various compounds have been synthesized on solid phase using the Fmoc/*t*Bu strategy, purified *via* HPLC and characterized by ESI- and MALDI-MS. These ligands have been conjugated to optical dyes or DOTA chelator for further radiolabeling with $^{68}GaCl_3$ and $^{177}LuCl_3$.

Main results

Multiple low-molecular-weight and peptidomimetic libraries have been successfully synthesized (≥95% purity) and radiolabeled (≥95% labeling efficiency). Radiolytic stability was assessed in PBS and human serum over 7 d. *In vitro* binding and internalization studies were performed in ERα+/PR+ (MCF-7, T47D), HER2+ (SKOV-3), and TNBC cell lines (MDA-MB-231, MDA-MB-468, HCC1937, and CHO-KISS-1R), revealing significant differences in binding performance, affinity, specificity, and stability. The first *in vivo* evaluation in mice is currently ongoing and will be reported in due course.

Conclusions

These findings demonstrate the successful development of receptor-targeted radioligand libraries with promising *in vitro* performance across multiple BCa subtypes, supporting their potential for future applications in molecular imaging and targeted radionuclide therapy within personalized oncology.

Acknowledgements

We sincerely thank Claudia and Hans-Peter Opitz for their generous financial support.

A FAST POSITRON LIFETIME TOMOGRAPHY METHOD AND INITIAL PHANTOM AND ANIMAL RESULTS

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Abstract

The feasibility of positron lifetime imaging (PLI) with time-of-flight (TOF) positron emission tomography (PET) by using b$^+$g emitters has been demonstrated. The positron lifetime spectrum consists of three components: the direct annihilation (DA) component, arising from positrons that annihilate directly with electrons, and the para-positronium (p-Ps) and ortho-positronium (o-Ps) components, arising from positronium formation in spin-singlet (S=0) and spin-triplet (S=1) states, respectively. In tissue, the DA:p-Ps:o-Ps population ratio is about 0.6:0.1:0.3. The p-Ps lifetime is approximately 125 ps, and the DA lifetime is 200-400 ps depending on the local electron density, whereas the o-Ps lifetime in biological tissues is variable between 1–5 ns, affected by processes that are sensitive to the free-volume and physicochemical properties of the microenvironment. Hence, the o-Ps lifetime may provide diagnostic information for disease in addition to that given by the PET tracer uptake. We are interested in the potential of the o-Ps lifetime as a surrogate of tissue oxygen concentration, which is an important biological parameter for cancer. At the current TOF resolution, accurate voxelwise estimation of the positron lifetime, called positron lifetime tomography (PLT), is a challenge. Many reported PLT methods are computationally intensive. To reduce complexity, these methods often neglect the DA and p-Ps components. We have reported that this leads to biased results that diminish the contrast of lifetime images [1]. Presented here is a novel fast PLT method for estimating the o-Ps lifetime that is insensitive to the DA and p-Ps components, based on a previously reported analytic method [2]. We tested this PLT method using data simulated for PET systems having TOF resolutions of 200 ps (representing the state-of-the-art systems) and 3000 ps (considered to provide an assessment of the lower-bound performance of the proposed method). Results showed that for 200 ps TOF the method produces nearly unbiased results at high event counts. At lower counts, bias increased but estimates could remain monotonic with the true value. At 3000 ps TOF, the resulting images maintained contrast; however, increased bias and variance were observed. The method was also shown to be robust to 10% perturbations in the DA and p-Ps components. Also reported are initial results obtained by applying the method to real data, including physical phantom acquisitions from a preclinical scanner and a Siemens Biograph Vision Quadra scanner, as well as animal data acquired with the preclinical scanner following injection with ^{44g}Sc-PSMA-617.

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This work was supported in part by the NIH (USA) R01 EB029948 and R01 CA236385, by the Jules J Reingold Fellowship Endowment Fund, and by the NSF (USA) DMS-1924792 and DMS-2318925.

FROM MEDICAL ISOTOPE RESEARCH TO FUNDAMENTAL NUCLEAR PHYSICS: SUB-THRESHOLD ^{99M}TC PRODUCTION SUGGESTS POSSIBLE BOUND DINEUTRON STATE

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Abstract

^{99m}Tc is the most commonly used radioisotope in nuclear medicine, making a reliable supply essential. Conventional production, via elution from generators containing ^{99}Mo produced in nuclear fission reactors, is vulnerable to supply chain disruptions. Consequently, cyclotron-based production of ^{99m}Tc has gained significant interest as an alternative to reactor-based methods. At the Bern Medical Cyclotron (BMC) facility, we performed an extensive campaign to mea-sure the excitation functions of various Tc radioisotopes using natural and enriched molybdenum targets [1]. These measurements provide essential data for optimizing yield and radionuclidic purity in accelerator-based ^{99m}Tc production for medical applications.

The expertise gained during this campaign, along with the ongoing collaboration between AEC-LHEP at the University of Bern and the group led by Ihor Kadenko at the Taras Shevchenko National University of Kyiv, enabled a detailed investigation of the low-energy tail of the ^{100}Mo(p, 2n)^{99m} Tc nuclear reaction. This region is of particular interest due to the possible formation of a dineutron ^{2}n - a bound system of two neutrons - in the outgoing channel of the nuclear reaction, as also observed in previous studies [2]. The existence of such a bound system and its implications - particularly for Big Bang nucleosynthesis [3] - remain a long-standing question in nuclear physics [4].

Proton irradiation of highly enriched ^{100}Mo powder targets at proton energies below the nominal 7.8 MeV threshold of the $(p, 2n)$ reaction produced measurable ^{99m}Tc activity. Preliminary data show, for instance, an activity of 0.67(7) Bq at a proton energy of 5.8(9) MeV. The observation of ^{99m}Tc at sub-threshold proton energies may indicate a ^{100}Mo(p, ^{2}n)^{99m} Tc reaction channel, in which the binding energy of the dineutron effectively reduces the reaction threshold relative to the emission of two unbound neutrons.

Experimental nuclear cross-section data for optimized accelerator-based ^{99m}Tc production are presented, with particular emphasis on the sub-threshold regime of the ^{100}Mo(p, 2n)^{99m} Tc reaction, and the implications for the possible existence of a bound dineutron state in the nuclear potential of the residual nucleus are discussed.

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Acknowledgements

This research was partially funded by the Swiss National Science Foundation (SNSF) (grant: IZURZ2 224901).

FEASIBILITY STUDY OF 3-GAMMA IMAGING WITH TOTAL BODY J-PET

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Abstract

The J-PET detector, based on plastic scintillators, enables the registration of multi-photon annihilation events [1-3], including three-gamma decays of ortho-positronium, and the first 3γ images were demonstrated using the 192-strip J-PET prototype [4]. The Total-Body J-PET (TB-J-PET), with its long axial field of view (AFOV), offers high sensitivity that enables practical implementation of 3γ imaging. This study aims to investigate the feasibility of 3γ imaging using the TB-J-PET scanner through Monte Carlo simulations and a dedicated reconstruction method. The TB-J-PET scanner consists of five detection rings with a total AFOV of 254 cm. Two short rings (33 cm modules) and three long rings (60 cm modules). Each ring consists of 24 modules, with three detection layers per module. Monte Carlo simulations were performed using GATE [5] v9.4.1, extended to enable accurate tracking of the third photon, including proper modeling of Compton and Rayleigh interactions. An energy threshold of 30 keV was applied in the digitizer. Ortho-positronium annihilation events were simulated using the dedicated three-gamma source in GATE. Event selection criteria and a trilateration-based reconstruction algorithm [4, 6] were implemented within the J-PET Framework. Preliminary simulation results indicate that the TB-J-PET scanner is capable of detecting and reconstructing 3γ events with high sensitivity. The evaluated performance characteristics, including sensitivity, scatter fraction, and spatial resolution, show the potential of the scanner for 3γ imaging.

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DISTINCT SPATIAL RESOLUTION ADVANTAGES OF COMBINING THE TB-J-PET WITH A BRAIN PET INSERT

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The J-PET (Jagiellonian Positron Emission Tomography) collaboration is working towards the real-ization of a large field of view Total Body J-PET (TB-J-PET) scanner, following the development of both a prototype [1] and a modular scanner [2]. The key distinctive feature is the utilization of more cost-effective plastic scintillators over conventionally used inorganic scintillation crystals (such as BGO or LSO) for the detection of the 511 keV annihilation photons. Motivated by the numerous develop-ments and potential applications of dedicated brain PET scanners [3], we study the combination of the TB-J-PET scanner with a Brain PET Insert (BI).
In this Monte Carlo simulation work, we focus on the unique advantages the proposed detector configuration has in terms of spatial resolution. For this purpose, we first developed a robust scheme to estimate the spatial resolution from Maximum Likelihood Expectation Maximization (MLEM) recon-structions. We thereby address known challenges of MLEM-based spatial resolution assessment, which often leads practitioners to revert to the outdated Filtered Back-Projection (FBP) algorithm. Building on this methodological foundation, we then investigate the impact of detector geometry on resolution performance. The BI uses smaller scintillators than the TB-J-PET (4 vs. 6 mm). We show that this is a resource-efficient approach to obtain high resolution inside the BI, since the coincidences between the TB-J-PET and the BI (which contribute 50% of the sensitivity) have particularly low uncertainty. We demonstrate that this configuration is geometrically optimal. In addition, the non-collinearity effect, which provides the motivation to build dedicated close-up scanners in the first place, is also suppressed in the proposed detector geometry. We also analyze the resolution with respect to the event selec-tion polices suggested in [4]. We provide intuitive insights into our observations, offering compelling arguments for the experimental realization of the detector geometry under investigation.

Acknowledgments
We acknowledge support from the National Science Centre (NCN), grant nos. 2021/42/A/ST2/ 00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, the Polish Ministry of Science and Higher Education (MNiSW), grants no. IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Areas; and the ERC Advanced Grant POSITRONIUM (no. 101199807).

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THE DRS4 CHIP FOR PALS MEASUREMENTS – THE PSI EVALUATION-BOARD AND THE INTEGRATED *LIFETIMESPEC* TABLETOP SPECTROMETER: A COMPARISON

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Since the first publications on digital data acquisition in positron annihilation lifetime spectroscopy (PALS) by fast oscilloscopes in 2001, the development of fast digitizers has stimulated the transition from NIM-based analog PALS toward digital concepts. Digital PALS enables software-based pulse timing, pulse-height selection and filtering of unwanted events prior to the generation of a lifetime spectrum. However, conventional high-speed digitizer cards providing both a sufficient sampling rate and digitization depth remain technically demanding and, therefore, expensive. In contrast, the *DRS4* evaluation board from the PSI, first used in a PALS setup by Petriska et al. [1], provides a competitive, cost-effective alternative by combining high sampling speed (5 GHz) with high digitization depth (14 bit). Based on this concept, we developed the open-source Software *DDRS4PALS* allowing user-friendly pulse acquisition, filtering and offline reprocessing of lifetime spectra [2].

Here, we compare a digital PALS-*DRS4-PSI* setup [3] with the recently developed commercial *LifeTimeSpec* system by Aero-Laser GmbH. For both setups, signal detection is realized by plastic scintillators but the setups differ fundamentally in the implementation of event discrimination. In the the *DRS4* evaluation board from the PSI, the internal trigger and readout architecture are not optimized for detector pulses with nanoseconds rise time and coincident-event rates required in PALS. Therefore, coincident events must be preselected by an external NIM-based branch consisting of constant-fraction discriminators and a coincidence unit, which then provided the external trigger for the PALS-*DRS4-PSI* setup [3]. *LifeTimeSpec* resolves this limitation by integrating the corresponding coincidence discrimination and trigger logic into a *DRS4*-chip-based acquisition board specifically developed for PALS. This removes the need for the external NIM-based trigger chain and turns the *DRS4* concept into a compact, method-specific digital PALS platform.

Both systems are evaluated using spectra acquired from in-situ 22-Na source configurations on selected high-purity metals and silicon (Mg, Al, Si, Sn, Pb, …) compared to source-sample-sandwiches. Our investigation focuses on spectral quality, analyzability, count rate performance and the practical robustness of the acquisition workflow. Our emphasis is on the influence of software-defined filtering and post-acquisition optimization, since both approaches allow unwanted events to be rejected after pulse acquisition rather than fixing all discrimination conditions during measurement.

All DRS4-based systems provide high-quality positron lifetime spectra suitable for reliable analysis. While the PALS-*DRS4-PSI* with *DDRS4PALS* is a transparent open-source approach to digital PALS, the *LifeTimeSpec* offers a more integrated and user-friendly implementation. By reducing the need for external nuclear electronics, it lowers the technical entry barrier for routine PALS measurements in academic and industrial laboratories.

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STATUS OF CPT SYMMETRY TEST IN ORTHO-POSITRONIUM DECAYS WITH THE MODULAR J-PET DETECTOR

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Abstract

The combined symmetry of charge (C), parity (P), and time reversal (T) is one of the most fundamental symmetries in nature. Any observation of its violation would indicate the presence of New Physics beyond the current theoretical framework. A direct test of the CPT symmetry has been recently performed for the electromagnetic decays of ortho-positronium (o-Ps) using the 192-strip Jagiellonian Positron Emission Tomograph (J-PET) [1]. Studies are done by measuring the CPT-violating angular correlation between the o-Ps spin and the momenta of its annihilation photons with a precision at the 10^{-4} level [2,3]. However, there is still a range of orders of magnitude unexplored to test its exactness in the pure leptonic system [4]. Here we present the status of a new measurement aimed at enhancing the sensitivity of the CPT symmetry test using the modular J-PET detector, consisting of 24 independent detection modules from plastic scintillators. The modular detector design offers improved detection efficiency of photons from o-Ps annihilations compared to the previous prototype. We will discuss the analysis criteria, and the prospects for further improving the CPT invariance limit with this new detector system.

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EVALUATION OF NOVEL Β⁺+Γ EMITTERS FOR POSITRONIUM LIFETIME IMAGING WITH THE MODULAR J-PET SCANNER

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Abstract

Positronium Lifetime Imaging (PLI) is a promising extension of Positron Emission Tomography (PET) **[1]**. In recent years, numerous phantom and human studies have demonstrated the feasibility of this approach in clinical and pre-clinical PET scanners, supported by the development of various reconstruction methodologies **[2]**.

This study presents, to our best knowledge, the first PLI investigations using three promising novel β^++γ emitters (^{44}Sc, ^{52}Mn, and ^{55}Co) performed with the Modular J-PET scanner. The Modular J-PET is a plastic-based PET scanner with a 50 cm axial-field-of-view and multi-photon detection capabilities **[1]**. Three separate experiments were conducted. First experiment was performed with a NEMA-IQ phantom containing six spheres filled with water mixed with ^{44}Sc (three largest spheres) and ^{18}F (three smallest spheres) **[3]**. For ^{52}Mn and ^{55}Co, experiments were performed using two Certified Reference Materials (polycarbonate and fused silica) with known mean ortho-positronium lifetimes, and two human tissue samples **[4]**. Events with two annihilation photons and one prompt photon were selected for the positron lifetime estimation. From the resulting lifetime spectra, the mean ortho-positronium lifetime (τ_{ops}) and mean positron lifetime (ΔT_{mean}) were extracted for ^{44}Sc-filled spheres and, for ^{52}Mn and ^{55}Co, for each sample.

Among all the radionuclide studied, ^{44}Sc appears to be most suitable candidate for PLI **[5]**. Its high β^++γ branching ratio (~94%) enable efficient event tagging and excellent signal purity. ^{55}Co also shows clear potential, particularly as the second-best candidate after ^{44}Sc. With a high β^+ branching ratio (~76%) and a simpler decay scheme, it provides a superior peak-to-background ratio (~133) compared to ^{52}Mn (~87), making it well suited for cobalt-based tracers and delayed imaging in PLI. In contrast, although ^{52}Mn's three-photon cascade may increase effective tagging yield, its large electron-capture fraction (~71%) increases background. Nevertheless, its long half-life and manganese chemistry may still be advantageous for selected applications. These novel β^++γ emitters, combined with the planned Total-Body-J-PET system, and dedicated PLI reconstruction methods, are expected to achieve enhanced sensitivity and improved image quality. The results on comparative assessment of ^{44}Sc, ^{52}Mn, and ^{55}Co for the PLI will be shown and discussed at the conference.

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(PLG/2024/017688, PLG/2025/018762).

ADVANCED ON-BOARD IMAGING FOR PRECISION SMALL ANIMAL PROTON AND LIGHT ION RADIATION RESEARCH

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Abstract

Precision small-animal radiation research is an important emerging field that provides a critical link between fundamental radiobiology and clinical particle therapy through studies of radiation response in well-controlled tumor and normal tissue models. This is essential for validating biological models and facilitating the translation of innovative therapies into clinical practice. However, the widespread use of murine models poses considerable challenges for beam delivery precision due to their small size, requiring dedicated solutions for beam formation and image guidance.

Over the past decade, our team at LMU Munich has developed a range of dedicated solutions for advanced on-board imaging, supporting treatment planning, in vivo treatment monitoring, and biologically guided proton and light-ion therapy. This talk will summarize the rationale, key developments, and first in vivo applications of these imaging solutions, integrated into a versatile mobile platform that can be deployed across different particle therapy environments, ranging from passively collimated beams [1] to the novel SIRMIO beamline for multi-field intensity-modulated proton therapy [2].

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Acknowledgements

Parts of the work to be presented received funding from the ERC projects SIRMIO and BARB, the Bavarian High-Tech Agenda project EQAP and the Eurostars project ACACIA. All past and current contributing members from the LMU team along with the national and international research collaborators from DCPT, GSI, TUM and NIRS-QST are gratefully acknowledged. We also thank the company Advacam for their support on proton imaging.

ARTIFICIAL INTELLIGENCE IN MEDICINE

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Abstract

Artificial intelligence (AI) is transforming modern medicine by enabling advances in medical imaging, radiation therapy, nuclear medicine and data-driven clinical decision-making. This keynote will explore how modern AI methods—ranging from deep learning to physics-informed models—are reshaping the acquisition, reconstruction, and interpretation of biomedical data.

From the perspective of medical physicists, AI offers significant opportunities to enhance image reconstruction, automate segmentation, optimize treatment planning, and support adaptive and personalized therapies, ultimately improving precision and efficiency in patient care. However, the clinical deployment of AI introduces complex challenges, including model interpretability, data bias, generalizability, and integration into heterogeneous healthcare systems.

Medical physicists play a central role in addressing these challenges by extending their traditional responsibilities in quality assurance and system validation to AI-driven technologies. They act as independent evaluators of AI models, ensuring accuracy, robustness, and consistency across diverse clinical environments, while also developing quality assurance frameworks to monitor performance over time and detect model drift. Their contributions further extend to regulatory compliance, standards development, and data stewardship, ensuring that AI systems are built on reliable, ethical, and high-quality datasets.

Beyond oversight, medical physicists contribute to education, training, and research in AI, promoting appropriate use and advancing the development of interpretable and clinically robust models. As AI continues to evolve, the role of the medical physicist is expanding from hardware-focused support to comprehensive system-level assurance, where human expertise, software intelligence, and medical technology converge. This dual role—driving innovation while ensuring safety and reliability—is essential for the responsible integration of AI into medicine and for achieving improved patient outcomes.

PET-GUIDED ENDOVASCULAR MEDICINE

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Abstract

Background: Conventional systemic delivery of therapeutics is inherently limited by biological barriers and off-target toxicity. PET-guided endovascular medicine represents a shift toward regional pharmacology, using arterial conduits to achieve high local drug concentrations. A critical component of this paradigm is the use of PET to quantify the "first-pass benefit" - the immediate extraction of the payload by the target organ before systemic recirculation. Furthermore, spatial fractionation—treating discrete organ segments across multiple sessions—offers a strategy to preserve functional reserve and lower peak exposures, addressing the safety limitations of monolithic whole-organ exposure.

Objective: To investigate the efficacy of PET-guided endovascular delivery for biologics across various body areas, and to evaluate enhanced osmotic protocols for maximizing barrier permeability.

Methods: Studies were conducted in murine models using real-time MRI to guide intra-arterial (IA) catheterization and monitor perfusion. For brain delivery (n=44), osmotic blood-brain barrier opening (OBBBO) was performed using 25% mannitol alone or in combination with 4% NaCl[1]. For head-and-neck delivery, mRNA, AAV9-luciferase, and radiolabeled antibodies were infused *via* the external carotid artery[2]. Quantitative distribution was assessed using PET/CT with ^{89}Zr radiolabeling to verify spatial targeting and calculate Standardized Uptake Values (SUV). Safety was monitored through longitudinal MRI and postmortem histology.

Main Results: In the brain, the combination of 25% mannitol and 4% NaCl significantly expanded the OBBBO territory compared to mannitol alone (area ratio 1.99±0.17 *vs* \$1.41±0.15; p <.001), increasing the disruption area from <20% to approx. 50%. PET imaging confirmed a substantial increase in antibody uptake (SUV 2.77±1.80 vs 1.0 ±0.23; p <.001)[1]. In head-and-neck region, IA delivery of mRNA resulted in 100-fold higher expression in targeted tissues (tongue, jaw) compared to systemic delivery, where expression was virtually undetectable. PET quantification of ^{89}Zr-bevacizumab showed significantly higher uptake in the targeted neck region *via* IA vs. IV routes (SUV 0.65±0.12 *vs* 0.29±0.11; p <.01)[2]. Safety assessments showed no edema, stroke, or neuroinflammation.

Conclusions: PET is critical for verifying spatial targeting and quantifying the pharmacological advantages of endovascular delivery. By leveraging first-pass effects and high-resolution imaging, clinicians can achieve unprecedented local availability for biologics. The adoption of spatially fractionated protocols can further raise the safety ceiling by avoiding the "all-or-nothing" toxicity risk of systemic administration, preserving organ reserve while ensuring comprehensive therapeutic coverage over iterative sessions[3].

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This work was supported by the NIH grants R01NS120929 and R01DA056739

POSITRONIUM LIFETIME IMAGING USING AN ITERATIVE RECONSTRUCTION ALGORITHM WITH J-PET AND BIOGRAPH VISION QUADRA

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Abstract

Positronium Lifetime Imaging (PLI) is a novel multiphoton technique that uses the properties of positronium in combination with the positronium lifetime in tissue as a probe for the microenvironment and provides additional and complimentary information to conventional PET imaging [1,2]. Reliable implementation of PLI requires an efficient and robust image reconstruction framework. In our earlier work, PLI reconstruction relied on region-of-interest (ROI) methods and multiple-peak fitting procedures, which can be sensitive to selection biases and limited in spatial generality [3]. To address these limitations, we have developed an iterative reconstruction algorithm based on maximum likelihood expectation maximization (MLEM) [4]. We validated the proposed reconstruction pipeline using data acquired with the modular J-PET scanner and the clinically attractive radionuclide ^{44}Sc (half-life 4.04 h), characterized by a high positron branching fraction (~94.3%) and the emission of a 1157 keV prompt gamma (γ) that provides a start signal for positronium formation. The dataset was filtered to select triple-coincidence events consisting of two 511 keV annihilation photons and the prompt gamma, using the dedicated J-PET Framework. The selected events were stored in list-mode format and subsequently used to reconstruct activity images with MLEM. In addition, a voxel-wise positronium rate constant lambda (λ) image was reconstructed using a penalized-MLEM formulation [4].

As the next step, we are extending the workflow to clinical data acquired with Biograph Vision QUADRA PET/CT system using ^{124}I at Bern, Switzerland [5]. The current analysis focuses on filtering and post-processing candidate 2γ+prompt events, followed by reconstruction of both activity images and activity-filtered lambda (λ) images. Since this work is still at a preliminary stage, the first results will be presented at the conference.

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ADVANCES IN POSITRONIUM MICROWAVE SPECTROSCOPY

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Abstract

The electron-positron bound state positronium (Ps) [1] is a simple atomic system that has some superficial similarities to hydrogen, but whose structure is very different once you look beyond the simple Bohr level. Indeed, because Ps has no hadronic components and negligible weak force contributions, it is almost fully described by bound-state quantum electrodynamics (QED) [2]. This means that Ps is an ideal system with which to test QED theory, and as a clean system, can in principle also be used to look for "New Physics" [3]. Unfortunately, while PS may be theoretically appealing it is experimentally complicated, and performing precision spectroscopic measurements with this metastable system is much more difficult than the corresponding measurements using hydrogen (for example). The short lifetime of Ps states means that linewidths are generally much broader, and the low mass means that Ps speeds are generally large, leading to various additional broadening effects. Moreover, the difficulty in producing Ps atoms also means that signal rates are usually low [4]. Nevertheless, some progress has been made in recent years in optical [5] and microwave spectroscopy of Ps [6]. Here I will describe some of this work, focusing on recent advances in positronium microwave spectroscopy carried out at UCL.

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BIOLOGICAL MULTIPLEXING WITH PET: INTERROGATING MULTIPLE DISEASE BIOMARKERS IN A SINGLE PET SCAN

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Abstract
In this paper we describe methods that enable what we believe will be an important new direction for PET: The ability to image more than one positron-emitting tracer in a single PET imaging session. Molecular-based characterization of the hallmarks of cancer, neurological disorders, and cardiovascular disease relies on the ability to assess the status of multiple disease biomarkers. However, to date, commercially available PET scanners do not have the ability to visualize and quantify more than one biomarker per study, owing to the indistinguishability of positron annihilation photons emitted by the associated radiotracer contrast agents administered into the patient. Performing separate PET scans with different tracers on sequential days is logistically very challenging and thus never done in regular clinical practice, and the status of the different biomarkers would change if the separate scans were scheduled weeks or months apart. However, if a tracer is labeled with a positron emitter that also emits a prompt gamma ray with energy higher than 511 keV (**�$^{+}$-y**), it is possible to distinguish that tracer from another labeled with a pure positron emitter (**�**$^{+}$) in one scan, as the former yields *triple* photon coincidences, comprising two 511 keV photons + one higher energy interaction, and the latter results in only double photon coincidences. Furthermore, the use of **�**$^{+}$-y radiometals to achieve this PET multiplexing also facilitates *positronium lifetime imaging*, which adds complementary microstructural information about diseased tissue to the multiplexed molecular information provided by the multi-tracer distribution. In this abstract we discuss PET system design, signal processing, and radiolabeling requirements that enable clean *unmixing* of three (or more) distinct radionuclide distributions that, if successful, will allow us to interrogate at least three different disease biomarkers in a single PET scan. We hypothesize that this capability would give us a more complete "molecular" picture of the patient's disease, leading to more effective treatments.

AN NLP-BASED AI SYSTEM FOR POST-RADIATION PATIENT TRIAGE

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Abstract

Background: Assessment of ionizing radiation exposure is a critical challenge in the domains of nuclear and radiation accidents, as well as in the field of medical physics, particularly in the contexts of triage and particle therapy monitoring. Recent studies have identified the FDXR gene as a highly reliable biomarker for exposure [1]. The development of efficient and rapid computational methods is essential for the improvement of diagnostics.

Objective: To develop and evaluate an artificial intelligence natural language processing (NLP) based pipeline differentiating between samples exposured to low and high absorbed ionizing radiation doses using long-read RNA sequencing data.

Methods: The process is comprised of three fundamental stages: sequence encoding, filtering, and classification. Encoding involves the transformation of RNA sequences into numerical vectors through the utilisation of the "Bag of Words" method, thereby generating an initial complete feature space consisting of 1024 k-mers, as outlined in [2]. In the second stage, the reads are preliminarily classified as "Possible FDXR" and "Others". In the concluding phase, the classification is executed by employing exclusively the NLP profiles of reads from the "Possible FDXR" group. In the classification stage, the following commonly used machine learning algorithms are employed: logistic regression (LR), random forest (RF), and XGBoost (XGB). A rigorous feature selection process was implemented, incorporating forward feature selection (requiring a Bayes' ratio > 20) for LR, and piecewise linear regression analysis of permutation importance metrics to ascertain optimal feature thresholds for RF and XGB.

Main Results: The applied feature selection strategies successfully identified the most critical descriptors. The classifiers maintained exceptional performance, consistently achieving over 98% accuracy even when the feature space was reduced to 17 on the very limited subset of reads. Validation on an independent, external dataset confirmed high system specificity and generalization.

Conclusions: Integrating sequence encoding, targeted filtration, and optimized classification into a single, cohesive pipeline provides a highly accurate and computationally efficient approach to radiation dose assessment.

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Partially financially supported by the United Kingdom Health Security Agency, CRCE Capital Programme, grant no CRCE/CAP/20–21/406, IDEA: bIological DosimEtry Assessment device.

QUANTUM ENTANGLEMENT OF POSITRON ANNIHILATION QUANTA: FROM EXPLORATION OF FUNDAMENTAL ASPECTS TO APPLICATION IN PET IMAGING

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Abstract

Annihilation of positrons, either direct or via formation of positronium, presents an opportunity to study various fundamental topics such as quantum entanglement and conservation of discrete symmetries, while it is also the underlying process of the biomedical imaging with Positron Emission Tomography (PET). At the University of Zagreb Faculty of Science, we have focused on Compton scattering of the annihilation quanta, exploring it with scintillator-based single-layer polarimeters. I will present an overview of these activities pursuing two complementary research directions: the exploitation of quantum entanglement in PET, and detailed investigation of azimuthal correlations of annihilation quanta from positronium decay, supplemented by development and upgrade of the simulation framework.

In PET, we performed successful imaging of sources with clinically relevant activities, and we showed that using the quantum entanglement, manifested through azimuthal correlations of the annihilation quanta in Compton scattering, can reduce the random background fraction in the event sample [1, 2]. We also demonstrated that the inclusion of the polarization-correlated events may yield up to 10% sensitivity gain at preserved image quality.

On the fundamental side, we investigated ortho-positronium decays into three gamma photons, where correlations of the Compton azimuthal angles encode information about the quantum state of the initial system. The study using a modular system of three single-layer Compton polarimeters in a planar 3×120° configuration around a ^{22}Na source embedded in aerogel, will be presented.

To complement the experimental studies, we developed a simulation package, within Geant4 framework, that can artificially reconcile the otherwise physically incompatible Klein-Nishina statistics for single photons, with Pryce-Ward statistics for entangled photons, for the purpose of more efficient semi-classical simulations [3].

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This work was supported by the Croatian Science Foundation under the project number IP-2022-10-3878, and by the ‘‘Research Cooperability’’ Program of the Croatian Science Foundation, funded by the European Union from the European Social Fund under the Operational Programme Efficient Human Resources 2014–2020, grant number PZS-2019-02-5829, and by the European Union – NextGenerationEU through the National Recovery and Resilience Plan 2021-2026 Institutional grants of University of Zagreb Faculty of Science (ProPubFO).

FROM RADIOPHARMACEUTICAL DEVELOPMENT TO CLINICAL TRIALS – POLATOM'S EXPERIENCE

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Abstract

Recently, progress in the development of theranostic and personalised nuclear medicine has been observed globally. This progress stems from intensive studies of biological targets, targeting molecules, and radionuclide decay properties, all aimed at improving patient care. However, meeting regulatory requirements for clinical trials remains a challenge, particularly for novel radionuclides and innovative radiopharmaceuticals [1]. Recent clinical trial projects conducted at POLATOM in Poland, in collaboration with leading clinics at the national and European levels, will be presented. To name just a few, the ongoing multicentre DuoNEN phase III clinical trial examines the safety and effectiveness of radioligand therapy with mixed doses of [^{177}Lu]/[^{90}Y] DOTA-TATE, delivered by personalised dosimetry (Project No 2019/ABM/01/00077-00). Another personalised radioligand therapy approach is also being investigated for advanced MTC using the CCK2R-targeting compound [^{161}Tb]Tb-CP04, with safety, dosimetry, and preliminary efficacy evaluated in a first-in-human clinical trial (Project No 2024/ABM/02/00053). Collaborations within the SECURE, PRISMAP+, and ACCELERATE.EU initiatives at the European level are also endorsed.

To meet the growing demand for theranostic radionuclides, the new research facility at NCBJ/POLATOM is being launched, called "Center of Design and Synthesis of Radiopharmaceuticals for Molecular Targeting, CERAD". The 30 MeV cyclotron, Cyclone 30XP (Ion Beam Applications, IBA), is a key component. It accelerates alpha particles to an energy of 30 MeV with a maximum intensity of 50 µAe, ideally suited for the production of Astatine-211 [2], protons to energies ranging from 15 to 30 MeV with a maximum intensity of 400 µA, and deuterons to energies ranging from 9 to 15 MeV with a maximum intensity of 50 µA. It provides a powerful tool for producing innovative radioisotopes for medical applications that were previously unavailable in Poland and holds promise of further clinical developments.

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Acknowledgement

CERAD project is co-financed under the Smart Growth Operational Programme 2014-2020, Priority IV: INCREASING THE RESEARCH POTENTIAL, Measure 4.2. Development of modern research infrastructure of the science sector.

POSITRONIUM LIFETIME IMAGING ON THE BIOGRAPGH VISION QUADRA: FROM VALIDATION TO FIRST IN-VIVO CLINICAL RESULTS

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Abstract

Background. The mean lifetime of ortho-positronium (oPs) depends on the local molecular environment of the medium in which positronium forms, including its oxygenation [1]. This makes oPs lifetime a candidate biomarker that adds tissue-microenvironment information on top of conventional PET tracer uptake [2]. We report measurements obtained at Inselspital (Bern) in collaboration with Siemens Healthineers and the Jagiellonian University, establishing positronium lifetime measurement and imaging on a clinical long axial field-of-view (LAFOV) PET/CT, the Siemens Biograph Vision Quadra.

Methods. Quadra was operated in a singles acquisition mode that records every single-crystal interaction in list mode. We reconstructed three-photon events (3γE) offline by combining two 511 keV annihilation photons with one prompt photon from the radionuclide decay. The selection used a 20 ns triple coincidence window, isotope-specific energy windows, a 4.2 ns annihilation pair window, and a 30 crystal (~100 mm) prompt-annihilation separation cut to suppress the intrinsic ^{176}Lu background. The time-difference distribution (TDD) between prompt and annihilation photons was then fitted with a three-component model (para-positronium, direct annihilation, oPs) convolved with a Gaussian time response, using Bayesian inference and hierarchical extensions for cross-region comparisons [3].

Results. Reference measurements using different radioisotopes: ^{68}Ga, ^{124}I, and ^{82}Rb gave oPs lifetimes consistent with the literature water value [3]. A ^{124}I phantom of Amberlite XAD4–water mixtures established voxel-wise positronium lifetime imaging on a commercial scanner. Sample-level oPs lifetimes ranged from 1.82 ± 0.02 ns in water to 2.52 ± 0.03 ns in dry XAD4, and the four densities remained distinguishable down to $4 \times 4 \times 4$ mm^3 voxels [4]. A NEMA image-quality phantom acquired with ^{44}Sc was less successful: its 1157 keV prompt photon sits above Quadra's ~726 keV higher detection boundary, and the peak signal-to-background ratio was about four times worse than for ^{124}I at equivalent activity volume [5]. The first in-vivo data on a commercial LAFOV PET/CT were acquired in three subjects who received intravenous [^{68}Ga]Ga-DOTA-TOC, [^{68}Ga]Ga-PSMA-11, and [^{82}Rb]Cl. Organ-level oPs lifetimes in kidneys, liver, lungs, spleen, parotid gland, and a meningioma were compatible with reported tissue values. In the [^{82}Rb]Cl perfusion scan, mean oPs lifetimes in the right (venous) heart chambers were longer than in the left (arterial) chambers: right ventricle 1.96 ns (68 % HDI 1.69–2.18) versus left ventricle 1.44 ns (1.22–1.60), and right atrium 1.76 ns (1.46–1.99) versus left atrium 1.50 ns (1.15–1.72).

Letting arterial and venous blood have separate oPs lifetimes fit the data slightly better than treating them as one, and the difference pointed the expected way: venous blood, being less oxygenated, showed the longer lifetime [6]. We then performed voxel-wise positronium lifetime imaging in three thyroid cancer patients receiving oral [^{124}I]NaI as part of clinical staging. Six neck lesions in one patient (1.3–6.3 mL, 8.5–34.1 kBq mL^{-1}) yielded lesion-level τ3 values of 1.77–2.52 ns (per-lesion uncertainty 0.15–0.48 ns) and a combined-lesion estimate of 1.92 ± 0.11 ns, with the best individual 7 × 7 × 7 mm^3 voxel achieving τ3 = 1.77 ± 0.26 ns. To our knowledge these are the first in-vivo voxel-wise positronium lifetime maps from a commercial PET/CT [7]. The in-vivo data carry some limitation. The random three-photon fraction was high, 85–98 % across the VOIs we analyzed, and we did not model the type II random events specific to imaging-based oPs measurements. Since 3γE localization depends on time-of-flight along the line-of-response, some spill-in and spill-out between neighboring VOIs occurs. The ~726 keV photopeak ceiling excludes high-energy prompt emitters such as ^{44}Sc and reduces performance with ^{68}Ga and ^{82}Rb. Per-voxel precision at present is 0.15–0.50 ns at 7 mm, still larger than the ~0.1 ns separation expected between oxygenation states. The three-subject cohort per study supports proof-of-principle, not population-level inference.

Conclusions. Positronium lifetime measurement and imaging are feasible on a commercial LAFOV PET/CT under clinically routine conditions. Of the isotopes we tested, ^{124}I is currently the most favourable on Quadra: its 602.73 keV prompt photon sits inside the detection chain, and it accumulates in lesions at clinically relevant activity concentrations. The arterial–venous lifetime difference we see in the [^{82}Rb]Cl scan goes in the direction expected from blood oxygenation, but the cohort is too small to call this established; larger studies and better handling of random three-photon events should clarify whether the effect is reproducible and clinically useful.

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Acknowledgements

Supported by the Swiss National Science Foundation (SNF-Lead grant 216944) and the National Science Centre of Poland (OPUS24+LAP 2022/47/I/NZ7/03112). We thank the clinical teams at Inselspital and the Quadra singles-mode development team at Siemens Healthineers. The extended version of this work was also supported by the PRISMAP – The European Medical Radionuclides Program (Project_1729020993_aniX3).

TESTING MATTER-ANTIMATTER AND OTHER DISCRETE SYMMETRIES IN PARTICLE PHYSICS

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Abstract

Discrete symmetries have played a central role in the development of modern particle physics, deeply influencing our understanding of fundamental interactions and conservation laws. After a brief introduction to the concepts of charge conjugation (C), parity (P), and time reversal (T) symmetries, and their combinations CP and CPT, the talk will review the first pioneering tests performed in particle physics systems and the profound implications of the observed matter-antimatter (CP) symmetry violations for the Standard Model and cosmology. Selected modern experimental tests of discrete symmetries will also be presented, along with future perspectives in the field.

MEASURING THE POLARIZATION CORRELATION OF ANNIHILATION PHOTONS IN E^+E^- DECAYS USING MODULAR J-PET

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Photons emitted from positron–electron annihilation in the singlet state ($^1S_0$) of positronium exhibit entangled polarization states as predicted by quantum electrodynamics (QED) [1,2]. Since the use of conventional polarimeters is not feasible at MeV energy scale, Compton scattering serves as an effective polarization analyzer, exploiting the strong dependence of the scattered photon direction on the polarization of the incident photon. The Klein-Nishina differential cross section provides the theoretical foundation for polarization analysis through measurement of the angle between the scattering planes of the two annihilation photons [3,4]. The degree of polarization correlation can thus be quantified through the asymmetry parameter extracted from the angular distribution of Compton-scattered photons [4]. Although feasible with various detector technologies, precise determination of this observable benefits significantly from a detector with high efficiency for Compton interactions.

J-PET, a plastic scintillator-based positron emission tomograph, constitutes a uniquely suitable detector for such studies, as 511 keV photons predominantly interact via Compton scattering in plastic scintillators rather than through photoelectric absorption [5]. This characteristic allows direct measurement of the polarization-dependent angular distributions essential for the analysis. Recent J-PET measurements have revealed non-maximal entanglement between annihilation photons in porous polymer media, with the degree of polarization correlation showing sensitivity to the annihilation environment [6,7]. Motivated by these findings, we performed the measurement with the modular J-PET, the next-generation J-PET prototype offering improved detection efficiency, to investigate the polarization correlation of photons in e^+e^- decays and to explore how it varies with the annihilation environment.

This presentation will outline the experimental methodology with the modular J-PET, and the analysis framework developed for extracting the polarization correlation observable in vacuum and in different media, along with the broader implications for developing quantum-informed mechanisms in medical imaging [6,8].

Acknowledgements

We acknowledge support from the ERC Advanced Grant POSITRONIUM no. 101199807, the National Science Centre of Poland through grants no. 2021/42/A/ST2/00423, 2021/43/B/ST2/02150, 2024/53/N/ST2/04279, PLGrid infrastructure under grant no. PLG/2024/017688 and PLG/2025/018762, the SciMat and qLife Priority Research Areas budget under the program Excellence Initiative – Research University at Jagiellonian University.

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INTERACTION PROFILING OF $\beta^{+}\gamma$ ISOTOPES WITH AN EDGE-ON CZT-BASED IMAGING SYSTEM: A MONTE CARLO SIMULATION STUDY

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Abstract

The use of non-pure positron emitters in Positron Emission Tomography (PET) introduces additional prompt gamma emissions alongside the conventional 511 keV annihilation photons [1]. These prompt gammas can be exploited in $\beta^{+}\gamma$ imaging to provide a third coincidence signal that improves spatial localization of radiotracer decays, reduces uncertainty associated with positron range, enhances signal-to-background performance, and enables simultaneous imaging of multiple radiotracers. However, they also complicate signal discrimination by introducing spectral overlap with scattered prompt gammas, elevating random and scatter backgrounds, and increasing the complexity of accurately classifying detected events. In thick Cadmium Zinc Telluride (CZT)-based detector systems, the high cross section of Compton scattering and excellent energy resolution provide an opportunity to exploit these prompt gammas for enhanced imaging, while simultaneously requiring careful management of contamination and misclassification effects [2]. In this work, we present a Monte Carlo-based comparative evaluation of three clinically relevant non-pure positron emitters - Scandium-44 (^{44}Sc), Iodine-124 (^{124}I), and Cobalt-55 (^{55}Co) within an edge on CZT detector framework.

Simulations were performed using the GATE platform [3] to model photon interactions, including photoelectric absorption, Compton scattering, and multi-interaction photon events (MIPEs), with 10^{7} primary decays simulated for each isotope. The analysis focuses on quantifying the prompt gamma leakage into clinically relevant energy window (460-560 keV). ^{44}Sc exhibits a relatively simple decay scheme dominated by a single high-energy prompt gamma (1157 keV) with a high branching ratio (~94%). In contrast, ^{124}I produce multiple prompt gammas (603, 723, and 1691 keV) with lower branching ratios (63%, 10.36%, 11.14%). ^{55}Co demonstrates intermediate behavior, with multiple prompt gammas (931, 1316, and 1408 keV) and moderate branching ratios (76%, 7%, 16.86%). Among the investigated isotopes, ^{124}I exhibited the lowest prompt-gamma leakage into the PET energy window (1.706% of detected prompt gammas), followed by ^{44}Sc (4.8%) and ^{55}Co (16.42%). When normalized to the total number of simulated disintegrations, the corresponding contamination fractions were 0.33%, 0.51%, and 2.38%, respectively. These results indicate substantially higher prompt-gamma interference for ^{55}Co, suggesting increased background contamination and reduced signal purity in conventional PET energy windows compared with ^{124}I and ^{44}Sc. In addition, we performed a comprehensive sensitivity audit of possible triple-coincidence modes and MIPE chains across the investigated isotopes. This extensive characterization provides a foundation for future event-classification and interaction-sequencing methodologies in CZT-based $\beta^{+}\gamma$ imaging systems.

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Acknowledgements

This research was supported by the National Institutes of Health (Grant Nos: UG3EB034686 and UH3EB034686).

HOW AI IS RESHAPING NEXT-GENERATION PET SYSTEMS DESIGN

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Abstract

Since its introduction more than five decades ago, positron emission tomography (PET) has evolved from coarse single-ring scanners with discrete BGO blocks into total-body, time-of-flight (TOF) capable systems with sub-nanosecond coincidence timing and millimetre-scale spatial resolution. Each generation has been driven by intense engineering effort directed at the detector itself: faster scintillators, denser crystal segmentation, multi-channel SiPM readout, depth-of-interaction (DOI) encoding, and increasingly capable front-end readout ASICs [2]. However, sophisticated light-sharing geometries such as semi-monolithic slabs and DOI light-sharing concepts, which combine high 3D spatial resolution with excellent timing resolution, have not yet made it into commercial products. A central reason is the recalibration burden required to maintain their specified performance. In parallel with detector development, equally large effort has had to be spent on the mechanical accuracy of detector placement, particularly for high-resolution and MRI-integrated PET, where sub-millimetre alignment is required and mechanical tolerances are constrained by the magnet bore [3, 6].

More recently, the calibration paradigm itself has begun to shift. Benchtop measurements of light spread and timing in light-sharing detectors have provided the high-statistics datasets needed to train data-driven timing models that exploit the full single-event detector response. Such learned models have been shown to surpass classical analytical skew and walk corrections by explicitly resolving light transport, photon statistics, sensor response, and DOI effects, both at the waveform level [1, 4] and through structured residual formulations [5].

The same data-driven, in-system perspective can be applied to detector alignment. Recasting alignment as a maximum-likelihood distribution-matching problem, the rotations and translations of every detector block are optimised directly on TOF-binned list-mode coincidence data by stochastic gradient descent, so that the expected coincidence counts best match the true measurements under the alignment parameterized expectation model. This formulation removes the need for motor stages, rotating sources, or carefully separable point-source acquisitions and supports arbitrary tracer distributions and generic, non-cylindrical geometries while exploiting TOF and DOI information [6]. On a semi-monolithic preclinical prototype with deliberately perturbed initial geometry, this recovered detector positions to ~50–100 µm and orientations to ~0.1–0.3°, restoring 1 mm rod separability and matching the PSNR/SSIM of the precisely known blueprint configuration. We have extended this calibraiton framework/ paradigm to a single-event detector-conditioned approach to TOF timing: a shared network predicts single-interaction time offsets, with coincidence time differences reconstructed by subtraction; on a 24-module semi-monolithic prototype with 28 M coincidences from 450 ^{22}Na point-source positions, this improves CTR from 486 ps (skew) and 469 ps (walk) to 431 ps, while compact Transformer and Edge-MLP variants preserve nearly the full gain and generalise to detector pairs unseen in training.

Most recently, we have unified these previously separate calibration domains in a joint differentiable in-system framework: a single physics-constrained optimisation simultaneously infers detector poses, interaction-position estimation, energy response, and timing corrections from sparse point-source acquisitions, supervised only at the coincidence level through TOF-consistent line-of-response physics.

On the same prototype, it matches or slightly exceeds the conventional blueprint-plus-fan-beam workflow on hot-rod phantom reconstructions (PSNR, SSIM, COV; RC and PVR improved for five of six rod diameters) while replacing multiple specialised stages with a single four-hour in-system procedure [3, 6].

The trajectory is clear: AI is no longer a post-hoc correction layer but the connective element that ties detector physics, geometry, and system-level performance into a single learnable model. The natural next step is to close the loop and let differentiable, physics-informed models drive detector and system design itself — jointly optimising scintillator topology, sensor layout, readout granularity, and reconstruction under realistic noise and timing constraints. Viewed from this perspective, next-generation PET systems will not only have been calibrated using AI, but may even have been developed in collaboration with AI.

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Acknowledgements

This work was funded by the Federal Ministry of Education and Research (BMBF) and the Ministry of Culture and Science of North Rhine-Westphalia as part of the National High-Performance Computing for Computational Engineering Sciences (NHR4CES) consortium. We thank NVIDIA for four RTX 6000 Ada GPUs through its Grant Program.

QUANTITATIVE RECONSTRUCTIONS OF ACTIVITY AND ATTENUATION FROM TIME-OF-FLIGHT PET DATA

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Abstract

Time-of-flight (TOF) PET data provide an effective means for attenuation correction (AC) when no (or incomplete or inaccurate) attenuation information is available. In this talk, I aim to demonstrate that with accurate modelling/corrections, results of joint reconstructions are comparable to the current clinical gold standard - ordered-subsets expectation maximization - using CT-based AC in PET/CT, as well as the current state of the art in PET/MR using zero time echo (ZTE)–based AC.

AI-BASED DELINEATION OF LYMPHOMA LESIONS IN FDG PET

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Abstract

Background: Total Metabolic Tumor Volume (TMTV) is a known prognostic biomarker in multiple cancer types. For TMTV determination, delineation of tumor lesions in PET images is required. This can be very time-consuming and susceptible to inter-observer variability when performed using semi-automatic methods. Deep Learning (DL) approaches hold promise to mitigate these problems by automating the delineation process. We have previously shown the efficacy of DL-based solutions in delineation of head and neck [1] and lung [2] cancer lesions and have recently developed a DL tool for lymphoma delineation in PET/CT called *LyROI* [3]. Here, we present extension of *LyROI* to PET-only operation and its validation on a modern digital PET scanner not seen during the training.

Methods: Automated delineation was performed with an ensemble of 3D U-Net convolutional neural networks (CNNs) developed using the *nnU-Net* framework in three different configurations. 1192 [^{18}F]FDG PET/CT scans of Non-Hodgkin lymphoma patients from the PETAL [4] trial were used for network training and testing using a 5-fold cross-validation scheme (results for PET-positive scans reported here). The ground truth delineations were developed iteratively by an experienced observer with assistance of intermediate CNN models. The network training was performed with either PET only or PET and CT images as input. The PET-only network was additionally validated on data acquired using a Siemens Biograph Vision 600 (N=76) to assess its generalizability to a newer scanner generation.

Results: Compared with the PET/CT CNN, the PET-only CNN achieved a similar median Dice coefficient in the cross-validation of 0.914 vs. 0.919, as well as comparable lesion detection performance for lesions >1 ml, with a positive predictive value (PPV) of 0.900 vs. 0.916 and a sensitivity of 0.867 vs. 0.863. The Mean Absolute Error (MAE) of TMTV determination was 47.3 ml vs. 47.8 ml, respectively. For the additional validation data, the PET-only network reached a median Dice coefficient of 0.891, PPV of 0.883, and sensitivity of 0.808, with a MAE of TMTV determination of 54.2 ml.

Conclusions: The additional benefit of CT-derived information for DL-based delineation of non-Hodgkin lymphoma appears to be limited. *LyROI* generalizes well to the data from the newer PET scanner with only minor degradation in delineation performance. All developed CNN models and tools are freely available at https://github.com/hzdr-MedImaging/LyROI.

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SPECTROSCOPY OF PIONIC ATOMS AND H' MESIC NUCLEI

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Abstract

Recent progress in the spectroscopic studies of mesic atoms and mesic nuclei will be reported including the present status and future perspectives in the pionic atoms and the eta' mesic nuclei. The spectroscopy of the bound systems provides information on the low-energy strong interaction between the mesons and the nuclei, where the QCD exhibits interesting features due to its non-perturbative nature. The high density of the nuclear medium may modify the strong interaction through the wave function renormalization effects. Precision spectroscopic information of the bound states deduces the medium effects and provides information on the non-trivial structure of the QCD vacuum.

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FROM PALS TO PLT: RANDOMS-LIMITED PRECISION AND ACTIVITY OPTIMIZATION FOR POSITRONIUM LIFETIME TOMOGRAPHY

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Abstract

Positronium Lifetime Tomography (PLT) extends the principles of Positron Annihilation Lifetime Spectroscopy (PALS) to *in vivo* imaging, enabling spatially resolved measurements of ortho-positronium (o-Ps) lifetime. While conventional PALS experiments are typically performed at low source activities where random coincidences are negligible, PLT requires substantially higher activity levels to compensate for the limited scan duration available in clinical imaging and the short half-lives of commonly used PET isotopes. As a result, random coincidences become a major source of background and can fundamentally limit the precision of o-Ps lifetime estimation.

In this work, we investigate the precision limits of PLT using the Cramér–Rao Lower Bound (CRLB) framework. Real measurements of true and random coincidence rates from ^{44}Sc, ^{68}Ga, and ^{82}Rb are used to model realistic PET acquisition conditions. The analysis reveals the trade-off between improved counting statistics and increased random coincidences as activity increases. By comparing CRLB predictions across activity levels and isotopes, we identify optimal operating points that minimize lifetime estimation uncertainty and evaluate the relative performance of each isotope for PLT applications. These results provide theoretical performance benchmarks and practical guidance for activity selection and protocol optimization in future positronium lifetime tomography studies.

BRAIN IMAGING OF CHRONIC PAIN: INSIGHTS FROM NUCLEAR MEDICINE

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Abstract

Objective: Chronic pain is typically attributed to tissue injury or damage to the nervous system. However, some patients experience persistent pain in the absence of identifiable tissue or neural abnormalities. This type of pain has recently been classified as nociplastic pain (NP), which is thought to arise from altered pain processing involving both the central nervous system and descending inhibitory pathways. Nevertheless, its underlying mechanisms remain poorly understood. As a result, patients with NP are frequently diagnosed as pain of unknown origin and may not approach optimal treatments. We have demonstrated the cases presenting chronic pain accompanied by similar symptoms of attention-deficit/hyperactivity disorder (ADHD), whose pain improved following treatment with ADHD medications. We investigated cerebral function alterations in patients with NP who were treated with ADHD medications using cerebral blood flow (CBF) SPECT. **Methods**: We retrospectively identified 65 patients (mean age 53 ± 14 years; 30 men and 35 women) who underwent CBF-SPECT before and after ADHD medication initiation. Clinical scores included the Clinical Global Impression-Severity (CGI-S) scale, pain Numerical Rating Scale (NRS), Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale (PCS), and Conners' Adult ADHD Rating Scale-Self Report (CAARS-SR). Voxel-based statistical analyses were performed to compare pre- and post-treatment CBF-SPECT images to identify brain regions associated with clinical measures. **Results**: Compared with post-treatment scans, pre-treatment CBF-SPECT demonstrated significantly increased perfusion in the precuneus, insular cortex, and thalamus (paired t-test, cluster-defining threshold $p<0.001$, cluster-level $p<0.05$, with family-wise error correction). The hyperperfusion in the precuneus was positively correlated with the CGI-S score and was significantly decreased following methylphenidate treatment. **Conclusions**: These findings suggest that altered brain function, particularly in the precuneus, may contribute to the pathophysiology of nociplastic pain. Furthermore, CBF-SPECT may help identify patients with chronic pain who are likely to benefit from ADHD-targeted pharmacotherapy.

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HYPERONIC INTERACTION STUDIES AT THE LHC TO UNDERSTAND NEUTRON STARS

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Abstract

Neutron stars provide a unique environment for studying matter at densities far beyond those reached in ordinary nuclei. In such conditions, strange baryons, such as Λ and Ξ hyperons, may appear in the stellar core [1]. Their presence, however, creates a long-standing tension: many theoretical descriptions predict that hyperons soften the equation of state, reducing the maximum neutron-star mass below the values observed astrophysically. Resolving this issue requires a better understanding of the interactions between hyperons and ordinary nucleons, particularly the hyperonic three-body forces [2]. So far, efforts to include three-body contributions have largely relied on limited experimental input from hypernuclei, used to anchor the low-energy constants of effective field theories. However, existing data are less precise than theoretical uncertainties and remain particularly scarce for Ξ−hyperon systems. Femtoscopic measurements in high-energy collisions at the LHC offer a novel and complementary approach to probe hyperon–nucleon–nucleon interactions [3]. In particular, preliminary theoretical studies of the p–p–Λ correlation function indicate sensitivity to three-body forces, with potentially sizable effects [4]. In this contribution, recent measurements and developments in the study of p–p–Λ correlations across different collision systems are presented. Comparisons between systems and event centralities provide insight into how the sensitivity to three-body forces evolves with the size of the collisions. In addition, new results on p–p–Ξ^- correlations, probing systems with double strangeness, are discussed together with future perspectives.

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Acknowledgements (optional)

This project has received funding from the European Research Council (ERC) under the European Union's Horizon Europe research and innovation programme (Grant Agreement No. 101220549 — HUNTING-3BFs).

IMPLEMENTATION OF ETHOS AUTOMATED ADAPTIVE THERAPY IN PATIENTS TREATED FOR MALIGNANT PROSTATE TUMORS.

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Abstract

This study presents dosimetric optimization of online adaptive radiotherapy (ART) implemented in the Varian Ethos system for prostate-cancer treatment using an end-to-end (E2E) verification methodology. The work included generation of a reference treatment plan, online adaptation based on CBCT images, and absolute dose measurements in a RUBY adaptive phantom using a Semiflex 3D ionization chamber. Agreement between measured and calculated doses was assessed for the baseline, scheduled, and adapted plans, with additional independent verification in the Mobius system. The highest agreement was observed in the CTV region, whereas larger yet clinically acceptable deviations were found in organs at risk located in high-dose-gradient regions. A measurement uncertainty budget was estimated in accordance with ISO GUM, TRS-398, and TG-51 recommendations; the total standard uncertainty was approximately 2.69% (1σ), corresponding to an expanded uncertainty of approximately 5.4% (k = 2). The findings confirm dosimetric stability and clinical acceptability of the adaptive workflow for prostate radiotherapy,

Adaptive radiotherapy is one of the fastest-developing techniques in radiation oncology. Over the last several months, the use of adaptive radiotherapy has increased rapidly in radiotherapy departments worldwide. At present, the Varian Medical Systems Ethos platform is installed in more than 60 centers worldwide and in 5 centers in Poland. Wroclaw is the second center in Poland to implement treatment based on the ETHOS system and the first to perform integrated dosimetric optimization based on an E2E test.

Definitive radiotherapy of the intact prostate is particularly relevant in patients with so-called early advanced disease and involves irradiation of the entire organ (intact radiation therapy). The rationale for definitive adaptive radiotherapy (ART) in radical treatment is based on two assumptions: high antitumor effectiveness through physical or biological dose escalation, and good treatment tolerance through toxicity reduction.

Dose escalation. Clinical studies show that the higher the absorbed dose delivered to the prostate, the greater the probability of complete tumor control (biochemical control). Thanks to online adaptation, it is possible to deliver a high total dose, for example 80 Gy, with improved safety because each fraction is closely matched to the current geometry of the organ and the topographic anatomy of the lesser pelvis.

Toxicity reduction. Limiting dose to the rectum and bladder may reduce adverse effects such as bleeding, urinary frequency, and pain. In non-adaptive radiotherapy, wider tissue margins around the prostate (PTV) are required, which means that adjacent healthy organs receive part of the therapeutic dose. In ART, margins can be minimized because the dose distribution is adjusted to changes in target geometry caused by organ motion and variations in prostate shape and size. ART therefore provides a high degree of treatment individualization.

Adaptive radiotherapy focuses on dose delivery by adjusting the treatment plan to the patient's changing anatomy and/or physiology, with the aim of improving treatment outcomes while minimizing complications related to normal-organ function. At present, ART may be more formally defined as radiotherapy in which the delivered dose is monitored for clinical acceptability during treatment and modified daily when necessary to improve clinical outcomes. By generating a derivative dose distribution each day and modifying the original treatment plan to reflect changes in target and critical organs as well as changes in patient body habitus, ART ultimately aims to maximize homogeneous dose delivery to the tumor while minimizing the dose to healthy tissues. In some cases, dose distributions in normal tissues may be less favorable than in the original plan despite optimization intended to minimize exposure.

The main objective of this study was the dosimetric optimization of adaptive radiotherapy implementation in the Ethos system for the treatment of prostate cancer using the end-to-end method, together with cross-validation of absolute dosimetry against independent Mobius calculations.

To achieve the primary objective, the following specific aims were defined.

1. To assess agreement between the dose measured with an ionization chamber and the dose calculated in the reference, updated, and adapted plans.

2. To analyze the impact of autosegmentation and subsequent manual correction on the final dosimetric result.

3. To identify potential sources of measurement uncertainty in high-dose-gradient regions.

DALITZ PLOT STUDY FOR ORTHOPOSITRONIUM DECAYS INTO THREE PHOTONS WITH THE J-PET TOMOGRAPH

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on behalf of the J-PET collaboration

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*Corresponding author: sushil.sharma@uj.edu.pl The Dalitz plot for the three-body decay of positronium has so far been only scarcely investigated experimentally [1]. Recent advances in positronium studies have been enabled by the Jagiellonian Positron Emission Tomograph (J-PET) [2-4], a detector based on organic scintillator strips with nearly full solid-angle acceptance. In this talk, we will present the first experimental determination of the Dalitz plot for the threephoton annihilation of ortho-positronium (o-Ps) over almost the entire available phase space. These results open new opportunities for precision studies of positronium and for testing higher-order QED corrections starting at O(α) [5,6] in a purely leptonic bound-state system.

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J-PET MODULES AS A RECONFIGURABLE DETECTION SYSTEM FOR ANTIMATTER PHYSICS

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Abstract

Direct tests of weak equivalence principle (WEP) for antimatter are pursued along two complementary routes: with antihydrogen at CERN and with positronium at the University of Trento [1,2]. At CERN, the AEgIS experiment aims to measure the gravitational acceleration of a horizontally boosted, pulse antihydrogen beam, produced via charge exchange between Rydberg positronium and antiprotons as it traverses a moiré deflectometer [1,3]. At Trento, the Antimatter Laboratory (AML) is commissioning a pulsed positron beam intended to drive a metastable 2^3S positronium beam through a deflectometer to measure the inertial sensing on Ps atoms [4,5]. The same beamline will be used to perform the studies of three-photon annihilation entanglement. Both programmes share a common detection requirement: position-sensitive reconstruction of the annihilation vertex, together with the beam profile, at the precision the gravity measurement demands [6,7]. The J-PET detector, built from plastic scintillators, addresses these demands with reconfigurable geometry. Its modular prototype comprises 24 portable detection units, each housing 13 plastic scintillator strips read out by SiPM matrices with an FPGA-based, triggerless data-acquisition system [8,9]. Each module can operate as a stand-alone, portable detector and can be reconfigured to match the beam under study.

In this talk, I will present the portable, reconfigurable J-PET module concept, with emphasis on the extended field of view that enables photon- and pion-specific configurations for the antimatter-gravity programme at AML and at AEgIS, respectively.

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ANALYTICAL BLANK SCAN MODELLING FOR DETECTOR SCATTERED ATTENUATION CORRECTION (DSAC)

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Abstract

Quantitative Positron Emission Tomography (PET) requires Computed Tomography (CT) for attenuation correction, but this comes with an extra radiation dose, hardware costs, and registration complexities [1]. Due to these problems, we look for CT-less PET imaging techniques to perform attenuation correction without CT [2]. We propose Detector Scattered Attenuation Correction (DSAC), which is a method specifically designed for plastic scintillator-based PET systems [3, 4]. These systems involve a large number of detector scattered coincidences due to the low atomic number of plastics, which leads to significant Compton scattering [4, 5].

The fundamental problem with DSAC is the lack of a blank scan, which we fulfil by providing an analytical blank scan model for generating a blank scan from attenuated direct coincidences. We validate our model using Simplified Monte Carlo Simulations & also with GATE [6]. Using this analytical blank scan, we have successfully converted the DSAC framework into a CTAC-like problem. This method also eliminates the need for joint reconstruction (DS-MLAA) by decoupling the activity from the attenuation along detector scattered coincidences.

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We acknowledge support from the National Science Centre (NCN), grant nos.

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KLEIN-NISHINA MEETS PRYCE-WARD: THE BEST FROM BOTH WORLDS FOR THE SEMI-CLASSICAL SIMULATIONS OF THE ANNIHILATION PHOTONS CORRELATIONS

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Abstract

A joint Compton scattering of the two maximally entangled photons in a singlet state of orthogonal polarizations – such as those from the ground state para-positronium annihilation – exhibits increased angular correlations, relative to the scattering of the two independent photons. These increased correlations may be artificially implemented in the otherwise classical photon tracking simulations, treating the two photons as separate entities. However, the singlet entangled state in question is rotationally invariant, lacking any and all physical information on the single photon polarizations; only the state of an entire entangled system is well defined. Therefore, the single-photon-polarization degrees of freedom still available in the semi-classical simulations are clearly at odds with the assumption of their entangled state.

The joint Compton scattering of thus entangled photons is governed by the double-differential Pryce-Ward cross section. On the other hand, the scattering of each independent photon is described by the Klein-Nishina cross section, its azimuthal dependence defined relative to a given photon's initial polarization. Since the singlet entangled state lacks any information on the single photons' polarizations, the azimuthally-dependent Klein-Nishina cross section is incompatible with the Pryce-Ward correlations. However, for purposes of the semi-classical simulations (retaining the single-photons' polarizations as the unphysical degrees of freedom) the Klein-Nishina and Pryce-Ward descriptions can be made compatible by sampling an artificially modified form of the cross section, subsuming both the single-photons' Klein-Nishina statistics and their Pryce-Ward correlations.

We present a recommended form of the modified cross section, as the general solution is not unique. Artificially reconciling the otherwise physically incompatible aspects of the two-photon system not only allows for a more efficient utilization of the computational resources, but also ensures that the two photons are treated consistently within a semi-classical approach.

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Acknowledgements

This work was supported by the Croatian Science Foundation under the project number IP-2022-10-3878 and by the European Union – NextGenerationEU through the National Recovery and Resilience Plan 2021-2026 Institutional grant of University of Zagreb Faculty of Science (ProPubFO).

Towards Rigorous Entanglement Detection of Para-Positronium Annihilation Photons

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Abstract

The annihilation of ground-state para-positronium (*p*-Ps) into two photons is a fundamental process in quantum electrodynamics (QED). While conservation of angular momentum and parity dictates that the resulting photons emerge in a maximally entangled polarisation singlet state, unambiguous experimental verification of this entanglement remains an open challenge. However, newly developed detectors such as J-PET [1], which rely on Compton scattering where photon polarisation information is preserved, open the door to witnessing entanglement without making strong assumptions about the initial photonic state.

In this work, we employ the S-matrix formalism of QED and analyse the relevant Feynman diagrams to rigorously derive the differential cross-sections for correlated photons [2]. Having established these foundations, we review the validity and constraints of the commonly used R-factor [3, 4], identifying the specific classes of initial photonic states for which it can be reliably used as an entanglement witness and quantifier [5].

We consider the well-established class of two-qubit X-states, extending our analysis to provide tools that go beyond the R-factor for the verification of entanglement from scattering data. By applying these quantum information methods, we investigate the precise dependence of entanglement quality on the R-factor and derive a rigorous analytical form of the differential cross-section applicable to a wide range of photon states. Our results reveal that while the R-factor is well-defined only for a specific subclass of X-states, noise analysis demonstrates it remains a robust measure even under the classical mixing of polarisation angles. Ultimately, the framework proposed provides a foundation for generalising entanglement witnesses to ortho-positronium and other multi-photon decays.

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TEMPERATURE DEPENDENCE OF FREE VOLUME SIZE DISTRUBUTION IN NAFION MEMBRANE CHARACTERIZED USING POSITRONIUM

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Abstract

The Nafion membrane, a perfluorosulfonic acid polymer manufactured by DuPont, is widely used as a proton exchange membrane (PEM) in electrolyzers due to its exceptional chemical stability, mechanical strength, thermal stability, and proton conductivity. It is also utilized as a solid electrolyte in proton exchange membrane fuel cells (PEMFCs). In recent years, Nafion has played an increasingly important role in biomedical and healthcare sectors as a key component in sensors, implantable biomedical devices, smart drug delivery platforms and antimicrobial coatings.

Nafion consists of a PTFE (polytetrafluoroethylene) backbone with pendant side chains that end in sulfonic acid groups. When exposed to water, which the polymer readily absorbs, these sulfonic acid groups aggregate to form "clusters." These clusters are thought to contribute to the unique mechanical and transport properties of Nafion.

The size distribution of free volume within Nafion is influenced by the distribution of these clusters. Upon the absorption of water, the size of the clusters increases, leading to a reduction in the size of the free volume cavities and resulting in a narrower size distribution. However, there is limited information available regarding the effect of temperature on the free volume size distribution in this polymer. The aim of the present study is to investigate the impact of temperature on the free volumes in Nafion, using positronium (Ps) as an atomic-sized probe.

Our investigations conducted in the temperature range of 140 to 420 K revealed that the lifetime of pick-off annihilation of ortho-positronium (o-Ps) increases with temperature, indicating a rise in the number of free volume sites. Notably, this temperature dependence shows distinct changes in slope at 223 K and 378 K, which correspond to glass transitions occurring in the cluster region and an increase of the mobility of the backbone chains. As temperature rises, the average size of free volumes in Nafion increases, and the distribution of these free volumes becomes broader. In contrast, the yield of Ps decreases with increasing temperature. This decline suggests that free electrons generated during positron thermalization are captured by positively charged free radicals at elevated temperatures, which competes with the formation of Ps.

MONTE CARLO SIMULATION OF POSITRONIUM LIFETIME IMAGING WITH MATERIAL-DEPENDENT PICK-OFF ANNIHILATION AND OXYGEN QUENCHING

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Abstract

This work presents a Monte Carlo simulation framework for positronium lifetime imaging that computes tissue-specific ortho-positronium lifetimes from the Tao-Eldrup free-volume model with oxygen quenching, integrated directly into the transport loop of a clinical PET scanner simulation. Positronium lifetime provides insight into the tissue microenvironment where positrons are emitted, as the ortho-positronium (o-Ps) pick-off annihilation rate depends on intramolecular void size and the molecular composition of the surrounding medium. The decay rate is also affected by dissolved oxygen concentration through spin-exchange interactions with molecular oxygen [3]. Current simulation software does not model interactions between positronium atoms and the medium, such as conversion or pick-off processes that reduce o-Ps lifetime and lead to two-photon annihilation [1]. Instead, most studies use fixed lookup tables or estimate pick-off rates from bulk electron density, without considering void size. The Tao-Eldrup model [2] links the pick-off annihilation rate to the void size where o-Ps forms: smaller voids increase overlap with surrounding electrons, shortening the lifetime. When combined with an oxygen quenching term proportional to local partial oxygen pressure
[3] and material-specific formation intensities, this model can predict lifetimes for tissue states not yet characterized by positron annihilation lifetime spectroscopy (PALS). This study used GATE 9.4.1 with custom Geant4 11.3 physics processes and a validated Siemens Biograph Vision Quadra digital twin. Three phantoms were simulated with both the Tao-Eldrup model and the lookup table for comparison: (i) a multi-tissue phantom (water, adipose, muscle, brain, tumor) with Sc-44, (ii) a reproduction of the Mercolli et al. XAD-4 phantom experiment [4] with I-124, and (iii) a hypoxia gradient phantom spanning partial oxygen pressures from 2 to 40 mmHg. Cross-source predictions across four independent adipose-tissue samples agreed within mean residual 3.8%, and simulated lifetimes were recovered within 5.7% of configured values across eight tissues. For the XAD-4 phantom [4], the framework distinguished four humidity states across a 360 ps range, while the lookup table cannot represent humidity-dependent variation. For the hypoxia phantom, the total lifetime shift between pO2 = 2 and 40 mmHg was 3.4 ps, which is about 63 times below the scanner's coincidence resolving time. Although o-Ps response to dissolved oxygen is highly linear [3], achieving sufficient count statistics for spatially resolved oxygen imaging remains challenging at clinical activity levels.

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Refractive Index Dependence on Detection Efficiency and CTR in Simulated Cherenkov-based TOF-PET Detectors

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Abstract

In PET, time-of-flight (TOF) information of annihilation photons can localize the source position along the line of response, yet the coincidence time resolution (CTR) of state-of-the-art scanners remains around 200 ps. Detectors measuring Cherenkov photons for timing have attracted attention; a CTR of 30 ps has been achieved with using a pair of Cherenkov-radiator-integrated microchannel plate photomultiplier tubes (CRI-MCP-PMTs) [1]. However, the detector configuration using 3.2 mm-thick lead glass window (n=~1.5) was optimized for CTR, at the cost of detection efficiency, and a detector simultaneously achieving ultrafast CTR and practical detection efficiency is required for clinical PET implementation. In this study, we focused on the refractive index of the radiator as a design parameter and investigated its effect on coincidence detection efficiency and CTR. We hypothesized that a higher refractive index, by increasing the number of Cherenkov photons produced based on the Frank-Tamm formula, would improve both detection efficiency and CTR. We modeled point-source measurements with a CRI-MCP-PMT pair using a Geant4-based simulator [2] incorporating measured single-photon response, PMT gain fluctuation, and electrical noise, validated against experimental data. Lead fluoride was used as a window material, with Cherenkov photon behavior modeled over 240–840 nm. The window thickness was kept at 3.2 mm to highlight the effect of refractive index difference on CTR. Simulations were performed for flat refractive indices of 1.5, 2.0, 2.1, 2.5, and 3.0, and for the true dispersive refractive index [3] (1.7–2.1). Detection efficiencies for refractive indices of the true value, 1.5, 2.0, 2.1, 2.5, and 3.0 were 1.5%, 0.5%, 1.9%, 2.1%, 2.6%, and 3.0%, with corresponding CTRs of 51.6±0.3, 41.8±0.4, 41.6±0.2, 42.0±0.2, 44.6±0.2, and 49.6±0.2 ps. Detection efficiency increased with refractive index as expected; however, CTR deteriorated for $n > 2.0$, attributable to the reduced speed of light in the medium c/n increasing timing jitter. Furthermore, despite the true refractive index lying between 1.7 and 2.1, its CTR was worse than both flat $n = 1.5$ and $n = 2.1$ cases, suggesting that wavelength-dependent dispersion degrades CTR. These results indicate that while a higher refractive index improves detection efficiency, it may degrade CTR, and a spectrally uniform refractive index may be important for fast timing.

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Copper-64 chloride as a precursor for modern radiopharmaceuticals - characterization of ^{64}Cu-DOTATOC in NET Diagnosis

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Abstract

The use of Copper-64 (^{64}Cu) in nuclear medicine represents a significant step towards personalized theranostics. Due to its three decay modes (β+, β- and EC) and a half-life of 12.7 h, this nuclide bridges the gap between short-lived Ga-68 and therapeutic Lu-177 [1-2].

The extended half-life of Cu-64 compared to Ga-68 allows for better distribution logistics and delayed PET imaging, which significantly enhances diagnostic sensitivity. Furthermore, the lower positron energy of Cu-64 results in a shorter positron range in tissue, providing higher spatial resolution images and improved detection of very small neoplastic lesions [2]. This research focuses on the efficient production of copper-64 chloride and its application in labeling the somatostatin analog – DOTATOC (edotreotide). The employed DOTATOC peptide is characterized by strong targeting of SSTR2 and SSTR5 receptors, which are overexpressed in tumor cells [3].

The copper-64 radionuclide was produced by proton irradiation of an enriched Ni-64 target in a cyclotron. Separation was performed using an automated module with ion-exchange resins. The DOTATOC labeling process was conducted under optimized pH and temperature conditions. Radiochemical purity (RCP) was verified using radio-HPLC and iTLC.

Cu-64 chloride was obtained with a radionuclide purity of over 99,9%. Optimization of the labeling process resulted in radiolabeling 64Cu-DOTATOC yield exceeding 98% without the need for final purification. The promising results of the production process optimization and the positive evaluation of radiochemical parameters served as a basis for initiating clinical trials in patients, which will open a new pathway in precise receptor diagnostics.

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This work was supported by the project „**Przeprowadzenie prac badawczo-rozwojowych produktu radiofarmaceutycznego do diagnostyki raka prostaty i guzów neuroendokrynnych**", cofinanced by the **Medical Research Agency**.

Positronium imaging with the 8π gamma-ray spectrometer

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Abstract

Conventional positron emission tomography (PET) uses the detection of pairs of coincident gamma-rays produced in electron-positron annihilation to non-invasively visualize and examine physiological processes in the body. In tissue, more than 40% of annihilations occur following the formation of positronium, an unstable bound system consisting of an electron and a positron, which exists either in a singlet or a triplet state. Due to the conservation of charge conjugation parity, the latter produces odd numbers of gamma-rays upon self-annihilation, with the emission of three gamma-rays being the most probable. Interactions with the surrounding environment can cause positronium to switch states through a process known as spin-conversion. Consequently, measurement of the ratio of 2-gamma to 3-gamma events, can provide insights into properties such as oxygenation and porosity, enabling inferences to be made about the health of the surrounding tissue. While conventional PET has higher spatial resolution with no sensitivity to the surrounding environment, 3-gamma imaging has limited spatial resolution but offers the ability to provide information on the environment in which the annihilation occurred. By coupling conventional and 3-gamma PET, information on the localization of positron annihilation in space can be augmented with information on the conditions in which the annihilation occurred, offering more insight than obtained from individual modalities.

As of yet, there is no standardized method for reconstructing a 3-gamma image. The present work sets about to examine one of the possible approaches. The 8π gamma-ray spectrometer in the Nuclear Science Laboratory (NSL) at Simon Fraser University (SFU) was used to measure the energy of gamma-rays in triple coincidence emitted in positronium annihilation following ^{18}F positron decay. The ^{18}F was produced in the neutron-activation of a Teflon disk. Subsequent data analysis lead to successful reconstruction of a three-dimensional 3-gamma PET image of the ^{18}F source. In this experiment, the 8π spectrometer employed an array of 72 bismuth germanium oxide (BGO) detectors arranged in icosahedral symmetry, representing ~95% solid angle coverage. Currently, the addition of 20 high purity germanium (HPGe) Compton-suppressed spectrometer (CSS) is underway, with the goal of improving spatial resolution through increasing detector energy resolution.

Previous results, current developments and planned future studies will be presented and discussed.

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Development of a Cherenkov-based Compton Camera for High-Efficiency Gamma Imaging in the MeV Regime

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Abstract

Compton cameras are promising imaging devices with applications in nuclear medicine and radiation therapy involving high-energy gamma emitters. In contrast to conventional techniques such as PET and SPECT, Compton cameras operate without mechanical collimation and exploit the dominant interaction processes of gamma radiation above approximately 500 keV. However, their detection efficiency in the MeV regime is often limited by the low interaction probability in the scattering layer, which is typically constrained to small thicknesses to preserve spatial and angular resolution.

We present a novel Compton camera concept under development at the University of Siegen that aims to overcome this limitation by employing Cherenkov ring detection in the scattering layer. By reconstructing the Cherenkov cone from detected ring patterns, the interaction point of the scattered electron can be localized, enabling the use of thicker scatterers without sacrificing reconstruction capability. This approach can increase efficiency and enable quasi real-time imaging.

A key application of this concept is the imaging of radionuclides used in TAT, such as Actinium-225. Current dose verification relies on SPECT, however, image quality is severely limited due to low administered activities and the inefficiency of collimator-based systems. The proposed Compton camera targets the 1.57 MeV gamma emission of Actinium-225, offering the potential for significantly improved imaging performance.

The detector design comprises a UV-transparent PMMA-based scattering layer coupled to an array of silicon photomultipliers (SiPMs) and a scintillator-based absorption layer with SiPM readout. We report first experimental results demonstrating the feasibility of the concept. Measurements with a scaled-down 5×5 SiPM array coupled to PMMA and irradiated with a Sr-90 source reveal a Cherenkov light distribution, with a clear dependence on the electron beam position. For the absorption layer, studies of scintillator crystals enabled absorption point reconstruction, energy calibration, and timing characterization. A 3D image reconstruction algorithm based on LM-MLEM has been developed, where the ARM and SPD are modelled based on energy and positional uncertainties. In addition, a machine learning algorithm for reconstruction of the Compton scattering vertex has been developed using the individual Cherenkov photon hit positions on the SiPM array. These results represent an important step toward the realization of a first prototype system.

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STUDY OF AZIMUTHAL CORRELATIONS OF COMPTON-SCATTERED GAMMAS FROM ORTHO-POSITRONIUM

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Abstract

Ortho-positronium decays in three gamma-photons which, among others, carry information about quantum states of the initial system accessible through determination of azimuthal correlations of Compton-scattered photons. A modular system based on three single-layer Compton polarimeters comprising scintillator matrices read out by silicon photomultipliers was used to study different types of azimuthal correlations. We present the results of measurement with Na-22 source sandwiched between two small aerogel cylinders and modules placed around the source in a planar 3 ×120º configuration.

Acknowledgements

This work was supported by the Croatian Science Foundation under the project IP-2022-10-3878 and by the European Union – NextGenerationEU through the National Recovery and Resilience Plan 2021-2026 Institutional grant of University of Zagreb Faculty of Science (ProPubFO).

Study of ortho-positronium lifetime with the modular J-PET system

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Abstract

Ortho-positronium (o-Ps), a bound electron–positron system, predominantly decays into three photons and, due to the absence of hadronic effects, provides a clean environment for precision studies within Quantum Electrodynamics (QED). Precise measurements of the o-Ps lifetime enable stringent tests of QED predictions and offer sensitivity to hidden-sector phenomena such as Mirror Matter [1].

We present an ongoing analysis of o-Ps decays using the modular J-PET detector [2,3,4], optimized for high-resolution timing and angular reconstruction. Dedicated reconstruction algorithms, supported by Monte Carlo simulations, are used to identify o-Ps $\rightarrow 3\gamma$ events accompanied by a de-excitation photon and to suppress dominant background contributions. The detection of the de-excitation photon allows for precise determination of the positronium formation time, which is crucial for accurate lifetime measurements.

The primary goal is a high-precision determination of the o-Ps decay rate at the level of $\sim$100 ppm. Any deviation from QED predictions may indicate oscillations into mirror states, leading to invisible decay channels and enabling constraints on photon–mirror photon kinetic mixing. The experiment aims to improve current limits, $\Gamma = 7.039979(11) \times 10^6 s^{-1}$ [5], by at least an order of magnitude.

The analysis includes data from J-PET runs, detector calibration, Monte Carlo simulations, and the development of machine learning methods for signal–background discrimination, forming the basis for a precision measurement of the o-Ps lifetime.

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Acknowledgements (optional)

We acknowledge support from the National Science Centre of Poland through Grants No. 2019/35/B/ST2/03562, 2020/38/E/ST2/00112, SPUB/SP/627733/2025 and the SciMat and qLife Priority Research Area budget under the auspices of the program Excellence Initiative-Research University at Jagiellonian University. We also acknowledge Polish high-performance computing infrastructure PLGrid (HPC Center: ACK Cyfronet AGH) for providing computer facilities and support within computational grant no. PLG/2024/017688 and PLG/2025/018762.

THE ^{44}Ti/^{44}Sc GENERATOR: CURRENT STATUS, CHALLENGES, AND PROSPECTS

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Abstract

The ^{44}Ti/^{44}Sc generator has attracted growing attention as a potential source of scandium-44 (^{44}Sc) for positron emission tomography (PET). The interest is easy to understand. ^{44}Sc combines a suitable half-life with relatively low positron energy and an additional prompt γ emission, which together make it attractive not only for PET imaging but also for emerging positronium imaging approaches [1, 2]. At the same time, the long half-life of the parent nuclide, titanium-44 (^{44}Ti), opens the possibility of a generator capable of providing ^{44}Sc over extended periods, with reduced dependence on cyclotron infrastructure [3]. Despite this, the system remains difficult to implement in practice. The availability of ^{44}Ti is still very limited, largely due to low production yields and demanding irradiation conditions [4]. In parallel, the chemistry of Ti(IV) under generator conditions is far from straightforward [5]. Hydrolysis, variable speciation, and interactions with sorbent materials can all influence the retention of the parent nuclide and the quality of the eluate, which in turn affects downstream radiolabelling.

This contribution summarises the current status of ^{44}Ti/^{44}Sc generator systems and discusses the main challenges that continue to limit their broader use. Particular attention is given to the interplay between production constraints and chemical behaviour, as these factors ultimately define the practical feasibility of the approach. While the potential of ^{44}Sc is widely recognised, further progress will depend on resolving these underlying issues rather than on incremental optimisation alone.

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Acknowledgements

We acknowledge support from the European Union within the Horizon Europe Framework Programme (ERC Advanced Grant POSITRONIUM no. 101199807), the National Science Centre of Poland through grants no. 2021/42/A/ST2/00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, the Sci-Mat and qLife Priority Research Areas budget under the program Excellence Initiative – Research University at Jagiellonian University.

Quantum ghost imaging with annihilation photons – a Monte Carlo study

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Abstract

Quantum ghost imaging is an imaging technique in which an object is reconstructed using light that does not directly interact with it. The principle relies on measuring spatial correlations between photons in a coincidence detection setup. In the gamma regime, a pair of photons originating from positron annihilation possesses energies of 511 keV, emitted with nearly opposite momenta, making them suitable for quantum imaging applications. Recent experimental studies have demonstrated the feasibility of quantum imaging with annihilation photons for dense high-Z materials, achieving superior contrast compared to classical transmission imaging [1]. In this work, we present the first Monte Carlo study of quantum imaging using annihilation photons. We obtain ghost images without information on the entanglement of the photons, utilizing the kinematics of the positron-annihilation photons from Na-22 source. When classical transmission and quantum modality are combined, the contrast-to-noise ratio of the real images is approx. 48% higher than using only the classical modality. We will also show that this non-invasive technique can distinguish between solid and hollow high-Z objects, as well as detect density variations within materials in a highly noisy environment better than the classical transmission imaging. These findings indicate that quantum imaging with annihilation photons has strong potential for applications in industrial inspection and illicit cargo detection.

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Acknowledgements (optional)

This research was funded by the European Union – Next Generation EU and is part of the project Voxel Matrix Detector for Full Solid Angle Radiological Imaging – VMDScan - NPOO.C3.2.R2-I1.06.0084.

OPTICAL PROPERTIES AND TIME RESOLUTION OF PLASTIC SCINTILLATORS FOR THE TOTAL-BODY J-PET SCANNER

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Abstract

Total-body Jagiellonian positron emission tomography (TB-J-PET) is based on long plastic scintillators [1] which decrease cost of the scanner [2]. Total-body PET scanners enable positronium lifetime imaging of organs in human body [3] and tissue samples [4], measurements of polarization of photons [5], CPT symmetry [6], and beam therapy monitoring [7]. Development of TB-J-PET requires application of transparent plastic scintillators with low light attenuation [8] to build long modules with silicon photomultipliers attached at both ends of the scintillators. Modular TB-J-PET construction requires quality control of plastic scintillators and verifying its optical properties [9]. Purpose of this research is to verify time resolution of plastic scintillators for the TB-J-PET modules construction.

Six types of polyvinyltoluene-based plastic scintillators with emission spectra covering the maximum quantum efficiency of light detection of silicon photomultipliers, were measured. The plastic scintillators had dimensions of 6 mm × 30 mm × 500 mm, polished surfaces: faces as-cast and edges diamond-milled, and were manufactured by Eljen Technology. The time resolution was measured at three points along the scintillator using a setup consisting of silicon photomultipliers (Hamamatsu, S13361-6674), oscilloscope, power supply, black box, and collimated Na-22 source.

The best time resolution were achieved by the EJ-204, EJ-200, EJ-208 plastic scintillators combining short signal decay time, high light output, high transparency, and the best match of the emission spectrum to the maximum quantum efficiency of the photomultipliers. The best plastic scintillator type for the next generation total-body J-PET scanner is EJ-200. The EJ-200 plastic scintillator combines the best time resolution with uniform time resolution along the scintillator strip.

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μPPET Event Classes

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Abstract

μPPET[1] is a cosmic-ray experiment at the Jagiellonian University in Kraków dedicated to investigating the muon puzzle — a longstanding discrepancy between model predictions and experimental measurements of the muon count at ground level, observed consistently across multiple experiments over the past 15 years [2,3]. To probe this puzzle, μPPET uses J-PET detectors originally developed for medical imaging. The apparatus comprises two detector systems: the **Big Barrel** (BB) [4], located at ground level inside a Faraday cage and used to reconstruct muon trajectories; and the **Modular detector**[5], which can be reconfigured and distributed across a rooftop to form the Modular Array (MA), reconstructing the arrival direction of the primary cosmic ray.

To identify discrepancies between predicted and measured muon fluxes, we define three event classes based on the combination of sub-detectors that record a coincident signal: **Brass** (at least one MA module triggered), **Silver** (at least three MA modules triggered), and **Golden** (at least two MA modules and the BB triggered). In this work, we explore the potential of this classification within the current simulation framework for use in data quality and physics analysis.

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Towards the reconstruction of air showers with the J-PET system

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Abstract

The *μPPET* project addresses the longstanding muon puzzle by constructing a phenomenolog-ical model of hadronic interactions that accounts for QCD corrections from polarisation effects [1]. A central challenge is reconstructing muon trajectories relative to the primary cosmic ray direction. The J-PET Big Barrel (BB) [2] serves as the muon detector, with its geometric res-olution already established. For primary direction reconstruction, the Modular J-PET [3] is reconfigured and distributed across the rooftop of the Department of Physics, Astronomy, and Applied Computer Science at Jagiellonian University, forming the Modular Array (MA). MA will provide time synchronisation of the shower.

In this work, we present early-stage progress towards the simulation and analysis foundation of the *μPPET* reconstruction pipeline. Using the J-PET framework and its calibration method-ology [4], a GEANT4-based description of the array response to air-shower secondaries is under development alongside the analysis of cosmic muon data, with attention to extracting energy-related observables from timestamps. We studied the potential of this configuration, and this foundational work is intended to support subsequent studies of shower geometry.

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Performance of a scintillator detector for particle beam fragmentation measurements in charged particle therapy

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Background: Particle therapy (PT) is an external beam radiotherapy where the dose is delivered using beams of light ions. Due to their favorable physical and radiobiological properties, conformal dose can be delivered. However, nuclear fragmentation processes introduce significant uncertainties in biological dose distributions, due to uncertainties in radiobiological effectiveness. Accurate experimental measurements of fragmentation are therefore essential, both to improve biological dose estimates in treatment planning as well as to enable advanced particle monitoring techniques based on secondary fragment detection.

Objective: The FOOT (FragmentatiOn Of Target) experiment aims to measure double differential fragmentation cross sections (in energy and angle) for ion beams at therapeutic energies. This work presents the status of the experiment, focusing on the performance of the Delta E–TOF detector and its role in fragment identification, including helium beams.

Methods: Measurements were performed using helium beams in the energy range of 100–220 MeV/u with a partial FOOT setup. The Delta E-TOF detector, composed of a thin Start Counter and a Time-of-Flight wall, was used to measure energy loss and time-of-flight, enabling reconstruction of fragment charge via the Bethe-Bloch formalism. These activities are part of a broader experimental program involving multiple beam species (He, C, O) and facilities such as HIT, CNAO, and GSI.

Main results: The Delta E-TOF detector shows stable performance, with energy resolution between 5.0% and 8.1%, time-of-flight resolution between 116 ps and 157 ps, and charge resolution between 2.7% and 4.5%, allowing clear separation of helium ions from lighter fragments. Distinct particle populations are observed in Delta E–TOF, demonstrating effective fragment identification. These results are consistent with the broader progress of FOOT, where recent measurements have achieved high-precision fragmentation cross sections. The collaboration has obtained angular and elemental cross sections for a 400 MeV/u ^{16}O beam on different targets, which will be reported. Additional studies have also demonstrated the capability to extract cross sections for hydrogen targets and to benchmark nuclear interaction models.

Conclusions: The Delta E-TOF detector meets the requirements for fragment identification. The FOOT measurements are highly relevant for particle monitoring applications, where accurate knowledge of types, amounts, angles and energies of secondary particles is important.

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Acknowledgements We thank GSI and CNAO for the operation of their facilities during the data taking, and INFN for building and running the detector.

CROSS-SECTION OF BOUND DINEUTRONS FORMATION WITH SIMULATION OF EXPERIMENTS FOR DIRECT DINEUTRON DECAY OBSERVATION

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Possible statistically significant indications of a bound dineutron in fast neutron-induced reactions on ^{159}Tb and ^{175}Lu have been reported previously, consistent with theoretical predictions by Migdal and Dyugaev suggesting the formation of a loosely-bound dineutron state in the nuclear potential well outside the volume of a nucleus. Direct observation of dineutron decay remains an open challenge, motivating detailed studies of its expected experimental signatures.

The objective of the present work is to evaluate the feasibility of experimentally observing bound dineutron formation and decay in neutron-induced nuclear reactions and to quantify the sensitivity of realistic detector systems to this process.

In this work, we investigate the sensitivity of simulated experiments to the cross section of bound dineutron formation using a GEANT-based model for future measurements, focusing on neutron-induced reactions on nuclei from the list in [1]. The simulations were performed within our dedicated multi-stage framework that integrates TALYS-based nuclear reaction calculations, a custom Python pipeline for activity evaluation and time-ordered event generation, and Monte Carlo particle transport with detector response modeling in a GEANT4-based application. The difference between the detected beta-spectra with and without dineutron formation, including detailed contributions from gamma-emissions of residual nuclei, is considered as a potential observable signature of bound dineutron formation followed by its decay. This spectral difference is strongly dependent on the assumed dineutron formation cross-sections and decay characteristics.

Our results indicate that, within a physically reasonable range of model parameters, the effect of dineutron formation can produce measurable distortions in the beta-spectrum that exceed statistical fluctuations and detector-related uncertainties. We determine the minimum detectable values of dineutron production yields and provide corresponding estimates of the formation cross-sections for selected rare-earth nuclei. These findings support the hypothesis that the dineutron-induced contribution may be experimentally accessible under optimized conditions.

In conclusion, we demonstrate that the proposed simulation framework enables a consistent assessment of the detectability of bound dineutron formation in neutron-induced reactions. The presented results provide quantitative guidance for the design of such experiments and contribute to the ongoing investigation of exotic nuclear correlations beyond the conventional nuclear structure paradigm.

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Feasibility of measuring polarization correlations of annihilation photons from Positronium decays with multilayer modular J-PET

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Abstract

Understanding the polarization correlations of annihilation photons emitted in positronium (Ps) decays is important for both fundamental studies of quantum entanglement and for the emerging modality of quantum-entanglement imaging [1,2,3]. The annihilation photons have energies of 511 keV, for which polarization cannot be accessed by conventional optical methods but can be inferred through Compton polarimetry [4]. Since the Compton scattering plane of an incident photon is correlated with its linear polarization [5], the relative polarization of an annihilation-photon pair can be probed through the angle between their scattering planes. Plastic-scintillator detectors are particularly well suited for such studies because interactions of 511 keV photons are dominated by Compton scattering. The scattering planes of each photon can be reconstructed by registering each primary photon together with its subsequent scattered interaction [4]. Thus, for entanglement studies an event of interest will typically consist of at least 4 hits inside the detectors. The J-PET detector, equipped with a triggerless data acquisition system, enables the efficient registration of multiphoton events [6]. Previous studies have demonstrated the feasibility of polarization-correlation measurements with a three-layer J-PET prototype [7]. It was observed that geometric acceptance remains a critical factor in improving the sensitivity of these studies that can be achieved by the rearrangement of the modular J-PET scanner [7].

In this work, we present results based on Geant4 simulations for a double-layer Modular J-PET geometry composed of 8 inner and 16 outer modules. Two-layered configuration increases the probability of multiple interactions and extends the accessible phase space for both forward- and backward-scattered photons, thereby improving the acceptance for polarization-correlation studies.

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Exploring charge conjugation invariance in positronium with J-PET detector

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Abstract

The positronium (Ps) is a metastable state of electron-positron pair, and a low-energy laboratory for fundamental discrete symmetry tests. The absence of any internal substructures within its constituents makes it fully describable via Quantum Electrodynamics (QED). As a result, the decay of Ps is heavily constrained by the Charge conjugation (C) symmetry. Under C-symmetry the singlet,
para-Positronium (p-Ps) and triplet ortho-Positronium (o-Ps) can decay into odd and even numbers of photons respectively. The decay dynamics of p-Ps is additionally constrained by the rotations of the tetrahedral symmetry group due to the bosonic nature of the final state photons. This limitation forbids p-Ps to decay into a configuration of 4 photons flying off in the direction of the regular tetrahedron vertices. Observation of o-Ps decaying into 4 photons in this particular configuration is a direct test of the C-symmetry violation, free from QED allowed p-Ps background. With the multiphoton registration and the triggerless data acquisition in the modular J-PET detector, detection of such rare decay seems plausible. We obtain a non-zero detection efficiency for such unique configurational final state
photons. In this presentation, the study of this ongoing exploration with the J-PET detector shall be discussed.

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Polish Ministry of Science and Higher Education (MNiSW), grants no. IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Areas; and the ERC Advanced Grant POSITRONIUM (no. 101199807). We also thank the PLGrid (HPC Center: ACK Cyfronet AGH) for computational resources under grant no. PLG/2024/017688 and PLG/2025/018762.

Multimodal 3D Ultrasound of Pancreatic Tumor Progression and Survival

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Abstract

Multimodal 3D ultrasound imaging was used to assess pancreatic tumor progression and survival in an orthotopic pancreatic ductal adenocarcinoma (PDAC) model. PDAC is characterized by a highly hypoxic tumor microenvironment that contributes to therapy resistance and poor clinical outcomes, while reliable longitudinal assessment of tumor growth kinetics and treatment response remains limited in preclinical studies. Orthotopic PDAC (Pan_O2) tumors were implanted in C57BL/6J mice, which were randomly assigned to six groups: sham, gemcitabine (45 mg/kg i.v.), Abraxane (30 mg/kg i.v.), erlotinib (50 mg/kg/day p.o.), gemcitabine plus Abraxane, and gemcitabine plus erlotinib. In the gemcitabine–erlotinib group, erlotinib was administered 24 hours prior to gemcitabine injection to optimize treatment efficacy. Therapies were delivered every 72 hours for five cycles (days 0, 3, 6, 9, and 12), following a sequential combination schedule. Tumor progression was monitored using serial high-resolution ultrasound imaging to quantify tumor growth kinetics across treatment groups, incorporating 3D B-mode and power Doppler ultrasound. Survival was recorded from the day of tumor implantation until predefined endpoint criteria. Combination therapies showed reduced tumor progression compared to monotherapy and control groups, as revealed by serial imaging of tumor growth kinetics. Improved overall survival was observed in a treatment-dependent manner, consistent with imaging-based assessment of therapeutic response. Overall, multimodal ultrasound imaging provides a robust non-invasive platform for longitudinal quantification of pancreatic tumor growth and evaluation of therapeutic efficacy in preclinical PDAC models.

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This work was funded by NCN (grants 2022/45/B/NZ5/01695) and NCBiR (grant ENM3/IV/18/RXnanoBRAIN/2022). The Vevo F2 ultrasound system was funded by the Jagiellonian University, within the Strategic Programme Excellence Initiative.

FEASIBILITY OF J-PET FOR IN VIVO RANGE MONITORING IN UPRIGHT HADRON THERAPY: APPLICATIONS TO PROTON BEAMS.

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Abstract.

Hadron therapy, particularly proton beam therapy, is a radiotherapy that utilizes charged particles such as protons and carbon ions to target and treat cancer cells with high precision. The strength of hadron therapy lies in the unique physical and radiobiological properties of these particles that can penetrate the tissues with little diffusion and deposit the maximum energy just before stopping, at a peak shape called Bragg peak. Bragg peak which allows for the delivery of a lethal dose to the tumor while significantly sparing healthy tissue distal to the tumor site. With the use of hadrons, the tumor can be irradiated while the damage to healthy tissues is less than with the conventional photon beams.

Proton interactions in tissue involve both electromagnetic processes, responsible for energy deposition, and nuclear interactions that lead to the production of positron-emitting isotopes such as ^{11}C, ^{15}O, and ^{13}N. These isotopes form the basis for positron emission-based range monitoring techniques. By detecting annihilation photons resulting from β^+ decay and leveraging the principle of modular Jagiellonian Positron Emission Tomography (J-PET) technology based on plastic scintillators, as a cost-effective tool, one can indirectly verify the range of proton beam within the patient. Our proposed approach allows for in vivo monitoring whether the dose will be delivered exactly where intended, compensating for anatomical variations or setup uncertainties.

Furthermore, we evaluate the emerging interest in monitoring proton range in the upright position. Positioning patients in the upright position, i. e. sitting or standing, allows for significant reductions in treatment cost, increased patient comfort, and even therapeutic benefits resulting from physiological alignment and better anatomical separation of critical structures. This study presents the basic principles of proton therapy, the mechanisms of positron-emitting isotope production, and in vivo range monitoring, with particular emphasis on their application in upright treatment geometry using the modular J-PET scanner.

We acknowledge support from:

The UPLIFT project is funded by the European Union under Grant Agreement No. 101168955. The National Science Centre (NCN), grant nos. 2021/42/A/ST2/00423, 2021/43/B/ST2/02150,

2022/47/I/NZ7/03112, and 2023/50/E/ST2/00574; the Polish Ministry of Science and Higher Education (MNiSW), grants no. IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Areas; and the ERC Advanced Grant POSITRONIUM (no.101199807).

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CONCEPT OF USING SECONDARY NEUTRONS TO PRODUCE 99MO IN A COMPOSITE TARGET

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Cyclotron production technologies are widely used to produce medical radioisotopes by (p,xn) nuclear reactions on targets, which are mostly composed of enriched stable isotopes. This leads to secondary neutron fields with an intensity of 10^{12}-10^{13} n/s even for low-energy cyclotrons in the energy range of 10-20 MeV [1-2]. These neutrons can be used to produce additional radioisotopes by neutron-induced reactions on raw materials placed near the original target, thus forming a composite target of different layers. In this work, we present the idea to increasing the yield of cyclotron-produced ^{99m}Tc from enriched ^{100}Mo by further neutron capture in ^{98}Mo and subsequent decay of the activated ^{99}Mo to ^{99m}Tc.

Along with the ^{100}Mo and ^{98}Mo layers, we considered other stable elements that could be inserted between the enriched Mo isotopes to generate neutrons of lower energies. Here, we identified ^{7}Li, ^{9}Be, ^{45}Sc, ^{48}Ca, ^{76}Ge, and ^{100}Mo itself as the most promising candidates for this role. PHITS simulations of different layer configurations were performed to find the optimal one that gives the maximum neutron yield. The detector in the simulations was placed immediately after the neutron generation layer in a volume of Ø 6×3 mm, which was determined as a potential ^{98}Mo site. Although ^{7}Li has the largest integral neutron emission cross section, the highest total neutron fluence in the evaporation spectrum up to ~8 MeV was found for the combination of thicknesses ^{100}Mo (170 μm) / ^{7}Li (1200 μm). In this case, the fraction of neutrons below 1 MeV was 28%. To increase the low-energy part of neutrons, elements with thresholds (p,xn) 0.5÷1 MeV higher than for ^{7}Li were analyzed, among which the most suitable for spectrum shift was the isotope ^{9}Be. Further PHITS simulations were performed for the 3-element composition of ^{100}Mo, ^{7}Li and ^{9}Be: the maximum increase in the lower part (<1 MeV) of the spectrum was obtained for the combination ^{100}Mo (260 μm) / ^{9}Be (40 μm) / ^{7}Li (1,200 μm) – from 28% to 58%. At the same time, the maximum product of the neutron flux and the reaction cross section of ^{98}Mo(n,γ) was achieved for the following combinations: for the 2-element variant – ^{100}Mo (170 μm) / ^{9}Be (340 μm); for the 3-element variant – ^{100}Mo (210 μm) / ^{9}Be (190 μm) / ^{7}Li (140 μm).

The results obtained for such layer configurations can be used as a basis for further development of a composite target for hybrid production of ^{99m}Tc simultaneously by direct ^{100}Mo(p,2n) and indirect ^{98}Mo(n,γ) methods.

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Signal Efficiency Mapping studies for CP symmetry test using the J-PET Detector.

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The J-PET detector provides a powerful platform for investigations of fundamental discrete symmetries, particularly in the context of charge-parity (CP) symmetry tests [1–8]. Positronium, as a purely leptonic bound state and a simultaneous eigenstate of both charge conjugation (C) and parity (P) operators, offers an exceptionally clean environment for studying CP violating effects beyond the Standard Model [1–10]. Within the J-PET experimental framework, CP symmetry studies are enabled through the reconstruction of photon polarization plane in ortho-positronium (o-Ps) annihilation processes. This unique capability of the J-PET detector provides access to CP odd observables, such as the operator ($\boldsymbol{\varepsilon}_i \cdot \mathbf{k}_j$), constructed from momentum vectors of annihilation photons before and after the Compton scattering [1–10]. The precise measurement of these correlation operators, supported by the high time and spatial resolution of the modular J-PET detector, enables high-precision tests of CP symmetry. Depending on the achievable statistics and control of systematic uncertainties, the sensitivity is estimated to reach atleast the order of 10^{-5}, a regime that remains experimentally unexplored for CP symmetry studies [7–11]. This work presents preliminary results obtained from signal efficiency mapping studies for CP symmetry tests using J-PET detector.

Acknowledgements:

The authors acknowledge support from the National Science Centre (NCN), Poland through grants Nos. 2019/35/B/ST2/03562, 2021/42/ A/ST2/00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, the Polish Ministry of Science and Higher Education (MNiSW), grants no. IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Area budget under the auspices of the program Excellence Initiative — Research University at the Jagiellonian University; and the ERC Advanced Grant POSITRONIUM (no. 101199807). We also thank the PLGrid (HPC Center: ACK Cyfronet AGH) for computational resources under grant no. PLG/2024/017688 and PLG/2025/018762.

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Comparative ToF-SIMS Metabolic Profiling of Diabetic Rat Liver Tissue under Metformin and Flaxseed Mucilage Treatment

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Abstract

Type 2 diabetes mellitus (T2DM) is a global metabolic disorder characterised by insulin resistance and profound disturbances in hepatic metabolism. This condition leads to the dysregulation of hepatic lipid as well as amino acid homeostasis [1]. The liver, as a central metabolic hub, undergoes pathological remodelling, including enhanced de novo lipogenesis and accumulation of lipotoxic intermediates, such as ceramides [2]. Although metformin remains the first-line pharmacological treatment for T2DM, increasing attention has been directed toward complementary natural alternatives, such as flaxseed mucilage, known for its antioxidant and gastroprotective properties [3-5].

In this study, Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS) equipped with a Bi^{3+} liquid metal ion gun operated at 30 keV was employed to compare metabolic alterations in hepatic tissue of a T2DM rat model following treatment with metformin and flaxseed mucilage. The experimental groups included untreated diabetic controls (P1), metformin-treated animals (P2) and animal treated with two different doses of flaxseed mucilage (P3 and P4). Measurements were conducted under ultra-high vacuum conditions in static SIMS mode and the total ion fluence was maintained below 1 x 10^{-12} ions/cm^2. Spectra were acquired across the m/z 0–911 range from 250 x 250 µm^2 areas and the data were normalized to total ion counts (TIC).

Hyperglycemia was associated with pronounced alterations in hepatic molecular profiles detected by ToF-SIMS and marked metabolic changes. A decrease in ions associated with phospholipids and fatty acids was observed in diabetic liver tissue compared to controls. This was accompanied by an increase in ceramide-related ions and alterations in amino acid-related signals. Metformin treatment (P2) partially reversed these alterations, resulting in a partial restoration of lipid and amin acid profiles compared with untreated diabetic controls (P1). Preliminary investigations into flaxseed mucilage highlight its dose-dependent potential to modulate hepatic metabolic pathways and restore molecular balance. These results demonstrate the power of ToF-SIMS as a tool for spatially resolved metabolic profiling. This provides novel insights into the varied effects of different pharmacological interventions.

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3Dπ PET: A Novel Xenon-Doped Liquid Argon–Based Total-Body PET Concept with Ultra-Fast Timing and Low-Dose Capability

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Background: The 3Dπ scanner is a Total-Body, Time-of-Flight Positron Emission Tomography (PET) imaging device with silicon photomultipliers (SiPMs) and a xenon-doped liquid argon (LAr) scintillator, aimed at ultra-low-dose imaging for pediatric and pregnant patients. The scanner features an axial field-of-view of 200 cm and consists of nine double-sided concentric rings of SiPM panels. Xenon doping of the LAr scintillator provides several advantages: fast scintillation, suppression of the long scintillation tail, and wavelength shifting to xenon emission. These improve the time resolution and detection efficiency for positron–electron annihilation signals. Operating the SiPMs at LAr cryogenic temperatures further reduces their dark count rate. The 3Dπ project is a medical imaging application of the ongoing R&D of the DarkSide collaboration, focused on dark matter direct detection using LAr targets, and its simulation package is derived from the DarkSide Geant4-based framework.

Methods. System performance was evaluated via Monte Carlo simulations following NEMA NU 2-2018 standards. Ongoing experimental work includes commissioning of a xenon-doped LAr cryogenic system, SiPM characterisation at cryogenic temperatures, and timing resolution studies using a pulsed laser system. Readout electronics development is underway using the ALCOR ASIC chip, with test boards from INFN Torino under cryogenic validation, and the DENEB ASIC, originally designed for the DUNE neutrino experiment. In parallel, image reconstruction algorithms and system geometry optimisation are under active development.

Results. Simulations show a noise equivalent count rate (NECR) of 3.2 Mcps at 17.3 kBq ml^{-1}, rising to 4.3 Mcps at 40 kBq ml^{-1}. Spatial resolution averages 2.7 mm FWHM across axial positions, and system sensitivity reaches 373 kcps MBq^{-1} at the centre of the field of view. A TOF resolution of 151 ps at 5.3 kBq ml^{-1} is achieved, enabling high-quality, low-noise image reconstruction [1].

Conclusions. The 3Dπ system demonstrates the potential of particle physics detector technology applied to clinical PET imaging. We present recently published NEMA performance results and discuss the ongoing hardware and software development programme toward experimental validation of the 3Dπ concept.

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Support for this work was provided by multiple sources, including FNP IRA programmes: AstroCeNT, (MAB/2018/7), funded from the ERDF, and Astrocent (FENG.02.01-IP.05-A015/25) co-financed by the European Union under FENG 2021–2027; and Teaming for Excellence grant Astrocent Plus (101137080) funded by the European Union with complementary national funding from the MNiSW (MNiSW/2025/DIR/811), European Union's Horizon 2020 research and innovation program (952480 DarkWave), NCN Poland (2021/42/E/ST2/00331 and 2025/09/X/ST2/00794), the National Science Foundation Graduate Research Fellowship (Award 2136513), the University of Houston's Houston Scholars society, INFN, Università degli Studi di Cagliari, Fondazione CON IL SUD, the resources of the uHPC cluster (acquired through NSF Award Number 1531814), U.S. National Science Foundation (NSF) Grants (Grant Nos. PHY-2310091 and PHY-2310038), ANR (Grants N. ANR-22-CE31-0021), and IN2P3–COPIN (No. 20-152).

A Geant4-based simulation framework for positronium beam detection in atomic-interferometry experiments

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Abstract

Inertial sensing with positronium atoms provides a promising approach to studying the response of a purely leptonic matter-antimatter system to external forces, including gravity [1-4]. However, its experimental realization requires a positronium (Ps) beam with controlled velocity, angular divergence, emission time, and survival probability, together with a detection system capable of resolving small changes in the annihilation vertices [5,6]. We develop a Geant4-based simulation framework for positronium-beam detection in atom-interferometry experiments [7]. The package will generate Ps beams with configurable phase-space and lifetime properties. The beam will propagate through simplified interferometry or deflectometry geometry, and simulate annihilation-photon transport, detector interactions, timing response, and vertex reconstruction in a J-PET-like modular detector [8-10]. The interferometer response can be included through an external or parametrized model, while Geant4 is used to evaluate the experimentally measurable detector response. The expected outputs include detection efficiency, reconstructed vertex resolution, timing, and the sensitivity of the detector geometry to shifts in the Ps annihilation pattern. This study will provide a feasibility tool for optimizing beam parameters and detector configurations for future positronium-based inertial-sensing measurements.

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Acknowledgement:
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Ex-vivo Positronium Lifetime Imaging of Human Thrombi: Validation with Positron Annihilation Lifetime Spectroscopy

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Abstract
Positronium lifetime imaging (PLI) has recently emerged as a novel extension of positron emission tomography (PET), enabling access to nanoscale structural information beyond conventional tracer-based imaging (1,2). Previous studies have demonstrated the use of positron annihilation lifetime spectroscopy (PALS) for probing nanoscale structure in fibrin-based blood clots (3,4), while initial investigations using the modular J-PET system have explored positronium imaging in thrombotic material (5).

In this study, we extend these approaches by performing *ex vivo* positronium lifetime imaging of patient-derived human thrombi using the J-PET scanner and the prompt gamma-emitting radionuclide ^{44}Sc. The reconstructed ortho-positronium (o-Ps) lifetimes ranged from 1.85 to
1.99 ns, demonstrating sensitivity to nanoscale structural heterogeneity within thrombi. These variations are attributed to differences in fibrin network density, red blood cell content, and local biochemical environment.

To validate the imaging-derived parameters, independent PALS measurements were performed on the same samples using a ^{22}Na source. The PALS-derived lifetimes (1.90–2.01 ns) were in very good agreement with PLI results, confirming that the measured positronium lifetimes reflect intrinsic material properties rather than experimental artifacts.

The agreement between PLI and PALS demonstrates that positronium lifetime imaging provides reliable, spatially resolved information on nanoscale tissue structure. These findings highlight the potential of positronium lifetime as a novel imaging biomarker for thrombus characterization and suggest future applications in clinical diagnostics, particularly in ischemic stroke, where thrombus composition influences treatment outcomes (6,7).

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Development of a Geant4 Simulation Framework for Antimatter Annihilation Vertex Reconstruction

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Abstract

Testing the **W**eak **E**quivalence **P**rinciple with antimatter, to determine whether antimatter undergoes the same gravitational acceleration as matter, is still one of the most important questions in fundamental physics [1]. A promising route currently being explored by the antimatter community is the application of atomic interferometry technique with neutral antimatter systems, such as antihydrogen and positronium [2,3]. The realization of such advanced experiments requires precise optimization of several sensitive parameters. These include beam properties, atomic interferometry response, and the detector performance. It is technically difficult and not always practical to optimize these parameters during the experimental runs due to the limited availability of antimatter beams. Therefore, simulation tools can be used efficiently to study the influence of different parameters, which can later be validated with measured data under different experimental conditions.

We have developed a Geant4-based simulation framework to study how different experimental parameters influence the reconstruction of antimatter annihilation vertices using modular J-PET detectors [4,5,6]. Antihydrogen and positronium are used as representative test cases, since they provide complementary annihilation topologies relevant to ongoing antimatter experiments. In antihydrogen, the annihilation of the antiproton component produces charged pions together with other secondary particles [7,8], which can be used for charged particle tracking and vertex reconstruction. In positronium, the annihilation signature is instead purely electromagnetic, with the emission of two or three gamma photons depending on whether the atom is in the para-Ps or ortho-Ps state, respectively.

The framework allows different detector configurations, event topologies, and reconstruction strategies to be investigated under controlled simulation. In my presentation, I will describe the main components of the developed simulation package and discuss its performance for different annihilation topologies.

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DEVELOPMENT OF 3D-PRINTED ABDOMINAL PHANTOM FOR QUALITY ASSURANCE APPLICATIONS

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Abstract

Computed Tomography (CT) is a diagnostic modality that utilizes x-ray to obtain a volumetric scan of an object's body and is commonly used as an immediate imaging modality for emergency situations and diagnosis of possible malignancies especially for abdomen-related cases such as appendicitis and kidney injuries. Phantoms are employed to evaluate the performance of radiation-emitting equipment such as CT to ensure that such equipment can be used in clinical applications. Phantoms range from geometric to human anatomy-mimicking structures. Anatomy-mimicking phantoms offer a number of advantages over geometric phantoms such as providing a more realistic simulation of anatomical region of interest [1]. However, anatomy-mimicking phantoms are generally costly which could hinder use of this phantom type in the clinical setting. The research aims to develop a customized water-mimicking 3D abdominal phantom using 3D-printing technique. Volumetric measurements of the organs inside the phantom were derived from the average organ measurements of selected individuals. Resin 3D printing process was employed to fabricate the organs of the phantom. Diagnostic CT scanner was used to obtain volumetric scans of the phantom without and with water filling. ROI analysis was conducted to determine the Hounsfield Unit (HU) of the phantom under selected parameters. HU measurements of the phantom with and without water filling were within the tolerance indicated by the ACR and IAEA method. Results of this research could be used as a comparison of image quality between two different CT scanners for quality assurance applications. Moreover, results of this study can be employed in the development of phantom for dynamic and kinetic imaging using the total-body J-PET scanner [2].

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Acknowledgements

We acknowledge support from NCN (grants 2021/42/A/ST2/00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, 2023/50/E/ST2/00574), MNiSW (IAL/SP/596235/2023 and SPUB/SP/627733/2025),
SciMat and qLife Priority Research Areas, ERC Advanced Grant POSITRONIUM no. 101199807, PRISMAP (Project_1729020993_aniX3), and PLGrid infrastructure (PLG/2024/017688, PLG/2025/018762).

Oxygen Microbubbles for Ultrasound-Triggered Tumor Oxygenation: From Therapeutic Potential to Next-Generation Nanobubble Design

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Abstract

Tumor hypoxia limits the effectiveness of anticancer therapies and promotes aggressive tumor behavior. Oxygen microbubbles (OMB) enable ultrasound-triggered, localized oxygen delivery, but their efficacy is associated with vascular disruption and potential promotion of metastasis. This study evaluates therapeutic performance, vascular effects, and safety of OMBs, and motivates the development of next generation nanobubble systems.

Oxygen microbubbles were investigated *in vitro* and in murine 4T1 tumor models. Tumor oxygenation was quantified using EPR oximetry and oxygen mapping. Ultrasound pulses induced cavitation and oxygen release. Contrast-enhanced ultrasound and Doppler imaging were used to assess perfusion and vascularization. Effects on tumor growth, vascular structure, and metastatic spread were evaluated in combination with radiotherapy. In parallel, lipid-based oxygen nanobubbles with tunable gas cores were developed and characterized in terms of size, stability, and acoustic responsiveness.

OMBs showed high stability and efficient ultrasound-triggered oxygen release, increasing tumor pO_2 (up to ~120 mmHg in vivo). Oxygenation was heterogeneous and dependent on administration route. Ultrasound imaging provided strong contrast enhancement and visualization of tumor vascularization. Treatment induced vascular disruption and reduced pericyte coverage without major changes in vessel density. While OMBs improved radiotherapy response and reduced tumor growth, they were associated with increased metastatic dissemination after intravenous administration with ultrasound. Preliminary data indicate that nanobubbles exhibit smaller size, improved stability, and more controlled acoustic behavior.

Oxygen microbubbles enable effective, image-guided tumor oxygenation and radiosensitization but are limited by cavitation-induced vascular damage and pro-metastatic effects. These findings highlight the need for improved delivery platforms with enhanced stability and controlled bioeffects. Lipid nanobubbles with tunable gas composition are being developed as next generation theranostic systems with improved tumor penetration and controlled oxygen release.

Acknowledgements (optional)

This work was supported by the grant from the National Science Centre Poland OPUS No. 2015/17/B/NZ7/03005 and OPUS Project, 2022/45/B/NZ4/01215.

Experimental and methodical irregularities in the studying of biological samples using Positron Annihilation Lifetime Spectroscopy

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Abstract

A Positron Emission Tomography is a powerful technique for localization abnormal tissues and organic activity inside the body. At the same time, Positron Annihilation Lifetime Spectroscopy (PALS) could provide information about the structure (e.g. free volume sizes and distribution) or chemical activity (e.g. presence of free radicals) of wide range of materials. Combining these two techniques could give us an excellent tool for diagnostics of abnormal (e.g. tumorous, inflammation) tissues. However, achieving this requires conducting a wide PALS investigations of biological samples, such as tissues obtained from patients during surgery.

It is known, that many parameters, like patient's age, body hydration or tissue oxygenation significantly affect the PALS results. Equally important is the use of appropriate measurement procedures and procedures for handling biological material. Recognizing the importance of factors such as proper sample preparation and correct selection of PALS analysis parameters is crucial for the proper interpretation of obtained results.

In given presentation, many irregularities and errors, that can occur during planning and performing the measurements or analysing the PALS results will be discussed. The influence of time distance between obtaining the sample and performing the measurement on PALS results will be presented, as well as various methods of sample preservation. The irregularities that could be obtained as an effect of using incorrect method of analysis will also be presented.

Positronium diagnostic maps

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Abstract

A well-established position of positronium, as a probe of a medium's nanostructure in materials research, can be quickly implemented in medical diagnostics. The hydrogen-like positronium atom's ability to probe a medium results from the relatively simple correlation between the mean *o*-Ps lifetime and the size of the free volume in the medium and the physicochemical properties of the medium. Free volume in a medium is an area of reduced electron density, such as pores in polymers, vacancies, inter- and intramolecular spaces, and bubbles in liquids.

Free volumes also occur in biological matter. However, due to the complexity of chemical processes occurring in tissues, the diversity of metabolic processes, a number of individual patient characteristics, as well as the difficult access to samples—requiring ethical approvals— using the positronium probe has thus far had little role in biological tissues investigations.

Studies conducted using Positron Annihilation Lifetime Spectroscopy (PALS) on over one hundred samples of healthy and diseased tissues obtained from various human organs (liver, uterus, intestines, blood) demonstrate the strong position of Ps as a probe in oncological nanodiagnostics. Gradually, further correlations are emerging between PAL spectra parameters (lifetimes and intensities of fitted components) and diagnoses based on laboratory test results. These correlations are building our understanding of the factors influencing the positron annihilation process in the human body.

Key diagnostic progress has been achieved through the implementation of INTI mapping. In addition to the island-based segregation of tissues considered healthy and cancerous, it is now possible to consider the impact of therapy and assess disease stage. Previous and current studies conducted on samples obtained from tissue resections from organs offer promising prospects for implementing INTI mapping in nanodiagnostics alongside PET imaging.

Annihilation of e+ and Ps in blood - linked to blood cancer markers

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Abstract

Research on blood cancers such as chronic lymphocytic leukemia (CLL) and multiple myeloma (MM) constitutes one of the key challenges of contemporary medicine due to their complex pathogenesis, diverse clinical course, and still limited possibilities for permanent remission in many cases. Despite significant advances in molecular diagnostics and targeted therapies, these diseases remain associated with high mortality rates and impose a substantial burden on healthcare systems. This motivated the evaluation of the diagnostic efficacy of positron and positron emission probes, also considering their potential use in J-PET tomography.

Blood samples obtained from patients diagnosed with blood cancer, including CLL or MM, were investigated using Positron Annihilation Lifetime Spectroscopy (PALS). The studies were conducted on material collected and processed according to protocols and standards used in hematological diagnostics. Blood was collected in tubes with EDTA as an anticoagulant, ensuring the stability of blood cell shape and preventing aggregation. Diagnostic information was obtained for the samples, with particular emphasis on blood test results, including selected cancer markers.

PALS measurements were performed in a chamber dedicated to blood and plasma testing, ensuring controlled and reproducible conditions. The study includes samples from both healthy individuals and patients diagnosed with blood cancer. Spectral acquisition parameters were optimized to achieve a statistic of 2.5 million counts/spectrum in a relatively short measurement time of 40 minutes. The acquired spectra were analyzed by testing various spectral distribution variants, including those involving different numbers of components and analysis ranges.

Relations between the intensities and lifetimes of components identified in the spectrum, primarily of *ortho*-positronium (*o*-Ps) and selected markers of blood cancers were observed. The analysis focused specifically on correlations between parameters obtained from analyzed spectra and the following markers: lactate dehydrogenase (LDH), indicator of tissue damage and organ dysfunction; β_2 microglobulin, a protein serving as a cancer marker; as well as albumin and hemoglobin levels.

Controlling the Positron System of the AEgIS Experiment Using Sinara–ARTIQ Hardware–Software Infrastructure and CIRCUS–TALOS Framework for Autonomous Operation

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Abstract

The positron subsystem of the AEgIS experiment puts high requirements on timing determinism, synchronization fidelity, and operational stability, driven by the need for precise control of positron production, trapping, and manipulation processes. To address these constraints, a dedicated control architecture has been developed based on the Sinara–ARTIQ hardware–software ecosystem, complemented by the CIRCUS–TALOS framework for autonomous operation.

The Sinara-ARTIQ platform provides FPGA-based control of time-critical processes with ns precision and enables synchronization and flexible experiment sequencing across distributed devices. This approach ensures coherent coordination of multiple subsystems, including positron accumulation, transport, and diagnostic instrumentation. The same hardware–software paradigm has already been successfully integrated into other subsystems of the AEgIS experimental apparatus, where it demonstrated reliable performance and improved operational efficiency [1].

In parallel with the control system development, targeted hardware upgrades have been implemented, including the incorporation of new power supplies units and a redesigned electrode control scheme. These modifications will enhance voltage stability, switching performance, and overall robustness of the positron manipulation stages, while ensuring compatibility with the control framework.

At a higher level, the CIRCUS–TALOS framework introduces structured automation of experimental procedures, reducing operator intervention and enhancing reproducibility. Building on the proven performance of this architecture in existing AEgIS subsystems, the present work aims to extend its application to the positron system and achieve comparable gains in stability, scalability, and experimental output.

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Acknowledgements (optional)

This work was supported by the Research University – Excellence Initiative of Warsaw University of Technology via the strategic funds of the Priority Research Centre of High Energy Physics and Experimental Techniques; the Polish National Science Centre under agreements no. 2022/45/B/ST2/02029 and 2022/46/E/ST2/00255, and the Polish Ministry of Education and Science under agreement no. 2022/WK/06;

Methodology for determining absolute values of the 3γ/2γ annihilation rate ratio in positronium decays using the Modular J-PET detector

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Abstract

In positron emission tomography (PET), approximately 40% of positrons emitted by radiotracers form positronium (Ps), a short-lived bound state of an electron and a positron. Depending upon its spin state, positronium annihilates into either two photons (2γ) or three photons (3γ). In matter, the longer-lived component of Ps, ortho-positronium (o-Ps), interacts with surrounding molecules through processes such as pick-off annihilation and spin conversion. These interactions shorten the o-Ps lifetime and suppress the three-photon decay channel to two-photon annihilation. Hence, the observed ratio of the 3γ-to-2γ annihilation rate becomes sensitive to the local molecular environment in which positronium annihilation occurs [1]. This sensitivity is of particular interest for biomedical applications, as the 3γ/2γ ratio may serve as an indicator of tissue oxygenation levels, offering a potential biomarker for detection of hypoxia in tumors [2-4].

In this work, we investigated the 3γ/2γ annihilation ratio using the modular J-PET detector. The modular J-PET, built from plastic scintillator strips, offers large geometrical acceptance, better time resolution, and sensitivity to both 2γ and 3γ annihilation events. Here we discuss the methodology of calibrating the detector setup to characterize the detection efficiency for both 2γ and 3γ event topologies. This calibration would establish the baseline to the measured ratio, which is essential for further studies dependent on molecular environment with J-PET detector.

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Studies of attenuation effects in two- and three-photon positronium decays in phantom models

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Abstract

Background: Conventional PET detects two 511 keV photons from electron-positron annihilation, but ~40% of events proceed via positronium decay (p-Ps→ 2γ, o-Ps→ 3γ). Positronium lifetime and the $3\gamma/2\gamma$ annihilation ratio depend on tissue structure, forming the basis of positronium imaging – an emerging extension of PET that may enhance diagnostics [1, 2]. The $3\gamma/2\gamma$ method does not require de-excitation photon registration, allowing the use of all standard radionuclides (^{18}F-FDG), as well as emerging isotopes like ^{44}Sc, which we plan to utilize in J-PET.

Objective: Accurate image reconstruction requires corrections, e.g. for attenuation. While implemented in J-PET for 2γ imaging, it is not applicable to 3γ events, motivating dedicated corrections. This study investigates gamma absorption in phantom models and develops absorption maps, forming a basis for attenuation correction.

Methods: Monte Carlo (MC) simulations were used to study absorption in models including the XCAT phantom, using a custom ROOT-based toy MC and the GATE toolkit. Simulations with Total-Body J-PET geometry assessed detector effects, including acceptance and energy thresholds.

Main results: Photon survival strongly depends on decay location, as illustrated by the absorption maps. In XCAT, 24.9% of p-Ps photon pairs and 10.3% of o-Ps photon triplets escaped without interaction [3]. Detection efficiency is lower for 3γ than for 2γ events due to stronger attenuation of low-energy photons and limited acceptance, and is highly sensitive to energy thresholds.

Conclusions: Gamma absorption varies significantly with decay mode and position, with stronger attenuation for 3γ events. The generated absorption maps provide the first step toward dedicated attenuation correction for three-gamma positronium imaging, enabling accurate reconstruction in novel 3γ/2γ positronium imaging technique.

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Development of Image Correction Techniques for the J-PET scanner

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Abstract

Modular J-PET is a plastic-scintillator based PET scanner to facilitate cost-effective and scalable alternative to conventional crystal-based PET technologies [1]. Plastic scintillators have never been used for quantitative clinical PET imaging before. Due to its lower photon detection efficiency and higher scatter fraction, effective correction of scattered and random events is essential for achieving reliable quantitative imaging.

In this study, we present a comprehensive data correction framework and evaluate its performance in NEMA IQ phantom and human subjects through comparison with a commercial PET/CT system. Random events were estimated using a delayed time window approach, enabled by the customized trigger-less acquisition of the J-PET system [2]. Coincidences were identified within a 3 ns time window, while randoms were calculated using a 100 ns delayed window during offline processing. For scatter correction, we incorporated SimSET-based Monte Carlo simulations into a time-of-flight ordered-subsets expectation maximization (TOF-OSEM) reconstruction framework [3]. Scatter contributions were estimated on an event-by-event basis using block-based variance reduction and integrated into list-mode reconstruction [4]. For estimating the scattering contribution to improve computational efficiency, LYSO was tested as a surrogate material for BC-404 plastic in simulations, showing negligible impact on image quality while reducing computation time by nearly an order of magnitude. Attenuation correction was performed using CT images acquired on a commercial GE Discovery MI Gen 2 PET/CT scanner, with co-registration to the J-PET field of view. Initial validation and assessment of the developed correction techniques was performed on a NEMA IQ study and then Human studies were performed including four scans with different tracers ([18F]-FDG, [68Ga]-PSMA, and two [68Ga]-DOTATATE). Each subject underwent scan on both the J-PET and GE systems.

The results with the NEMA IQ phantom show that scatter correction improved contrast recovery coefficient, reduced background variability, and effective suppression of residual activity in cold regions and with the human subject it improves organ delineation and reduces residual background activity. Across all scans with the human subject, activity concentration ratios from J-PET were found in good agreement with those from the GE system within statistical uncertainties. Overall, the proposed correction framework enables consistent organ-level quantification in a plastic scintillator–based PET system. These findings represent a significant step toward establishing plastic-based PET technology as a practical and scalable solution for molecular imaging.

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MNiSW (IAL/SP/596235/2023 and SPUB/SP/627733/2025), SciMat and qLife Priority Research Areas, ERC Advanced Grant POSITRONIUM no. 101199807, and PLGrid infrastructure (PLG/2024/017688, PLG/2025/018762).

Evaluation of the Performance of a Plastic Scintillator Based Brain PET Insert

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Abstract

Positron Emission Tomography (PET) is an important imaging technique in modern medicine that can detect changes in tissue function before structural changes appear. The Jagiellonian Positron Emission Tomograph (J-PET) collaboration is developing a novel PET technology based on plastic scintillators which can lower costs and make PET imaging more widely available [1]. The J-PET system is designed as a total-body scanner with a long axial field of view (over 250 cm). This allows for faster scans, lower radiation doses, and the ability to image the entire body at once [2]. In addition, a brain PET insert based on plastic scintillators is being developed to improve brain imaging when used together with the full system.
To evaluate the performance of the scanner, Monte Carlo simulations were performed using the GATE platform [3]. The simulations were carried out according to standard NEMA protocols, including sensitivity, scatter fraction, and spatial resolution [4]. The results of the plastic scintillator-based brain PET insert will be presented, offering a comprehensive evaluation of its feasibility and performance for clinical and research applications.

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From Spreadsheets to a Unified Ecosystem: A Journey of Developing a Multimodal Database for UMCS

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Abstract

In contemporary biomedical research, especially within interdisciplinary domains utilizing Positron Annihilation Lifetime Spectroscopy (PALS), a persistent challenge is the unstructured management of experimental and clinical data. An often-inconsistent system of syncing clinical patient history with acquisition and spectroscopy parameters often results in fragmented data and ineffective correlations between physical parameters and their biological outcomes.

The AMIAp application was developed to address this gap as a specialized software solution that unifies comprehensive patient clinical records, histopathological tracking, and PALS data within a single digital environment. The application utilizes an SQL backend with Python coding with a custom GUI created with Tkinter. It implements a relational model that directly links patient information and medical histories with experimental data obtained from corresponding biological samples.

This application features an automated import/export functionality for generated Excel templates, to fetch PALS data in while minimizing the possibility of entry error. To maintain order in visual data, a naming convention module automatically renames clinical and histopathological images upon upload according to a predefined organizational pattern. The program uses a simultaneous modular design that allows for exploration of clinical record, histopathology tracking, and experimental unit simultaneously, facilitating quick generation of connections between clinical profile and experimental data. Real-time filtering is perfectly synchronised with the visualization of PALS, and dependency graphs are built based on exclusively data displayed.

By integrating patient clinical data directly with PALS parameters, the system eliminates the fragmentation typical of interdisciplinary research. At UMCS, this tool provides a practical environment for more transparent and structured analysis of intertwined biophysical data.

Prototype Development of an On-Chip PET System with Dual-Sided Crystal Readout for Enhanced Gamma-Ray Interaction Point Localization

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Abstract

Organ-on-chip (OOC) platforms mimic human tissue at millimeter scale and provide unique models for drug development and disease research. Quantitative imaging of radiotracer distribution within these devices can totally change their scientific utility, however no PET system exists at the physical scale and resolution required. We present a dedicated on-chip PET detector concept. It revolves around a new dual-sided readout architecture, whereby SiPM arrays placed on one large face and on the side face of the same monolithic LYSO crystal yield complementary spatial information, drastically enhancing scintillation location determination and image reconstruction quality. The physical prototype features two monolithic LYSO crystals (5×5 cm² in area, 15 mm thick) mounted face-to-face, with the OOC unit in the space between them. Dual-sided readout is carried out by each crystal: the large 5×5 cm² face on one side is equipped with a 16×16 array of 256 SiPM elements, while the 15 mm side face is covered by two 8×8 SiPM matrices, with channels not having direct crystal coverage being excluded from the analysis chain. Light patterns across the entire SiPM geometry were generated by GATE Monte Carlo simulations to train a Convolutional Neural Network (CNN) for predicting gamma-ray interaction points. The consistent part of large-face-only readout versus combined large-face and side-face readout was measured, thus directly quantifying the supplementary localization information encoded by orthogonal side-face matrices. Then, the simulation-trained CNN was used on experimental data from the physical prototype to confirm the generalization from simulated to real detector data. Spatial resolution was further restored by applying a deep learning positron-range correction algorithm based on U-Net architecture. The dual-sided readout design clearly brought a significant enhancement over the large-face-only layouts: side-face SiPM matrices provided depth-of-interaction information which could not be obtained from the large face only, thereby reducing the positioning error. In the optimized setup, the mean positioning error was 0.80 mm, the system sensitivity was 34.81%, and the mean spatial resolution of the reconstructed image was 0.55 mm FWHM according to the simulation. The positron-range correction using deep learning significantly enhanced spatial resolution by 32%, thus it recovered over 91% of the maximum theoretically achievable gain. Most importantly, the simulation-trained network when applied to the real experimental data still showed reliable positioning results which implies that the Monte Carlo training framework generalizes to the physical detector measurements without the need for retraining. The implementation of a two-crystal face-to-face configuration with dual-sided readout a 16×16 large-face panel combined with 8×8 side-face arrays for each crystal is the main hardware revolution of this system. Light distributions recorded at the same time from perpendicular crystal faces represent spatial coordinates in a complementary way, thus sub-millimetre reconstruction can be achieved without pixelated detectors. Establishing the workability of the system, the transport of simulation-trained AI models to real experimental data has been attested as effective. This detector design, merged with AI-based reconstruction, is capable of yielding the quantitative and spatial results necessary for the insertion of functional PET imaging directly with organ-on-chip devices, which allows radiotracer-based measurement of metabolic and pharmacokinetic processes in living microfluidic tissue models.

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Proton beam range monitoring and positronium studies in proton radiotherapy with J-PET system

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Introduction

Using protons (ions) in the radiation therapy has several advantages over conventional methods. Finite beam range, steep dose gradient and maximal energy deposition at the end of the path allow to reduce the dose delivered to the healthy tissue and to make the dose distribution in the tumor more conformal. To fully exploit those advantages, beam range has to be known with high precision. Hence, the beam monitoring system is needed. This role can play the J-PET detector, which is a plastic based PET detector, that allows beam range monitoring and also possibly positronium studies. Positronium studies should provide additional information about the irradiated tissue and the hypoxia level that would lead to better adjusted irradiation conditions.

Methods

During irradiation protons induce nuclear reactions in the tissue. Produced radioisotopes emit positrons, which annihilate and emit gamma quanta. J-PET scanner can register those gammas and obtain the information about the annihilation points that has to be transformed to information about interaction points. Combining Bethe-Bloch theory, Moliere theory and cross-sections for nuclear reactions one can make an attempt to compute the rate of the radioisotope production and distribution of the signal. Those computations later can be confronted with data from the proton therapy center. Data in the proton therapy center were taken with the J-PET scanner. Cuboid PMMA phantoms were irradiated with proton pencil beam of several energies which resulted in different ranges of protons in the phantoms.

Results/discussion

Beam monitoring can be conducted during the irradiation (in-beam) and after (off-beam) due to different lifetimes of radioisotopes. Most abundant isotopes produced in the tissue are: ^{11}C, ^{10}C, ^{15}O, ^{14}O, ^{13}N, ^{30}P and ^{38}K. ^{10}C and ^{14}O have short lifetimes ($\approx$ 20s and $\approx$ 120s respectively) whereas ^{11}C has the longest lifetime of about 20 minutes and thus can be useful in different stages of the monitoring process. Analysis of already collected data, proved that the J-PET system is suitable for proton beam range monitoring. The PMMA phantom was irradiated with proton pencil beam. We registered signal during the irradiation and several minutes after the irradiation. Data was analyzed with the J-PET framework and reconstructed images with CASToR software. Results show that our system is capable of conducting both on-line and off-line monitoring. ^{10}C and ^{14}O emit prompt gamma. This enables obtaining information of the positronium lifetime in the tissue. This would lead to gaining additional information about the tumor itself such as malignancy level and hypoxia level.

Conclusion

Our research presents novel and important approach to proton beam therapy monitoring. Obtaining spatial distribution of radioisotopes will provide finding the relation between annihilation points and Bragg peak which will increase the precision of the treatment. Positronium studies will have impact on the quality of the treatment when during the therapy one can obtain additional information about the conditions of the tumor.

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A Two-Axis Gantry System for a Total-Body J-PET/CT Scanner

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Introduction

Conventional PET/CT systems perform sequential imaging along a single longitudinal axis using a moving patient table, typically within one or two adjacent gantry enclosures. Although whole-body imaging is feasible, it is usually acquired over multiple discrete bed positions, which may increase susceptibility to motion-related artefacts compared with total-body imaging approaches. Total-body PET also enables imaging of an extended axial field of view and may allow examination of the same anatomical volume with a reduced radiopharmaceutical dose compared with conventional moving-bed whole-body protocols **[1]**.

Methods

The total-body Jagiellonian-PET (J-PET) project **[2,3]** adopts a crossed-axis concept in which PET and CT imaging modules operate around the same fixed patient table, but from different motion axes. This architecture is intended to reduce artefacts caused by involuntary patient motion while maintaining a compact installation footprint. The implementation of crossed-axis motion for heavy imaging modules requires stringent mechanical performance, including the transport of devices exceeding 1000 kg with sub-millimetre positioning accuracy on a shared floor-mounted motion system.

To address these requirements, we developed a cross-stage sliding gantry concept based on discrete rail placement and lead-screw-driven stages, enabling two-axis motion without the need for a classical stacked linear-motion arrangement [4]. The motion system uses a custom-fabricated aluminium-alloy base, hardened steel ball screws, two servo motors, and two servo drivers for controlled two-axis gantry displacement.

A dedicated patient table was also developed. The table is supported by two independently driven vertical-motion units connected to both ends of the patient support. Its structure is based on a lightweight sandwich design consisting of 3 mm carbon fibre, 24 mm PMI foam, and 3 mm carbon fibre. This configuration provides mechanical stiffness while reducing photon interactions within the patient support. The system is designed to enable examinations over lengths of up to 2.5 m, allowing extended total-body PET imaging on a stationary patient table.

Results

The three-dimensional design, mechanical construction, and installation of the two-axis gantry system have been successfully completed. The system has been installed at the Theranostics Center in Kraków. In the next stage, CT images will be acquired using the implemented motion platform, followed by integration of the total-body J-PET detector system for combined metabolic and anatomical imaging.

Conclusion

We present the design, construction, and installation of a two-axis sliding gantry system developed for total-body J-PET/CT imaging. The implemented architecture enables PET and CT modules to operate around a common fixed patient table from different axes, thereby supporting compact system integration and reducing the need for patient repositioning during examination. The current configuration demonstrates the feasibility of a stationary-patient, crossed-axis total-body J-PET/CT system aimed at motion-artefact reduction and extended axial imaging coverage.

Acknowledgements

We acknowledge support from NCN grants 2021/42/A/ST2/00423, 2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, and 2023/50/E/ST2/00574; MNiSW grants IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Areas; and ERC Advanced Grant POSITRONIUM no. 101199807.

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Temperature Dependence of Ortho-Positronium Lifetime in Liquid Water and Olive Oil in-PALS

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Abstract

The temperature dependence of ortho-positronium (o-Ps) lifetime is a fundamental property used to characterize molecular materials. In the context of biomedical research, fats like olive oil serve as excellent models for adipose tissue. Recently developed positronium imaging methods combining Positron Annihilation Lifetime Spectroscopy (PALS) with PET imaging allow the use of positronium properties as additional diagnostic parameters. Thus, characterizing these liquids is crucial for calibrating imaging systems and basic research into fatty acid composition.

Extra virgin olive oil and liquid water were analyzed in an aluminum chamber using a PALS system equipped with BaF2 scintillation detectors. Measurements were taken in the temperature range of 6°C to 40°C. A 22Na source (approx. 1.04 MBq) was used, sealed with Kapton and Parafilm. A 4-component analysis was applied to the PALS spectra, with fixed lifetimes for p-Ps (125 ps) and Kapton (386 ps). A Parafilm correction was included in the analysis to account for source sealing.

For olive oil, the o-Ps lifetime exhibited a clear monotonic increase with temperature, ranging from ~2.60 ns at 6°C to nearly 3 ns at 40°C before correction, consistent with thermal expansion of free volume. However, after adding a correction for Parafilm, the lifetime in olive oil stabilized at 2.82 ns, showing thermal degradation only above 37°C. These values are in good agreement with lifetimes in human adipose tissue (2.54-2.82 ns). For water, preliminary results suggested a lifetime above 2.10 ± 0.1 ns. After identifying and correcting for a fifth component related to Parafilm (which varied from 2.4 ns at 6°C to 2.92 ns at 38°C), the o-Ps lifetime for water was found to be almost stable at 1.8 ± 0.06 ns across the measured range.

The experiments identified o-Ps lifetimes in water and olive oil as a function of temperature, highlighting the importance of identifying all signal sources in the experimental setup. The correlation between temperature and o-Ps lifetime enables their use as calibration standards. Future studies will focus on distinguishing oil types and fatty acid concentrations using PALS parameters.

Acknowledgements

We acknowledge support from the National Science Centre (NCN), grant nos. 2021/42/A/ST2/00423,2021/43/B/ST2/02150, 2022/47/I/NZ7/03112, the Polish Ministry of Science and Higher Education (MNiSW), grants no. IAL/SP/596235/2023 and SPUB/SP/627733/2025; the SciMat and qLife Priority Research Areas; and the ERC Advanced Grant POSITRONIUM (no. 101199807).

CLINICALLY-RELEVANT PORCINE ENDOVASCULAR STROKE MODEL FOR TESTING THERAPEUTIC AGENTS AND MEDICAL DEVICES

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Abstract:
Background: Ischemic stroke accounts for 87% of all strokes and is the second leading cause of death and a major cause of long-term disability worldwide. Despite advances in mechanical thrombectomy, many patients fail to achieve optimal recovery even after successful reperfusion, underscoring an urgent need for adjuvant therapies that can be administered immediately after thrombectomy. Developing and testing such therapies requires clinically relevant animal models. Most preclinical work is performed in rodents for practical and financial reasons, yet many therapies that appeared promising in small animals have failed in clinical trials, and scientific committees recommend large-animal models to evaluate efficacy, durability, dose-response, and safety. The pig, with its gyrencephalic brain, closely mimics human stroke conditions, but its complex vascular anatomy has historically hindered stroke research. We previously overcame this barrier with a minimally invasive, real-time MRI-guided endovascular model of thrombin-induced ischemic stroke in swine[1], providing an endovascular, imaging-compatible testbed for both pharmacological agents and the medical devices used in mechanical reperfusion.

Objective: To establish a clinically relevant, minimally invasive porcine endovascular stroke model and, for the first time, to achieve recanalization that recapitulates the current clinical thrombectomy workflow, thereby providing a versatile platform for the controlled evaluation of both therapeutic agents and medical devices in a gyrencephalic brain.

Methods: Stroke was induced in juvenile domestic pigs (n = 8 in the quantitative cohort) under both anesthesia and, in selected cases, in awake animals. All procedures were approved by the Local Ethical Committee. Under X-ray angiographic guidance, an intra-arterial catheter was navigated to the ascending pharyngeal artery near the rete mirabile, and the animals were transferred to an MRI scanner. A gadolinium-based contrast agent (GBCA) was infused at varying rates until transcatheter cerebral perfusion was visible on MRI; a mixture of thrombin and GBCA was then infused to occlude cerebral vessels, with contrast retention confirming thrombus formation. The MRI protocol included dynamic GE-EPI for dynamic susceptibility-contrast (DSC) perfusion and monitoring of thrombin-mediated clotting, diffusion-weighted imaging with ADC mapping, perfusion-weighted imaging, SWI, T2w, and contrast-enhanced T1w sequences. Two hours after ischemia, recombinant tissue plasminogen activator (rtPA, 20 mg) was infused intra-arterially to evaluate restoration of circulation[2]. Follow-up MRI at 7 and 30 days, together with postmortem histological and immunohistochemical analyses, confirmed the lesions.

Results: Ischemia was reliably induced, with persistent hypointensities on DSC scans during intra-arterial thrombin infusion, and real-time MRI allowed direct observation of lesion formation and evolution. Diffusion imaging detected lesions within 15 minutes of thrombin injection, with an average ADC-based lesion volume of 8.18 ± 4.98 cm^3 (range 3.27-17.33 cm^3). Intra-arterial rtPA achieved recanalization of the thrombosed vessels, reducing the severely hypoperfused area (Tmax > 6 s) to only 1.168 ± 0.223 cm^3 and restoring perfusion toward near-baseline levels; ADC changes were partially reversible within two hours[2]. Persistent T2 lesions were observed in cortical and subcortical white matter at 7 and 30 days, indicating sustained ischemic injury despite reperfusion. Histology revealed neuronal loss within the lesion, astrocytic scar formation, and elevated levels of activated microglia, consistent with the time-dependent upregulation of damage-associated molecular patterns and VEGFA that this model reveals in the post-ischemic brain[3].

Conclusions: This minimally invasive porcine endovascular model is the first to demonstrate recanalization in a large-animal stroke model, closely reproducing the contemporary clinical thrombectomy workflow. Because it combines true endovascular access with continuous, real-time MRI throughout the procedure, the model is well suited not only to test therapeutic agents-as illustrated by neuroprotective strategies that limit calcium-mediated excitotoxicity in this setting[4]-but also to evaluate medical devices, such as catheters, thrombectomy systems, and other reperfusion hardware, under clinically faithful conditions, while also advancing diagnostic innovations and the study of stroke pathomechanism.

References

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